



MINISTRY OF HEALTH, JAMAICA

ZIKA PREPAREDNESS AND RESPONSE PLAN FOR OUTBREAK CONTROL

ZIKA FEVER (ZIKA VIRUS INFECTION) CLINICAL MANAGEMENT PROTOCOL

28 MAY 2015 (REVISION 5: 30 JANUARY 2016)

BACKGROUND

Zika virus (ZIKV) is an emerging arbovirus that causes an acute febrile illness. The virus was first isolated in 1947 from a febrile rhesus monkey in the Zika forest of Uganda during a research project on the transmission of jungle yellow fever. The virus was first isolated in humans in 1952 in Uganda and Tanzania. ZIKV belongs to the *Flavivirus genus*, family *Flaviviridae* the same as Dengue, Yellow Fever, Japanese encephalitis and West Nile virus.

The virus is transmitted from human to human by the bites of infected mosquitoes. The mosquitoes involved are *Aedes* species, typically *Aedes aegypti*, *Aedes albopictus* and *Aedes polynesiensis* which also transmit other mosquito-borne viruses, including Dengue. There have been reports of non vector borne transmission of the virus through perinatal transmission and sexual intercourse. Blood transfusion has been identified as a potential route for transmission.

Outbreaks of Zika fever beyond Africa have been described, inclusive of Asia. However these infections had been limited to sporadic cases or small outbreaks until 2007 when the first major outbreak of ZIKV occurred in the island of Yap (Micronesia). ZIKV has spread widely since 2013, causing outbreaks in French Polynesia and other South Pacific islands. ZIKV infections have been reported in returning travelers from Thailand, Cambodia, Indonesia, Cook Islands and New Caledonia.

In 2014 Chile reported cases of autochthonous transmission of ZIKV in the Easter Island. In May 2015, Brazil confirmed autochthonous transmission of ZIKV. In October 2015, Colombia reported the first autochthonous case of ZIKV infection.

Since January 2016, Barbados, Bolivia, Brazil, Colombia, Curacao, Dominican Republic, Ecuador, El Salvador, French Guiana, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Martinique, Mexico, Nicaragua, Panama, Paraguay, Puerto Rico, Saint Martin, Suriname, US Virgin Islands and Venezuela have reported autochthonous transmission of ZIKV.

Brazil has reported an increase in Microcephaly and other congenital anomalies in neonates during the Zika virus outbreak, raising concerns about the effects of Zika virus infection in fetuses and its implications for delivery of health care.

Due to the wide distribution of the mosquito vector capable of transmitting ZIKV and the high mobility of persons in and outside the region of the Americas and worldwide, future transmission could occur in Jamaica.

It should be noted that the description of the clinical presentation of Zika virus is based on a limited number of case reports and outbreak investigations. The body of knowledge continues to grow and updates will be made accordingly.

Clinical Presentation

The incubation period of ZIKV infection is usually **3 to 12 days**. It is postulated to be between 2 to 14 days based on experimental studies and historical information obtained from infected travelers.

The clinical presentation of Zika virus infection is similar to Dengue Fever without haemorrhagic manifestations.

The symptoms of ZIKV infection are:

- Fever
- Maculopapular skin rash (that starts on the face or trunk and then becomes generalized)
- Headache
- Retro-orbital pain
- Conjunctivitis (non-purulent)
- Arthralgia
- Myalgia
- Gastro-intestinal symptoms such as vomiting, diarrhea, constipation
- Ankle oedema
- Lymphadenopathy

The outbreak of ZIKV infection on the Yap Island, Micronesia, has provided the most information with regards to the clinical presentation of ZIKV. Rash was the most common symptom, affecting 90% of individuals, followed by fever (65%), arthralgia (65%), non-purulent conjunctivitis (55%) and headache (45%).

The illness is typically mild to moderate in severity and self-limiting. Symptoms usually last for 3 to 7 days.

Complications of ZIKV infection include Guillain-Barre syndrome (GBS), meningoencephalitis, myelitis, neuropathies, immune thrombocytopenia purpura and congenital anomalies. Ophthalmologic and cardiovascular complications have also been reported.

French Polynesia reported having 74 individuals out of a population of approximately 270,000 with neurological syndromes during the ZIKV outbreak in 2013 to 2014. Forty two (42) cases were consistent with GBS.

