Pan American Health Organization
World Health Organization
REGIONAL OFFICE FOR THE Americas

Epidemiological Alert

Zika virus infection

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The Pan American Health Organization (PAHO) / World Health Organization (WHO) recommends its Member States establish and maintain the capacity for Zika virus infection detection, clinical management and an effective public communication strategy to reduce the presence of the mosquito that transmits this disease, particularly in areas where the vector is present.

Situation summary

The Zika virus was first isolated in 1947 in Zika Forest (Uganda), in a Rhesus monkey during a study of the transmission of wild yellow fever. It was first isolated in humans in 1952 (Uganda, Tanzania).[1,2] In 1968 the virus was detected in human samples in Nigeria. [3,4]

In 2007 the first major outbreak of Zika virus fever occurred on the island of Yap (Micronesia) where 185 suspected cases were reported, of which 49 were confirmed and 59 were considered probable. The outbreak lasted 13 weeks (April to July). The probable vector was identified as being *Aedes hensilii*, however the presence of the virus in the mosquito could not be determined.

Subsequently an outbreak in French Polynesia, which began at the end of October 2013. Around 10,000 cases were registered, of which approximately 70 were severe cases, including neurological (Guillain Barré syndrome, meningoencephalitis) or autoimmune (thrombo-cytopenic purpura, leukopenia) complications. An investigation was carried out to determine the association between these complications and primary or secondary co-infection with other flaviviruses, especially dengue virus[5,6] The vectors responsible for transmission were *Aedes aegypti* and *Aedes polynesiensis*. In 2014, cases were also recorded in New Caledonia and in the Cook Islands.

To date, no death attributed to Zika virus infection has been reported in any of the outbreaks.

Zika virus infection

This is a disease caused by the Zika virus (ZIKAV), an arbovirus the flavivirus genus (family Flaviviridae), very close phylogenetically to viruses such as dengue, yellow fever, Japanese encephalitis, or West Nile virus.

The Zika virus is transmitted by mosquitoes of the genus Aedes, in urban areas (*A. aegypti*) as well as in the wild.

After an infected mosquito bite, the disease symptoms usually appear following an incubation period of three to twelve days.

The infection may present itself as asymptomatic or with a moderate clinical picture; no fatal cases have been detected to date.

In symptomatic cases, with **moderate disease,** the symptoms appear acutely and include fever, non-purulent conjunctivitis, headache, myalgia and arthralgia, asthenia, maculopapular rash, edema in the lower limbs and less frequently, retro-orbital pain, anorexia, vomiting, diarrhea, or abdominal pain. The symptoms last for 4-7 days and are self-limiting. Complications (neurological, autoimmune) are rare and have only been identified in the epidemic in French Polynesia.

In the past seven years, cases in travelers have sporadically been reported (Thailand, Cambodia, Indonesia and New Caledonia).

In February 2014, the public health authorities of Chile confirmed that there was a case of autochthonous transmission of Zika virus infection in Easter Island (Chile).[1] It coincided with the presence of other foci of transmission in the Pacific Islands: French Polynesia, New Caledonia, and the Cook Islands.[5,6,7] The presence of the virus was reported until June of the same year and was not detected later.

Currently, the public health authorities of Brazil are investigating a possible transmission of the Zika virus in the northeast of the country.

The recent outbreaks of Zika fever in different regions of the world, demonstrate potential spread of this arbovirus across territories where the vectors (*Aedes*) are present.

Recommendations

The broad distribution of the vector in the Americas combined with the high mobility of persons in and outside of this Region and worldwide, represent a risk for the spread of Zika virus in the Americas. PAHO/WHO reinforces the recommendations made previously regarding the same vector of dengue and chikungunya and urges Member States where the Aedes mosquito that transmits these diseases are present, to establish and maintain the capability to detect and confirm cases, manage cases, and implement an effective public communication strategy to reduce vector density.

Provided below are the key recommendations related to surveillance, case management, and prevention and control measures.

Surveillance

Zika fever surveillance should be set up based on the same existing surveillance system for dengue and chikungunya, taking into account differences in the clinical presentation. As appropriate to the epidemiological situation, surveillance should be directed to (i) determine if the Zika virus has been introduced to an area, (ii) to monitor the Zika virus once introduced, or (iii) to monitor the disease once it has been established.

In countries **without** autochthonous transmission of the Zika virus infection, it is recommended to:

- Test for Zika virus in a percentage of samples from patients presenting with fever and arthralgia or fever and arthritis with no known etiology (e.g., negative test for malaria, dengue, chikungunya, and febrile rash illnesses). Cross reactivity with dengue serology tests should be taken into account, especially if there has been prior dengue infection. Early detection will allow for proper response and characterization of the outbreak and identification of the circulating viral strains.

