Factsheet for health professionals

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Introduction

Zika virus disease is a mosquito-borne disease caused by Zika virus. Most infections are either asymptomatic or cause a mild illness with a transient maculopapular rash.

The *Aedes aegypti* mosquito is the main vector but other *Aedes* species can also transmit the virus. Sexual transmission via semen has been reported recently.

Viral circulation and a few outbreaks were documented in tropical Africa and in some areas in south-east Asia. Since 2007, several islands of the Pacific region have experienced outbreaks, and in 2015 outbreaks were reported in the Americas and the Caribbean. Zika virus disease is considered an emerging infectious disease [1-4].

A significant increase of patients with Guillain–Barré syndrome was reported during the 2014 outbreak in French Polynesia and the Americas since 2015. An unusual increase of congenital microcephaly was observed in some regions in north-eastern Brazil in 2015. According to WHO, there is scientific consensus that Zika virus is a cause of microcephaly, congenital nervous system malformations and Guillain-Barré syndrome [5].

There is no prophylactic or curative treatment or vaccine to protect against Zika virus infection. Therefore, preventive personal measures are recommended to avoid mosquito bites during the daytime.

The pathogen

Zika virus disease is caused by a virus from the *Flavivirus* genus, Flaviviridae family, from the Spondweni group. It was first isolated in 1947 from a monkey in the Zika forest, Uganda, then in mosquitoes (*Aedes africanus*) in the same forest in 1948, and in a human in Nigeria in 1952.

There are two Zika virus lineages: the African lineage and the Asian lineage, which has spread recently in the Pacific and the Americas [2,6,7].

Clinical features and sequelae

The incubation period likely ranges between three and 12 days after the bite by an infected mosquito. Most of the infections remain asymptomatic (approximately 80%).

Disease symptoms are usually mild, and the disease is commonly short-lasting and self-limiting. Its duration is between 2–7 days without severe complications, with no associated fatalities and a low hospitalisation rate.

The main symptoms are maculopapular rash (+/-itchy), with or without mild fever, arthralgia, fatigue, non-purulent conjunctivitis/conjunctival hyperaemia, myalgia and headache. The maculopapular rash often starts on the face and then spreads throughout the body. Less frequently, retro-orbital pain and gastro-intestinal signs might be present.

Differential diagnostic with dengue and chikungunya fever based on clinical symptoms remains challenging, and co-infection can occur. The other usual differential diagnoses are measles, rubella, parvovirus and enterovirus infections, and malaria.

Among women infected during pregnancy, congenital central nervous system malformations of the foetus (such as microcephaly) and foetal losses were notified during several recent Zika disease outbreaks. Unusual increases of Guillain–Barré syndrome incidence, coinciding with the Zika virus outbreaks, were reported in several countries in the Americas and French Polynesia.

Epidemiology

Serological surveys in Africa and Asia indicate most likely silent Zika virus circulation, with detection of specific antibodies in various animal species (large mammals such as orang-utans, zebras, elephants, water buffaloes) and rodents.

The knowledge of the geographical distribution of Zika virus is based on results of serosurveys and viral isolation in mosquitoes and humans, and on reports of travel-associated cases. Before 2007, the areas with reported Zika virus circulation included tropical Africa and south-east Asia. Very few outbreaks were documented prior to a 2007 upsurge on Yap Island, Federated States of Micronesia [8], which was the first outbreak of Zika virus identified outside of Africa and Asia. Between 2013 and 2015, several significant outbreaks were notified on islands and archipelagos in the Pacific region, including a large outbreak in French Polynesia. In 2015, Zika virus emerged in South America, with further spread across the Americas [3,7].

Transmission

Zika virus is transmitted by mosquitoes. It has been isolated from *Aedes aegypti* mosquitoes and experimental infections show that this species is capable of transmitting Zika virus.

Other *Aedes* mosquito species (notably *Ae. africanus*, *Ae. albopictus*, *Ae. polynesiensis*, *Ae. unilineatus, Ae. vittatus* and *Ae. hensilli*) are considered potential vectors of Zika virus. These species bite during the day. *Aedes albopictus* is experimentally able to transmit Zika virus.

Additional modes of transmission have been identified:

- Materno-foetal transmission can occur most probably by trans-placental transmission and during delivery when the mother is infected.
- Sexual transmission has been documented in several instances, in one case from a symptomatic male to a woman as late as 5–6 weeks after onset of the man's symptoms.
- There is a potential risk of Zika virus transmission through blood transfusion and organ transplantation.

More information on *Aedes* mosquitoes can be found here: *Aedes albopictus* and *Aedes aegypti*.

Diagnostics

Zika virus disease diagnostics is primarily based on the detection of viral RNA from clinical specimens (blood, saliva, urine, cerebrospinal fluid, amniotic fluid, semen, and breast milk).

The viraemic period appears to be short, allowing for direct virus detection from blood and saliva, usually during the first 3–5 days after the onset of symptoms (sometimes up to 7–8 days). In several cases, Zika virus RNA has been detected in urine up to 2–3 weeks after onset of symptoms. Virus presence in semen has been documented up to 62 days after symptom onset.

