E D I T O R I A L / U V O D N I K

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Another emerging pathogen – Zika virus

Zika virus – još jedan novoiskrsli patogen

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Zika virus (ZIKV) disease is caused by an emerging mosquito-borne virus from the *Flavivirus* genus, Flaviviridae family, from the Spondweni group. It was first isolated in 1947 in rhesus monkeys through a monitoring network of sylvatic yellow fever, 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 ZIKV lineages: the African lineage and the Asian lineage which has recently emerged in the Pacific and the Americas [1–4].

For many years only sporadic human cases were detected in Africa and Southern Asia. Serological surveys in Africa and Asia indicate a most likely silent ZIKV circulation with detection of specific antibodies in various animal species (large mammals such as orangutans, zebra, elephants, water buffaloes) and rodents [4, 5]. The knowledge of geographical distribution of ZIKV is based on the results of serosurveys and viral isolation in mosquitoes and humans, and with reports on travel-associated cases and very few published outbreaks. Before 2007, the areas with reported ZIKV circulation included tropical Africa and Southeast Asia. In 2007, the outbreak of Zika virus disease occurred in the Pacific. This was the first outbreak of ZIKV identified outside of Africa and Asia [6]. Between 2013 and 2015, several significant outbreaks were notified on the islands and archipelagos from the Pacific region including a large outbreak in French Polynesia. In 2015, ZIKV emerged in South America with widespread outbreaks reported in Brazil and Columbia [1–3]. Given the expansion of environments where mosquitoes can live and breed, facilitated by urbanisation and globalisation, there is a potential for major urban epidemics of Zika virus disease to occur globally.

The incubation period of disease is not clear, but is likely to be three to 12 days after the bite of an infected mosquito. Most of the infections remain asymptomatic (between 60% to 80%). The symptoms are similar to other arbovirus infections such as dengue. Signs and simptoms are usually mild and the disease is usually characterised by a short-lasting self-limiting febrile illness of 4–7 days duration without severe complications, with no associated fatalities and a low hospitalisation rate. The main symptoms are macular or papular rash, fever, arthralgia, 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 gastrointestinal signs are present [3].

Autoimmune, neurological and neurodevelopmental conditions such as Guillain-Barré syndrome and microcephaly in fetuses and newborns from mothers possibly exposed to ZIKV in the two first trimesters of the pregnancy were notified during recent Zika disease outbreaks in French Polynesia and Brazil, in 2013 and 2015, respectively. Further evidence is needed to establish a causal link between these neurological/neurodevelopmental impairments and infections with ZIKV [1, 2, 7].

Zika virus is transmitted to people through the bite of an infected mosquito from the *Aedes* genus, mainly *Aedes aegypti* in tropical regions. This is the same mosquito that transmits dengue, chikungunya and yellow fever. Other *Aedes* mosquito species (notably *Ae. africanus*, *Ae. albopictus*, *Ae. polynesiensis*, *Ae. unilineatus*, *Ae. vittatus* and *Ae. hensilli*) are considered as potential vectors of ZIKV. These species bite during the day (especially in mid-morning and between late afternoon and twilight) [8]. Till now in Serbia, we have not confirmed the presence of Zika vectors, but some underlying field investigations could show different picture.

Additional modes of transmission also have been identified. Perinatal transmission can occur most probably by transplacental transmission or during delivery when the mother is infected. Sexual transmission was reported in two case reports. There is a potential risk of ZIKV transfusion-derived transmission [9, 10].

The ZIKV disease diagnostics is primarily based on detection of viral RNA from clinical specimens in acutely ill patients. The viraemic period appears to be short, allowing for direct virus detection during the first 3–5 days after the onset of symptoms. ZIKV RNA has been detected in urine

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up to 10 days after onset of the disease. From the day five post-onset of fever, serological investigations can be conducted by detection of Zika-specific IgM antibodies and confirmation by neutralisation, seroconversion or four-fold antibody titer increase of Zika specific antibodies in paired serum samples. Diagnosis by serology can be difficult as the virus can cross-react with other flaviviruses, therefore serological results should be interpreted according to the vaccination status and previous exposure to other flaviviral infections [3].

Mosquitoes and their breeding sites pose a significant risk factor for this 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 using insect repellent; wearing clothes (preferably light-coloured) that cover as much of the body as possible; using physical barriers such as screens, closed doors and windows; and sleeping under mosquito nets. 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. Special attention and help should be given to those who may not be able to protect themselves adequately, such as young children, the sick or elderly.

Residents and travellers visiting affected areas (Table 1) [3], particularly pregnant women, must take individual protective measures to prevent mosquito bites all day round as Zika virus disease, chikungunya and dengue are transmitted by a

Table 1

Countries and territories with recent local Zika virus transmission (EECD)