In countries **with** autochthonous transmission of Zika virus infection, it is recommended to:

- Monitor the spread of the virus to detect the introduction into new areas;

[1] Information available at: http://web.minsal.cl/node/794

- Assess the clinical severity and impact on public health;
- Identify risk factors for Zika virus infection, and when the capacity exists;
- Identify circulating Zika virus lineages.

These efforts are the basis for developing effective control measures. Once the introduction of the virus is documented, ongoing surveillance should be continued to monitor changes in the epidemiology and in Zika virus vector transmission. Any changes detected by the surveillance system should be promptly communicated to the national authorities of prevention and control in order to ensure timely decisions for actions as warranted.

Laboratory detection

During the first 5 days after the establishment of the clinical picture (acute phase, viraemic period) detection of viral Ribonucleic Acid (RNA) can be performed from serum by molecular techniques (conventional or real-time RT-PCR). The reverse transcription-polymerase chain reaction (RT-PCR) for dengue as the main differential diagnosis should be negative. In addition, a generic assay against flavivirus, followed by genetic sequencing to establish the specific etiology could also be used.

For a case clinically suggestive of infection and where dengue has been discarded, further tests for other flaviviruses, including Zika virus, should be performed.

The serological tests (ELISA or inmunofluerescence) to detect specific IgM or IgG against Zika virus can be positive after 5 to 6 days following the onset of symptoms. It must demonstrate an increased antibody titer in paired samples, with an interval of about two weeks. However confirmation of positive results with plaque reduction neutralization test (PRNT) showing at least a four-fold increase in the titer of neutralizing antibodies to Zika virus is recommended. There can be cross-reactivity with other flaviviruses, especially dengue and yellow fever or, less frequently, with West Nile virus. Hence, a fourfold rise or more of the neutralizing antibody titer against dengue in a patient infected with Zika virus, particularly if the patient previously had dengue, could be detected. Given this cross-reactivity between flavivirus serology results should be interpreted with caution.

Case management

There is no specific antiviral treatment for Zika virus. Symptomatic treatment after excluding more severe conditions such as malaria, dengue and bacterial infections is recommended.

It is important to differentiate Zika virus infection from dengue due to severe clinical outcomes of dengue. In addition, cases of co-infection, Zika and dengue, could occur in the same patient. Compared with dengue, Zika virus infection has a more mild to moderate clinical picture, the onset of fever is more acute and shorter in duration; in addition, no shock or severe bleeding has been observed.

Because Zika virus outbreaks could cause additional burdens on all levels of the health care system, it is necessary to develop and implement institutional protocols for the triage, and rehabilitation of patients.

Treatment

- There is no vaccine or specific treatment for Zika virus infection. Therefore, treatment is mainly symptomatic.

- Treatment is symptomatic and supportive, including rest and the use of acetaminophen or paracetamol to relieve fever. The use of antihistamines to control pruritis usually associated with the maculopapular could be recommended.

- Using aspirin is not advised due to the risk of bleeding and developing Reye's syndrome in children younger than 12 years of age.

- Patients should be advised to drink plenty of fluids to replenish fluid lost from sweating, vomiting and other insensible losses.

Patient isolation

To prevent infection of other persons, a Zika virus-infected patient should avoid being bitten by *Aedes* mosquitoes during the first week of illness (viremic phase). Staying under a bednet – whether it is insecticide-treated (IT) or not – or remaining in a place with intact window/door screens is highly recommended. In addition, physicians or health care workers who attend to Zika virus-infected patients should protect against mosquito bites by using insect repellent (IR3535 or Icaridin) and wearing long sleeves and pants.

Prevention and control measures

Prevention and control measures directed at the reduction of vector density are fundamental, and if effective, can prevent transmission.

An effective and operational Integrated Management Strategy for the Prevention and Control of Dengue (IMS –Dengue) provides the basis for adequate preparedness to Zika virus. In the current situation, the intensification of comprehensive prevention and control of IMS-dengue is recommended. These recommendations include:

- Intersectoral participation and collaboration at all levels of government and of health, education, environment, social development and tourism agencies.

- Participation of non-governmental organizations (NGOs) and private organizations; at the same time, control programs must maintain risk communication and mobilize the whole community.

Mosquito control is the only measure that can interrupt the transmission of vector borne viruses, such as dengue, Zika, and chikungunya. Due to the importance of vector control, the key elements of a vector control program that should guide the response are listed below.