Since July 2015, Brazil has reported the detection of patients with neurological syndromes and a recent history of Zika virus infection. Fifty five percent (55%) of these cases were consistent with GBS. In January 2016, El Salvador reported having an unusual increase of GBS cases since December 2015, with GBS occurring 7 to 15 days after the onset of a viral syndrome with rash and fever.

Guillain-Barré syndrome (GBS) is an acute polyradiculoneuropathy that is autoimmune in origin. The syndrome manifests as a rapidly evolving areflexic motor paralysis with or without sensory deficits. The usual pattern is of an ascending paralysis accompanied by absent or decreased deep tendon reflexes. The lower extremities are usually more affected than the upper extremities. The lower cranial nerves may be involved, causing bulbar palsy. Autonomic dysfunction may complicate GBS causing tachycardia, bradycardia, other arrhythmias, hypertension alternating with hypotension, orthostatic hypotension, urinary retention, ileus, and loss of sweating. Recovery may occur over many months to a year. Most cases of GBS are preceded by an infection.

In October 2015, the Brazil International Health Regulations National Focal Point notified WHO/PAHO of the detection of an unusual increase in microcephaly cases. A twenty (20) fold increase in rates compared to previous years was reported.

Microcephaly is defined as a head circumference of 2 standard deviations (SD) below the mean for age and sex.

In November 2015, the Brazil Ministry of Health established the relationship between the increase in occurrence of microcephaly and Zika virus infection. The Zika virus genome was detected in blood and tissue samples of a deceased neonate. The neonate presented with microcephaly and other congenital anomalies and died shortly after birth. Also in November 2015, the Flavivirus Laboratory in Brazil detected the ZIKV genome through real time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) in amniotic fluid samples of 2 pregnant women whose fetuses had microcephaly by ultrasound.

In November 2015, French Polynesia reported an unusual increase of Central Nervous System (CNS) malformations in fetuses and newborns registered between 2014-2015, coinciding with their Zika virus outbreak. Out of 17 malformations, 12 were cerebral malformations and polymalformative syndromes, and 5 infants had brainstem dysfunction and absent swallowing reflex.

There had been no reported deaths due to ZIKV infection in past outbreaks until November 2015 when the Brazil Ministry of Health notified deaths associated with ZIKV infection. The first case was a man with Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis, alcoholism on corticosteroid

therapy. The second case was a 16 year old female. Her symptoms included headache, nausea, and petechiae. Other cases were neonates with congenital anomalies.

Table 1. Clinical Manifestations

Common	Less Common	Atypical Manifestations/Complications
<ul style="list-style-type: none"> ➤ Fever ➤ Maculopapular skin rash ➤ Arthralgia ➤ Headache ➤ Non-purulent conjunctivitis 	<ul style="list-style-type: none"> ➤ Myalgia ➤ Retro-orbital pain ➤ Nausea ➤ Vomiting ➤ Diarrhoea ➤ Constipation ➤ Ankle oedema ➤ Lymphadenopathy ➤ Haemospermia ➤ Prostatitis 	<ul style="list-style-type: none"> ➤ Guillain-Barre syndrome ➤ Meningoencephalitis ➤ Myelitis ➤ Neuropathy ➤ Immune thrombocytopenia purpura ➤ Microcephaly ➤ Central Nervous System malformation in fetuses and newborns ➤ Congenital anomalies

Differential Diagnosis

ZIKV infection may be indistinguishable from other disease entities with fever, skin rash and arthralgia/arthrititis. ZIKV may also coexist with other infections such as Dengue. Diseases that should be considered as possibilities are dependent on epidemiological features such as place of residence, travel history and exposures.

These include but are not limited to:

- “ Dengue
- “ Chikungunya
- “ Malaria
- “ Leptospirosis
- “ Acute HIV infection
- “ Measles
- “ Rubella
- “ Rickettsial infections
- “ Typhoid fever

- “ Epstein Barr Virus – Infectious Mononucleosis
- “ Rheumatic Fever
- “ Post infectious arthritis due to Chlamydia, Gonococcus, Shigella
- “ Rheumatoid Arthritis
- “ Juvenile Rheumatoid Arthritis
- “ Drug reaction
- “ Other Flaviviral infections

ZIKV and Dengue

ZIKV infection may be confused with Dengue. It is important to distinguish between the two, as Dengue may be associated with a more severe and complicated clinical course. In ZIKV infection, severe thrombocytopenia, hemorrhage and shock are rare. The onset is more acute and duration of fever is shorter in Zika fever. Defervescence in temperature is not associated with worsening of symptoms in Zika fever compared to Dengue. The maculopapular rash and conjunctivitis are seen more frequently in ZIKV than Dengue. It is also important to note that co-infections with ZIKV and Dengue have been reported.

