



RAPID RISK ASSESSMENT

Zika virus disease epidemic

Eighth update, 30 August 2016

Conclusions and options for response

Given the current circulation of Zika virus, the evidence of an association between Zika virus infection during pregnancy and congenital malformations of the central nervous system (CNS), the association between Zika virus infection and Guillain-Barré syndrome (GBS) and the risk of local vector-borne transmission in Europe during the 2016 summer season, EU/EEA Member States should consider a range of mitigation measures. The options for risk reduction and the definitions below are based on the current evidence, taking into account remaining uncertainties. These are subject to change as new evidence emerges.

Options for risk reduction

The predominant mode of transmission of Zika virus is through bites of infected mosquitoes but the virus can also be transmitted through sexual contact. Pregnant women are the most important risk group because Zika virus infection during pregnancy is associated with intrauterine CNS infection, congenital malformations and foetal death. Hence, pregnant women are the primary target for preventive measures.

A map and list of countries and territories with widespread and sporadic transmission during the past three months is available on the [ECDC website](#).

Zika affected areas

ECDC classifies Zika affected areas as having widespread transmission or sporadic transmission based on cases reported in the past three months:

- **Widespread transmission:** more than 10 locally transmitted cases of Zika virus in one area, OR local transmission of Zika virus in two or more areas, OR Zika virus transmission ongoing for more than three months.
- **Sporadic transmission:** no more than 10 locally transmitted cases reported in a single area in the past three months.

For more information about the classification of Zika affected areas, please visit the [ECDC website](#).

Zika unaffected areas

Unaffected areas are areas without mosquito-borne transmission of Zika virus.

The unaffected areas in the EU/EEA are classified according to their potential for mosquito-borne transmission as:

- **Receptive areas** for Zika virus transmission: areas with established and active populations of *Aedes aegypti* or *Aedes albopictus* mosquitoes.
- **Unreceptive areas** for Zika virus transmission: areas with no established or inactive populations of *Aedes aegypti* or *Aedes albopictus* mosquitoes.

Potentially infectious person

A **potentially infectious person** is defined as:

- A person who resides in an affected area; OR
- A person who has been in an affected area in the past eight weeks; OR
- A man who has been in an affected area in the past six months AND experienced symptoms while in the affected area or within two weeks after leaving the area; OR
- A person, regardless of gender who has had unprotected sex* in the past eight weeks with a potentially infectious person as defined in the three bullets above.

Preventive measures

Preventing mosquito transmission

Mosquito-borne transmission occurs when an infective mosquito bites a susceptible person. The risk of mosquito-borne transmission can be reduced by lowering the mosquito population density and by applying personal protective measures against being bitten. The aim is to prevent susceptible people from being bitten by infective mosquitoes, and preventing infected people from being bitten by competent mosquitoes and thus continue the chain of transmission.

Personal protective measures that reduce the risk of mosquito bites are:

- Use of mosquito repellent in accordance with the instructions indicated on the product label;
- Wearing long-sleeved shirts and long trousers, especially during daytime, when the *Aedes aegypti* and *Aedes albopictus* mosquitoes are most active;
- Sleeping and resting in screened or air-conditioned rooms, otherwise using mosquito bed nets, at night and during the day;

These measures should be applied indoors and outdoors.

Preventing sexual transmission

Zika virus sexual transmission can be prevented by:

- Abstaining from sexual contact with a potentially infectious person, OR;
- Consistent use of barrier methods* during sexual contact with a potentially infectious person.

Advice to populations at risk

Residents in affected areas

All residents in affected areas are at risk of Zika infection unless they are immune due to infection in the past. Residents should consider taking measures to prevent mosquito-borne and sexual transmission.

Pregnant women residing in affected areas should consult their healthcare providers for medical advice. They should strictly follow measures to prevent mosquito and sexual transmission for the duration of their pregnancy. Pregnant women should seek medical attention if they develop symptoms compatible with Zika infection.

Women of childbearing age should be made aware of the risks of Zika infection to the foetus during pregnancy and the possibility of sexual transmission through unprotected sex with a potentially infectious person. Women and men living in affected areas should discuss planned pregnancy with their healthcare provider and consider delaying pregnancy.

* Protected sex is defined a sexual contact during which appropriate barrier methods are correctly and consistently used in order to reduce the risk of sexually transmitted infections and sexually transmissible infections such as Zika virus. Barrier methods include: male or female condoms for penetrative sex, including sex toys, and male or female condoms or dental dams for oral-genital or oral-anal sexual contact. To increase their effectiveness they should be used consistently and correctly, for the entire duration of sexual contact. United Nations Program on HIV/AIDS. Position statement on condoms and the prevention of HIV, other sexually transmitted infections and unintended pregnancy, 7 July 2015. Internet. Geneva: United Nations Program on HIV/AIDS, 2015.