Serological investigations can be conducted from day 5 after the onset of disease, by detection of Zika-specific IgM antibodies and confirmation by neutralisation, seroconversion or fourfold antibody titre increase of Zika-specific antibodies in paired serum samples. Eight to 14 days after the onset of symptoms, diagnostic testing of urine with RT-PCR can be considered in addition to Zika virus serology. Serological results should be interpreted according to the vaccination status and previous exposure to other flaviviral infections (e.g. dengue, West Nile, Japanese encephalitis).

Case management and treatment

There is no specific prophylactic treatment.

Differential clinical diagnostic should be considered as well as co-infection with other mosquito-borne diseases such as dengue fever, chikungunya and malaria.

The treatment is symptomatic and mainly based on a good hydration, pain relief, and anti-histamines for pruritic rash. Treatment with acetylsalicylic acid and no-steroidal anti-inflammatory drugs is discouraged if the diagnosis of dengue is not excluded because of a potential increased risk of haemorrhagic syndrome. Acetylsalicylic acid is also discouraged because of the risk of Reye's syndrome after viral infection in children and teenagers.

Public health control measures

No vaccine or prophylactic treatment is available.

Integrated vector management aiming to reduce mosquito vector density in a sustainable manner is of primary importance. Intersectoral collaboration and efficient public communication strategies to ensure community participation are required for sustainable vector control programmes.

Activities supporting the reduction of mosquito breeding sites in outdoor/indoor areas by draining or discarding sources of standing water at the community level include:

- removal of all open containers with stagnant water in and surrounding houses on a regular basis (e.g. flower plates and pots, used tyres, tree holes and rock pools), or, if that is not possible, treatment with larvicides),
- tight coverage of water containers, barrels, wells and water storage tanks, and the
- wide use of physical barriers that reduce the risk of exposure to mosquitos bites (such as mosquito nets, window/door screens and air conditioning).

During an outbreak, elimination of adult mosquitoes through aerial spraying with insecticides can be considered but efficacy seems very limited.

In areas where the vector is active, the following is recommended:

- Symptomatic patients should strictly follow personal protection measures to prevent mosquito bites for at least the first week of illness to decrease the risk for human-to-mosquito-to-human transmission.
- Asymptomatic individuals returning from an area with Zika virus outbreaks should follow personal protection measures against mosquito bites for three weeks after their return.

More information on mosquitoes can be found here: *Aedes albopictus* and *Aedes aegypti.*

Infection control, personal protection and prevention

Primary prevention is based on protection against mosquito bites. *Aedes* mosquitoes have diurnal biting activities in both indoor and outdoor environments. Therefore personal protection measures should be applied all day, especially during the hours of the highest mosquito activity (mid-morning, late afternoon to twilight).

Personal protection measures to avoid mosquito bites should be applied when in risk areas:

- applying appropriate mosquito repellents and wearing long-sleeved shirts and long trousers to cover as much of the body as possible, especially during the hours of highest *Aedes* mosquito activity
- sleeping or resting in screened or air-conditioned rooms, otherwise use of insecticide-treated mosquito nets, even during the day
- removing mosquito breeding sites in nearby outdoor/indoor premises.

Use of mosquito repellents should be in accordance with the instructions indicated on the product label.

Pregnant women and women who are planning to become pregnant and planning to travel to areas with widespread transmission should postpone non-essential travel. Those who are planning to travel to areas with sporadic transmission should consult their physician or a travel clinic and consider postponing non-essential travel. Pregnant women residing in countries with active transmission (sporadic and widespread) should consult their healthcare providers for advice and follow strict measures to prevent mosquito bites.

Travellers with immune disorders or severe chronic illnesses should consult their doctors or seek advice from a travel clinic before travelling, particularly with regard to effective prevention measures. Similar protective measures apply to a symptomatic patients in order to prevent human-to-mosquito-to-human transmission.

Sexual transmission of Zika virus through semen has been documented, therefore practicing safer sex (including the use of condoms) is recommended throughout pregnancy to protect the foetus.

Additional information

Updated information for travellers and EU citizens is available from ECDC's risk assessment on Zika virus. The list of countries and territories with active Zika virus transmission over the past three months is available on the ECDC website.

More information on mosquitoes can be found here: *Aedes albopictus* and *Aedes aegypti.*

Online updates regarding Zika virus infection are available from:

- World Health Organization (WHO): Zika virus disease
- Pan American Health Organization (PAHO): Zika virus infection
- United States Centers for Disease Control and Prevention (CDC): Zika virus
- European Centre for Disease Prevention and Control (ECDC): Zika virus infection

References

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- See more at: http://ecdc.europa.eu/en/healthtopics/zika_virus_infection/factsheet-health-professionals/Pages/factsheet_health_professionals.aspx?preview=yes&pdf=yes#sthash.RAzaKEyw.dpuf