Zika Fever - Case Definition:

Suspected Case (Preparedness Phase):

Patient with rash or elevated body temperature (> 37.2 °C) with one or more of the following symptoms (not explained by other medical conditions):

- Arthralgia or myalgia
- Non-purulent conjunctivitis or conjunctival hyperaemia
- Headache or malaise

In someone who resides in or has visited epidemic or endemic areas within two (2) weeks prior to the onset of symptoms. Note: In the event that a Zika virus infection outbreak is established in any geographical area in Jamaica, the entire country would be considered an epidemic area.

In addition, persons presenting with neurological syndromes and autoimmune syndromes post a viral illness are to be considered a suspected case of Zika virus infection.

Clusters of rash and fever will also be considered as suspected Zika virus infection.

Confirmed Case:

A suspected case with laboratory positive result for the specific detection of Zika virus.

Laboratory

There are no specific pathognomonic laboratory findings seen in ZIKV infections. Abnormal laboratory findings can include:

- “ Mild thrombocytopenia (>100,000/mm³)
- “ Mild leucopenia
- “ Mild elevations in Liver Function Tests(LFT)
- “ Elevated Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP)

Laboratory tests used for diagnosing ZIKV include:

Nucleic Acid detection of Zika viral RNA using, real time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) performed on an “acute sample”, collected during the first five (5) days of illness, has been shown to be a rapid, sensitive and specific method of diagnosis.

Serological detection of anti-Zika IgM and IgG antibodies using Enzyme-Linked Immunosorbent Assay (ELISA) and immunofluorescence assays may be performed on blood samples collected 6 days after the onset of symptoms. Of note, however, there have been reports of cross-reactivity with other flaviviruses, (such as Dengue and Yellow Fever), results of serological testing should therefore be interpreted cautiously.

Cerebrospinal fluid may be obtained for viral cultures and molecular studies with guidance from the Microbiologists at the National Public Health Laboratory and the Microbiology Department, University of the West Indies, if there is presence of meningoencephalitis or other neurologic complications.

It is important to exclude other diseases mimicking ZIKV infection such as Dengue, Malaria, Typhoid Fever, Influenza and Leptospirosis.

Treatment

There is no specific antiviral therapy for ZIKV.

Supportive treatment is available for the specific disease manifestations of ZIKV infection. The majority of patients will recover without hospital admission. It is however important to identify those with risk factors for severe disease and complications, such as individuals with co-morbidities and pregnant females and then institute treatment measures promptly.

Depending on the clinical manifestations, or presence of neurological, hematological and cardiovascular complications, patients may be sent home or referred for hospital management.

All persons fitting the Case Definition should be notified immediately to the Parish Health Department and the National Epidemiology Unit, Ministry of Health.

Treatment is symptomatic and involves fluids, rest, antipyretic and analgesic agents. The antipyretic and analgesic agent that is recommended is acetaminophen or paracetamol.

Non-steroidal anti-inflammatory agents (NSAIDS) such as ibuprofen, diclofenac and naproxen should not be used due to a risk of bleeding complications from thrombocytopenia, a missed diagnosis of Dengue or possible co-infection with Dengue which has been associated with hemorrhagic complications. The use of aspirin is not advised due to the risk of Reye's syndrome in children and bleeding complications in both children and adults.

Antihistamines may be used to relieve the symptoms of pruritus associated with the maculopapular skin rash.

There are no vaccines currently available to prevent ZIKV infection.