Travellers to affected areas

All travellers to affected areas are at risk of Zika infection unless they are immune due to infection in the past. Travellers to affected areas should take measures to prevent mosquito-borne and sexual transmission.

Pregnant women should seek medical advice prior to travelling. They should postpone non-essential travel to affected areas with widespread transmission and consider postponing non-essential travel to areas with sporadic transmission for the duration of their pregnancy.

Women of child-bearing age who travel to affected areas should be made aware of the risks of Zika infection to the foetus during pregnancy and the possibility of sexual transmission. Women of child-bearing age who travel to affected areas should be made aware of the risks of Zika infection to the foetus during pregnancy and the possibility of sexual transmission. Therefore, they should take measures to delay pregnancy until eight weeks after returning from the affected area. If their male partner has been exposed and had symptoms of Zika virus disease, conception should be delayed for six months after onset of symptoms.

Travellers with immune disorders or severe chronic illnesses should consult their physician or seek advice from a travel clinic before travelling.

Persons returning from affected areas

All persons returning from affected areas should:

- Take measures to prevent sexual transmission for at least eight weeks after returning if asymptomatic and six months for men who experienced symptoms while in the affected area or within two weeks after leaving the area;
- Seek medical attention if they develop symptoms compatible with Zika infection within two weeks of arriving from the affected areas and mention their travel history.

Pregnant women returning from affected areas should:

- Inform their antenatal care provider about their travel to an affected area;
- Take measures to prevent sexual transmission for the duration of their pregnancy.

All persons who have been in affected areas and travel to receptive areas should:

- Take personal protective measures to prevent mosquito bites as described above, for three weeks after having left an affected area.

Information to healthcare providers in EU Member States

Efforts should be made to increase awareness among health professionals providing antenatal care of the risk of neurological congenital syndrome associated with maternal Zika virus infection, especially during the first two trimesters of pregnancy. Pregnant women with exposure to Zika virus (including sexual exposure) since the beginning of their pregnancy should be investigated as part of the routine obstetric monitoring ([Algorithm for public health management of cases under investigation for Zika virus infection](#)).

Antenatal monitoring should be adapted in accordance with the possibility of exposure to the virus through vector or sexual transmission [1,2]. ECDC maps showing [Zika transmission in the past nine months](#) are provided to aid medical practitioners assessing returning travellers, especially pregnant women, who have visited countries and territories with recent transmission of Zika virus.

Health services and practitioners should be aware of the association between Zika virus infections and GBS, the possible associations with other neurological conditions (such as meningitis, meningoencephalitis and myelitis) and with as yet undocumented complications of Zika virus infections, particularly among children, the elderly, immunocompromised individuals and those with sickle cell disease.

Safety of substances of human origin

ECDC published a report on "Zika virus and safety of substances of human origin – Guide for preparedness activities in the Europe" [3]. The objective of this document is to support the operational preparation and implementation of national preparedness plans for the safety of substances of human origin (SoHO) during outbreaks of Zika virus infection. This document includes detailed measures to be considered to mitigate the threats to the safety of SoHO posed by Zika virus.

Non-affected areas and areas with sporadic transmission

Blood donors and living donors of cells and tissues who are at risk of having been infected should be temporary deferred from donation.

Criteria for identifying donors at risk are:

- A medical diagnosis of Zika virus disease;
- Returning from areas with widespread transmission;
- Reporting sexual intercourse with a person who has been diagnosed with Zika virus infection or a person who have returned from areas with widespread transmission.

The deferral/acceptance periods for living donors should provide a sufficient safety margin for virus-free donation. Cells and tissues from deceased donors with a recent medical diagnosis of Zika virus infection should not be accepted for donation.

Areas with widespread transmission

Temporarily interrupt donations and import blood components or cells and tissues from unaffected parts of the country or continue with the selective donation of plasma, platelets and some tissues that should be pathogen inactivated and import other products that cannot be inactivated. The laboratory screening of all donated blood and all donors of cells and tissues for the presence of Zika virus RNA by nucleic acid testing (NAT) may be considered necessary to ensure the safety and sustainability of supply in areas with widespread transmission.

Irrespective of the presence of ongoing local virus transmission in the area, the risk of Zika virus transmission through organs donated by living or deceased donors should be recognised and assessed during a pre-donation evaluation and balanced against the benefits of the transplantation for each potential recipient.