Country/Territory	Affected in the past 2 months	Affected in the past 9 months
American Samoa	Increasing or widespread transmission	Yes
Aruba	Sporadic transmission following recent introduction	Yes
Barbados	Increasing or widespread transmission	Yes
Bolivia	Sporadic transmission following recent introduction	Yes
Brazil	Increasing or widespread transmission	Yes
Bonaire	Sporadic transmission following recent introduction	Yes
Cape Verde	Increasing or widespread transmission	Yes
Colombia	Increasing or widespread transmission	Yes
Costa Rica	Sporadic transmission following recent introduction	Yes
Curaçao	Increasing or widespread transmission	Yes
Dominican Republic	Increasing or widespread transmission	Yes
Ecuador	Increasing or widespread transmission	Yes
El salvador	Increasing or widespread transmission	Yes
Fiji	No	Yes
French Guiana	Increasing or widespread transmission	Yes
Guadeloupe	Increasing or widespread transmission	Yes
Guatemala	Increasing or widespread transmission	Yes
Guyana	Sporadic transmission following recent introduction	Yes
Haiti	Increasing or widespread transmission	Yes
Honduras	Increasing or widespread transmission	Yes
Jamaica	Sporadic transmission following recent introduction	Yes
Maldives	No	Yes
Marshall Islands	Sporadic transmission following recent introduction	Yes
Martinique	Increasing or widespread transmission	Yes
Mexico	Increasing or widespread transmission	Yes
New Caledonia	No	Yes
Nicaragua	Increasing or widespread transmission	Yes
Panama	Increasing or widespread transmission	Yes
Paraguay	Increasing or widespread transmission	Yes
Puerto Rico	Increasing or widespread transmission	Yes
Saint Martin	Sporadic transmission following recent introduction	Yes
Samoa	Increasing or widespread transmission	Yes
Solomon Islands	No	Yes
Suriname	Increasing or widespread transmission	Yes
Thailand	Sporadic transmission following recent introduction	Yes
Tonga	Increasing or widespread transmission	Yes
Trinidad and Tobago	Sporadic transmission following recent introduction	Yes
Vanuatu	No	Yes
Venezuela	Increasing or widespread transmission	Yes
US Virgin Islands	Sporadic transmission following recent introduction	Yes

Based on data reported by European Centre for Disease Prevention and Control, 19 February, 2016 (http://ecdc.europa.eu/en/publications/Publications/communicable-disease-threats-report--20-feb-2016.pdf)
This table contains information on countries and territories that have recently experienced or are currently experiencing local Zika virus transmission. The classification of countries above is based on: 1) the number of reported autochthonous confirmed cases; 2) the number of affected areas in the country; 3) duration of the circulation.

daytime-biting mosquito. Consequently, protective measures should be taken, especially during the day.

Travellers that are pregnant, have immune disorders or severe chronic illnesses, or are accompanied by young children should consult their doctor or seek advice from a local public health institute before travelling in order to receive recommendations on the use of repellents and other preventive measures. Travellers showing symptoms compatible with dengue, chikungunya or Zika virus disease within three weeks after returning from an affected area should contact their healthcare provider. Pregnant women who have travelled to areas with Zika virus transmission should mention their travel during antenatal visits in order to be assessed and monitored appropriately.

Blood safety authorities should consider the deferral of donors with a relevant travel history to areas with active Zika virus transmission, in line with measures defined for dengue virus [3, 11].

Zika virus disease is usually relatively mild and requires no specific treatment. The 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 pain relief, fever reduction and antihistamines for pruritic rash. If symptoms worsen, they should seek medical care and advice. There is currently no vaccine available. Treatment with acetylsalicylic acid and non-steroidal anti-inflammatory drugs was discouraged because of a potential increased risk of haemorrhagic syndrome reported with other flaviviruses as well as the risk of Reye's syndrome after viral infection in children and teenagers.

REFERENCES

1. *European Centre for Disease Prevention and Control.* Zika virus infection outbreak, Brazil and the Pacific region. Stockholm: ECDC; 2014.
2. *European Centre for Disease Prevention and Control.* Microcephaly in Brazil potentially linked to the Zika virus epidemic. Stockholm: ECDC; 2015.
3. *European Centre for Disease Prevention and Control.* Zika virus infection (factsheet for health professionals). Stockholm: ECDC; 2015.
4. *Dick GW, Kitchen SF, Haddow AJ.* Zika virus. I. Isolations and serological specificity. Trans R Soc Trop Med Hyg 1952; 46(5): 509−20.
5. *Kuno G, Chang GJ, Tsuchiya KR, Karabatsos N, Cropp CB.* Phylogeny of the genus Flavivirus. J Virol 1998; 72(1): 73−83.
6. *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(24): 2536−43.
7. *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 2014; 19(9): pii=20720.
8. *Ioos S, Mallet HP, Leparc Goffart I, Gauthier V, Cardoso T, Herida M.* Current Zika virus epidemiology and recent epidemics. Med Mal Infect 2014; 44(7): 302−7.
9. *Musso D, Roche C, Robin E, Nhan T, Teissier A, Cao-Lormeau VM.* Potential sexual transmission of Zika virus. Emerg Infect Dis 2015; 21(2): 359−61.
10. *Foy BD, Kobylinski KC, Chilson Foy JL, Blitvich BJ, Travassos da Rosa A, Haddow AD,* et al. Probable non-vector-borne transmission of Zika virus, Colorado, USA. Emerg Infect Dis 2011; 17(5): 880−2.
11. *Musso D, Nhan T, Robin E, Roche C, Bierlaire D, Zisou K*, et al. Potential for Zika virus transmission through blood transfusion demonstrated during an outbreak in French Polynesia, November 2013 to February 2014. Euro Surveill 2014; 19(14): pii=20761.