Stepwise approach to management of ZIKV Infection:

A history should be taken and include the following:

- Date of onset of fever (fever persisting for more than 5 days may be indicative of Dengue)
- Quantity of oral intake
- Nausea or vomiting
- Urine output (frequency, volume, time of last voiding)
- Neurological symptoms, drowsiness, headaches, meningism, seizures, paralysis
- Chest pain, Shortness of breath (SOB)
- Bleeding diathesis
- Co-existing conditions e.g. diabetes mellitus, cardiovascular disease, pregnancy
- A detailed travel history in someone who resides in or has visited epidemic or endemic areas within two (2) weeks prior to the onset of symptoms.
- Family or community ZIKV infection

Counsel the patient about early warning signs of severe Dengue.

A physical examination should include:

- Vital signs
- Assessment of hydration status
- Haemodynamic status
- Plot anthropometric measurements (Weight, Height & head circumference) in children
- Assessing for abdominal pain, ascites, hepatomegaly
- Assessing for rash

- Assessment of mental status
- Assessing for meningism, neurological deficits
- Assessing for bleeding manifestations

Investigations should be guided by the severity of clinical presentation and may include:

- Complete blood count (CBC)
- Serum electrolytes, urea and creatinine (U+E's)
- Glucose
- Liver function test (LFT) including bleeding indices (PT/PTT)
- Dengue serology/RT-PCR
- Chikungunya serology/PCR
- ZIKV serology/RT-PCR
- Malaria Blood smear
- Leptospirosis serology
- Lumbar Puncture
- Blood culture
- CT/MRI Scan Brain where necessary.

CT Scan of Brain- to identify possible calcifications (caution: judicious use of CT Scans in children due to radiation risks)

MRI - to identify congenital malformations

Management of ZIKV Infection

Diagnosis and assessment of disease severity

The history, physical examination and investigations (where indicated) should assist the clinician in determining severity of the infection and whether there are atypical manifestations or complications and the need for hospital admission.

Ambulatory patients

Patients who are sent home should be alert, able to tolerate oral fluids, urinate at least once every 6 hours, and not have atypical manifestations. Ambulatory patients should be reviewed for disease progression. Care givers should be instructed to take the patient to hospital immediately, if there is deterioration, persistent vomiting, severe abdominal pain, cold and clammy extremities, lethargy or restlessness, bleeding and oliguria.

In-Patient Management

Patients with atypical manifestations, neurological syndromes, co-existing conditions that may make the management of ZIKV infection complicated such as co-morbidities conditions including cardiovascular disease, haematological disorders, haemoglobinopathies (Sickle Cell Disease), rheumatological disorders (Systemic Lupus Erythematosus) and Diabetes Mellitus should be admitted to hospital.

Neurological Syndromes

Guillain-Barré Syndrome

The treatment of GBS is symptomatic and supportive utilizing a multi-disciplinary team approach. The patients should be managed in a hospital equipped with an intensive care unit (ICU), as approximately 30 % of patients develop respiratory failure requiring mechanical ventilation. In addition, severe autonomic dysfunction may occur in approximately 20 % of patients, warranting ICU monitoring. Other complications may include sepsis, deep vein thrombosis and pulmonary embolism. These should be prevented with appropriate care and monitoring.

The disease modifying therapy used to treat GBS is intravenous immune globulin (IVIG) or plasmapheresis. Both treatments are equivalent and improve outcome.

Meningoencephalitis

The management of meningoencephalitis is dependent of the clinical presentation and severity of illness. Supportive care is necessary in conjunction with management of the Paediatric specialist.

Microcephaly

Microcephaly is defined as a head circumference is at least 2 standard deviations (SD) below the average for sex and age OR about less than the 3rd percentile.. In some cases, it is associated with changes in the brain structure and neurological development impairment.

The WHO growth standard charts by sex are to be used to identify cases in full term newborns. The Fenton growth charts are to be used for preterm newborns.

NB. When measuring the head circumference, avoid rounding to centimetres; always record to one decimal point.

Neonates with microcephaly or congenital abnormalities who are stable should be referred to the nearest Hospital Paediatric Clinic for appropriate investigations and management. Surveillance reporting of cases to the Parish Health Department within 24 hours should be done so that the necessary interventions can be undertaken. Ill babies should be referred to the nearest hospital with Pediatric facilities within 24 hours for assessment.

Long term follow up with appropriate investigations may be required in some cases.