Integrated Vector Management (IVM)

An effective and operational dengue and chikungunya vector control program provides the basis for adequate preparation against Zika virus, because these viruses are transmitted by the same mosquito, *Ae. Aegypti*. Therefore, it is recommended to apply and intensify the surveillance and vector control measures developed for dengue and chikungunya as part of the Integrated Vector Management (IVM).

To ensure its success, it is key to include intersectoral participation and collaboration at all levels of government, including the health, education, environment, social, development and tourism sectors, among others. IVM is also relies on support of non-governmental organizations (NGOs) and private organizations; communication channels must remain open and community participation should be mobilized. It is important to provide clear and quality information to the public about these diseases via communication campaigns.

Given the broad distribution of *Ae. aegypti* and *Ae. albopictus* in the Americas, prevention and control measures should be aimed at reducing vector density, and obtaining the acceptance and collaboration of communities in adopting such measures.

Prevention and control measures by national authorities should include the following:

- Strengthening environmental management to prevent or minimize vector propagation and human contact with the vector-mosquito by eliminating vector breeding sites in each household and in common areas of districts and cities (e.g., parks, schools, cemeteries, etc.).

- Organizing mass sanitation campaigns for the elimination of breeding sites, specifically in areas where routine garbage collection has been interrupted.

- Implementing breeding site control measures by applying physical, biological and chemical methods, while actively involving families and communities.

- Identifying areas of high risk of transmission (risk stratification), and prioritizing those where people concentrate (e.g., schools, transport terminals, hospitals, health centers, etc.). Mosquitoes should be removed with a radius of at least 400 meter around these facilities.

- In areas where autochthonous or imported cases of dengue, chikungunya, and/or Zika virus are detected, it is suggested to use adulticide treatment (primarily through spraying), to remove infected adult mosquitoes and interrupt transmission. It is important to take into account that this action is exceptional and is only effective when executed by adequately trained personnel following internationally accepted technical guidelines and when carried out together with other proposed actions, as described above. Spraying is the primary manner to intensively interrupt transmission and obtain time to consolidate the removal of larval breeding sites.

- Selecting appropriate insecticide (in accordance with PAHO/WHO recommendations), verifying the product label and formula, and considering the susceptibility of mosquito populations to that insecticide.

- Maintaining and using spraying equipment in an appropriate manner and maintaining a stockpile of insecticides.

- Ensuring intensified monitoring (e.g., quality control) of fieldwork operators both during larval control and during adult insecticide treatment (fumigation).

Integrated (simultaneous or coordinated) actions for vector control, in space and time, (e.g., adulticide and larval control by trained personnel, coupled with sanitation and the promotion of community actions) are essential to achieve the greatest impact in the shortest amount of time.

It is crucial that the personnel involved in the actions of chemical control use, without exception, the appropriate personal protective equipment for this activity. It is the responsibility of vector control programs to supply this equipment to its staff, to audit its use, and to have enough stockpile stored under appropriate conditions.

Personal prevention measures

It is important for patients infected with dengue, chikungunya or Zika virus to minimize contact with the vector. This measure helps prevent the spread of the virus and therefore the disease. Patients, their household members, and the community, must be educated about the risk of transmission to others and the ways to minimize this risk by reducing vector population and human-vector contact.

The following actions are recommended to minimize vector-patient contact:

- Patients should rest under mosquito nets (bed-nets), treated with or without insecticide.
- Patients and other members of the household should wear clothes that cover the extremities.
- Apply repellents containing DEET, IR3535 or Icaridin to exposed skin or clothing; its use must be strictly in accordance with the instructions indicated on the product label.
- Use wire-mesh screens on doors and windows.

These personal prevention measures are also effective in preventing transmission of the virus to healthy people.

Travelers

Prior to departure

Health authorities should advise travelers heading to any country with documented circulation of dengue, chikungunya, and/or Zika virus to take the necessary measures to protect themselves from mosquito bites, such as using repellents, appropriate clothing that minimize skin exposure, and using insecticides or nets. It is also important to inform travelers of the symptoms of dengue, chikungunya, or Zika virus, in order to assist them in identifying it promptly during their trip. This advice could be relayed through travel medicine services, clinics, travel health web pages of the Ministry of Health, or other relevant government web pages.

While visiting places with dengue, chikungunya and/or Zika virus transmission

Advise travelers to:

- Take appropriate measures to protect themselves from mosquito bites through use of repellents or use of appropriate clothes that minimize skin exposure.
- Avoid mosquito-infested areas.
- Use nets and/or insecticide.

- Recognize symptoms of dengue, chikungunya, and Zika virus and seek professional health care if any of these symptoms occur.

Upon returning

Advise travelers returning home, that if they suspect they have dengue, chikungunya, or Zika virus they should contact their health care provider.

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