ZIKA VIRUS INFECTION DURING PREGNANCY

i. Clinical issues: No clinical differences have been described between pregnant and non-pregnant women. After the infected mosquito bites the patient, the symptoms of the disease typically appear after a 3 – 12 day incubation period. Overall, the cases are usually not lethal. Infection may progress asymptotically (70-80% of the cases), or present with the clinical features listed above.

Symptoms of Zika virus infection that should be considered for the diagnosis must be recorded in the pregnant woman's medical record. Symptoms last from 2 to 7 days, and are usually self-limiting.

ii. Diagnosis: The diagnostic steps recommended for pregnant women are exactly the same as those recommended for the general population, and they are defined above.

ii a. The clinical diagnosis is suspected, and it is characterized by the occurrence of one or several of the above-described symptoms. Suspicions will be based on better grounds if the subject was in an area or territory where the vector was present the days before presenting with symptoms; suspicions will be further strengthened if any cases of viral infection have been confirmed in the area; this will be a stronger element leading to a presumptive diagnosis of Zika virus infection.

ii b. The differential clinical diagnosis will be established with other infections causing exanthema and fever, particularly produced by a flavivirus, such as dengue, Chikungunya, to name but a few.

ii c. Confirmed diagnosis: Confirmation requires a local or reference laboratory capable of performing the tests described below. The team in charge of the pregnant woman's care must contact the appropriate health authority to coordinate the type of samples that need to be taken.

V. THERAPY MANAGEMENT OF PREGNANT WOMEN WITH ZIKA

The infection being generally almost asymptomatic, or self-limiting in the few cases that present with symptoms, there is almost no need for therapy. To date, no vaccines or specific therapy have been developed for Zika virus infection; consequently, the therapy is aimed at relieving symptoms.

i Rest and isolation: To prevent any further transmission to other persons, contact of Zika infected patients with any mosquitoes of the *Aedes* genus should be prevented, at least during the first week of the disease (viraemic phase). The use of mosquito nets (impregnated with insecticide or not) is recommended. Alternatively, people should stay in places protected with mosquito screens. The health care workers providing care to patients infected with the Zika virus must protect themselves from mosquito bites using repellents and wearing long sleeves and long trousers or skirts.

ii Fever: There is evidence that during pregnancy, fever "per se" is associated with birth defects as there are no drugs considered to be 100% safe. The recommendation is to initially reduce the pregnant woman's fever with physical measures (damp cloths, scanty clothes, baths or showers with mildly lukewarm water). When physical measures fail, pain relievers and anti-pyretics must be added, with acetaminophen or paracetamol being the first line therapy.

Recommended dose: 500 mg orally every 6 or 8 hours; patients must be warned not to exceed 4,000 mg/day, since high doses may damage the pregnant woman's liver.

It is also necessary to warn the pregnant woman that many over-the-counter drugs contain acetaminophen, so the upper limit of the dose could inadvertently be surpassed.

iii Headaches will also be treated with acetaminophen at the dosages prescribed for the management of fever.

Do not use aspirin, as it increases the risk of bleeding, nor NSAIDs, because of their effects in infections caused by dengue or Chikungunya.

iv Itching: Although there is no research either supporting nor refuting the safety of topical products, there is clinical experience suggesting their safety. The safety profile of systemic therapy with anti-histaminic agents is also high, so the different forms of Loratadine may be recommended (18).

v Hydration: Patients should be advised to drink plenty of fluids to replenish volume depletions through sweat, vomiting and other insensible losses.

VII POTENTIAL COMPLICATIONS OF ZIKA VIRUS INFECTION IN PREGNANCY

One of the relevant issues in the context presented is the possible association between the infection by Zika Virus and the increased number of reports of congenital microcephaly and other conditions at birth.

VII MONITORING OF PREGNANT WOMEN

i Applicable to all pregnant women: All pregnant women should be recommended to attend the scheduled antenatal visits regularly, and to comply with the performance of all the tests indicated by the health team. There are multiple agents with the potential of causing congenital defects, and microcephaly in particular; consequently pregnant women should be reminded to avoid alcoholic beverages, illicit drugs and medications (unless prescribed by a health care professional). Likewise, they should be advised to avoid any contact with people with ongoing infectious conditions.

As there is no specific therapy against this infection, prevention continues to be the key issue. Early contact with pregnant women continues to be promoted, so all antenatal visits may take place in accordance with national standards; at those visits, women should be provided with information on the environmental and individual measures recommended to reduce the risk of bites by the mosquito that transmits the Zika Virus.

Special attention must be paid to routine work-up for syphilis, toxoplasmosis, cytomegalovirus and rubella, which will be relevant in case of congenital defects that require etiological confirmation.

As the infection may go unnoticed in a high percentage of people, at each visit pregnant women should be asked about the occurrence of any of the clinical signs and symptoms described above.

ii Applicable to pregnant women with suspected Zika infection

in addition to all the actions defined by the national guidelines for the monitoring of pregnancy, and based on risk levels, the following are recommended:

ii a. Measure size of uterus and volume of amniotic fluid: There is little evidence about the monitoring of pregnant women with the Zika virus infection, but it is estimated that, as is the case with other congenital infections, it might be associated with a larger than normal size of the uterus (due to increased amniotic fluid) or a smaller than normal size (as a result of fetal growth defects or even fetal death). The recommendation is that ultrasound scans should be performed at a minimum of 4 week intervals.

ii b. Evaluate fetal vitality, including auscultation with Pinnard's stethoscope (20 weeks), or doptone at early gestational ages (14 weeks), which will tell whether the fetus is still alive. At later gestational ages, perception of fetal movements may suffice (20 weeks). Obstetric ultrasound may serve that purpose at early stages of pregnancy (6 weeks).

ii c. Evaluation of the fetal anatomy: Ultrasonography in the last trimester might rule out microcephaly and other abnormalities in the fetuses of women that were exposed to the Zika virus. Microcephaly can only be confirmed after birth by measuring the neonate's head circumference.

Obstetric ultrasonography has shown that its capacity to diagnose secondary microcephaly (in this case due to a congenital infection), increases after the 28th week of gestation (last trimester). The diagnostic approximation will be stronger when associated with other defects of the central nervous system, including brain microcalcifications, enlarged ventricles, hydrocephalia and/or other defects, including, but not limited to an enlarged liver, oedema of the placenta and fetal oedema. All these are sonographic signs of congenital infection.

Obstetric ultrasound is unable to confirm the existence of microcephaly, but it may suggest it.

VIII WHEN TO SUSPECT MICROCEPHALY WITH ULTRASONOGRAPHY

i Head circumference: Antenatal microcephaly may be suspected when the fetal head circumference is 2 standard deviations under the mean value for gestational age; however, most of these children have turned out to show a normal intellectual function. Whenever possible, it is advisable to repeat the ultrasound after 15 days, to perform anthropometric measures. For individual clinical cases, health care professionals must be aware that when a measurement of the head circumference lies 3 standard deviations under the mean value for gestational age, the correlation between microcephaly and impaired neurologic development is increased.

The correct determination of gestational age is relevant in all pregnancies, but it is even more relevant when investigating alterations that require anthropometric measurements based on gestational age. The ultrasound evaluation of the fetus's head circumference depends on the correct assessment of gestational age.

ii Head circumference / femur length ratio or Head circumference

Ultrasonographers offer standardized tables for the various anthropometric measurements to be used in accordance with the characteristics of the local population.

— **Abdominal girth ratio:** There are tables available with the values of these ratios based on gestational age. These measurements have not proven to be any better than head circumference alone, when there is certainty about the gestational age. A recent study (even using a 3-standard deviation cutting point) establishes that it would lead to an antenatal overdiagnosis of microcephalia; hence, it should be used

with caution

When microcephalia is suspected based on an isolated ultrasound scan, ultrasound monitoring may be warranted to measure the evolution of the head circumference and other fetal anthropometric data, as well as to detect the occurrence of other congenital defects, when the needed resources are available.

Breast Feeding

There is no proof at this time of mother-to-child transmission during lactation. There are no recommendations to suspend breast feeding at this time.

Prevention of transmission

Zika virus infected individuals should avoid being bitten by mosquitoes during the first week of symptoms (viraemic phase) so as to reduce possible transmission to unaffected individuals. Use of insect repellants such as DEET (N, N-diethyl-3-methylbenzamide), Icaridin or IR3535 and bed nets (insecticide treated or not) is advised.

The repellents recommended by the health authorities offer the highest safety levels during pregnancy and breastfeeding. They should be applied on exposed body areas, and even over clothes, whenever indicated, and re-applied as suggested by the manufacturer on the product label. The repellent will have no protective effect unless it is used following the manufacturers' recommendations.

For newborns and children under three (3) months of age, repellents are not recommended; instead, bed nets should be used. Health care workers should protect themselves from mosquito bites using insect repellents and other protective measures such as wearing long sleeve tops and pants.

Prevention

Mosquitoes and their breeding sites pose a significant risk factor for Zika virus infection. Prevention and control relies on reducing mosquitoes through source reduction (removal and modification of breeding sites) and reducing contact between mosquitoes and people.

This can be done by :

1. using insect repellent(as per manufacturer's recommendation;
2. wearing clothes (preferably light-coloured) that cover as much of the body as possible;
3. using physical barriers such as screens, closed doors and windows;
4. Sleeping under mosquito nets.
5. It is also important to empty, clean or cover containers that can hold water such as buckets, flower pots or tyres, so that places where mosquitoes can breed are removed.

REFERENCES

1. PAHO. Epidemiological Alerts and Updates. Zika virus infection. 7 May 2015
2. PAHO. Epidemiological Alerts and Updates. Zika virus infection. 16 October 2015
3. WHO. Zika virus outbreaks in the Americas. *Wkly Epidemiol Rec*. 2015 Nov 6;90(45):609-10
4. WHO. Zika virus infection-Suriname. *Disease Outbreak News* 13 November 2015
5. PAHO. Epidemiological Alerts. Neurological syndromes, congenital malformations and Zika virus infection. Implications for public health in the Americas. 1 December 2015
6. PAHO. Epidemiological Alerts. Neurological syndromes, congenital malformations and Zika virus infection. Implications for public health in the Americas. 17 January 2016
7. Duffy MR, Chen TH, Hancock WT, Powers AM, Kool JL, Lanciotti RS, et al. Zika virus outbreak on Yap Island, Federated States of Micronesia. *N Engl J Med*. 2009;360:2536–43
8. Summers DJ, Acosta RW, Acosta AM. Zika Virus in an American Recreational Traveler. *J Travel Med*. 2015 May 21
9. 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*. 2014 Apr 3;19(13)
10. Musso D, Roche C, Robin E, Nhan T, Teissier A, Cao-Lormeau VM. Potential sexual transmission of Zika virus. *Emerg Infect Dis*. 2015 Feb;21(2):359-61
11. Foy BD, Kobylinski KC, Chilson Foy JL, Blitvich BJ, Travassos da Rosa A, Haddock AD, et al. Probable non-vector-borne transmission of Zika virus, Colorado, USA. *Emerg Infect Dis*. 2011;17:880–2
12. Dupont-Rouzeyrol M, O'Connor O, Calvez E, Daurès M, John M, Grangeon JP, Gourinat AC. Co-infection with Zika and dengue viruses in 2 patients. New Caledonia. 2014. *Emerg Infect Dis*. 2015 Feb;21(2):381-2
13. Zammarchi L, Stella G, Mantella A, Bartolozzi D, Tappe D, Günther S, Oestereich L, Cadar D, Muñoz-Fontela C, Bartoloni A, Schmidt-Chanasit J. Zika virus infection imported to Italy. clinical, immunological and virological findings, and public health implications. *J Clin Virol*. 2015 Feb;63:32-5
14. Hayes EB. Zika Virus Outside Africa. *Emerg Infect Dis*. 2009 Sep;15 :1347–50
15. Musso D, Nilles EJ, Cao-Lormeau VM. Rapid spread of emerging Zika virus in the Pacific area. *Clin Microbiol Infect*. 2014; .10.1111
16. Cao-Lormeau VM, Roche C, Teissier A, Robin E, Berry ALT, Mallet HP, et al. Zika virus, French Polynesia, South Pacific, 2013. *Emerg Infect Dis*. 2014;20:1085–6
17. 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
18. Derraik JG, Slaney D. Notes on Zika virus—an emerging pathogen now present in the South Pacific. *Aust N Z J Public Health*. 2015 Feb;39(1):5-7
19. European Centre for Disease Prevention and Control. Rapid Risk Assessment: Zika Virus Infection Outbreak, French Polynesia. Stockholm (SWE): ECDC; 2014 February 14