Laboratory screening of SoHO donors/donations

Commercial Zika tests for screening are still under development. SoHO establishments and laboratories may develop in-house or adapt available commercial diagnostic tests for screening purposes. The use of such screening tests should be validated and approved by the responsible national authority. WHO reference material of Zika virus RNA for comparative evaluation of both diagnostic and screening assays is expected to be officially endorsed in October 2016 but can already be obtained from the Paul-Ehrlich-Institute (Germany) [4].

The commercial laboratory tests that are reviewed favourably in the WHO Emergency Use Assessment and Listing (EUAL) [5] and listed as eligible for WHO procurement could also be used for an emergency application until final registration/approval for commercial use is available.

The recent non-binding recommendation by the US FDA for the universal testing of donated whole blood and blood components for Zika virus in the USA and its territories will be reviewed in the European context.

Surveillance of imported cases and local transmission in continental Europe

In order to reduce the risk of local transmission in continental Europe, EU Member States should:

- Ensure that medical practitioners and travel health clinics are aware of the evolution of the Zika virus outbreak and the areas around the world with active and past transmission (see ECDC website) to allow them to consider Zika virus infection in their differential diagnosis for travellers coming from those areas or for symptomatic individuals who have not travelled but had sexual activity with a returning traveller from those areas. Medical practitioners should be aware that Zika virus infections can be paucisymptomatic.
- Increase awareness among obstetricians, paediatricians and neurologists that the possibility of Zika virus infection should be investigated in patients presenting with congenital CNS malformations, microcephaly and GBS.
- Enhance vigilance towards the early detection of imported cases of Zika virus infection in EU Member States, EU Overseas Countries and Territories (OCTs) and EU Outermost Regions (OMR), in particular where Zika vectors are present, in order to reduce the risk of onward autochthonous transmission.
- Ensure timely reporting of autochthonous cases, in particular in the receptive areas of EU Member States in continental Europe.
- Clusters of unexplained illness with a rash, detected in receptive areas of continental Europe between 1 May and 31 October should be investigated, and Zika virus infection should be considered as a possible cause.
- Strengthen laboratory capacity and capabilities to confirm Zika virus infections in the EU/EEA and to differentiate Zika virus infections from other arboviral infections (e.g. dengue, chikungunya).

Source and date of request

ECDC internal decision, 5 August 2016.

ECDC issues this risk assessment document according to Article 7(1) of Regulation (EC) No 853/2004 establishing a European centre for disease prevention and control. In the framework of ECDC's mandate, the specific purpose of an ECDC risk assessment is to present different options on a certain matter. The responsibility for the choice of which option to pursue and which actions to take lies exclusively with the EU/EEA Member States.

Public health issue

This document assesses the risks associated with the Zika virus epidemic in currently affected countries, in EU Overseas Countries and Territories (OCTs) and Outermost Regions (OMRs) and in the EU Member States within continental Europe. Since February 2014, ECDC has published nine risk assessments related to Zika virus epidemics [6-16].

Consulted experts

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ECDC acknowledges the valuable contributions of all experts. Although experts from the World Health Organization (WHO) reviewed the risk assessment, the views expressed in this document do not necessarily represent the views of WHO. All experts have submitted declarations of interest and a review of these declarations did not reveal any conflicts of interest.

Disease background information

Zika virus disease is caused by an RNA virus transmitted to humans by *Aedes* mosquitoes, especially by the *Aedes aegypti* species. More information about Zika virus disease can be found in the previous risk assessments [6-16] and in the ECDC [factsheet for health professionals](#) (last update 23 June 2016).

Epidemiological developments

Since the 7th risk assessment [Zika virus disease epidemic](#), published on 8 July 2016, the outbreak has continued to evolve in Central America and the Caribbean countries and territories and autochthonous transmission has reached the state of Florida (USA) where competent vectors are present and active during the northern hemisphere summer season.

Between 30 June and 17 August 2016, seven new countries and territories reported locally-acquired cases (Antigua and Barbuda, Bahamas, Cayman islands, Turks and Caicos, United States of America, Guinea-Bissau and Federated States of Micronesia) and one new country reported non vector-borne Zika virus transmission (Spain) [17,18]. During the same period, three new countries (Honduras, Paraguay and Suriname) reported their first cases of microcephaly or CNS malformation associated with Zika virus infection and four new countries (Jamaica, Costa Rica, Grenada and Guatemala) notified cases of GBS associated with Zika virus infection [17,18].

In South America, Brazil has reported 174 003 suspected and 78 421 confirmed Zika virus infections as of week 26 2016, [19,20]. On 25 July, the Ministry of Health of Colombia declared the end of the Zika epidemic phase [21]. The country remains the second most affected in the Americas with 93 281 suspected and 8 826 confirmed cases reported up to week 32 in 2016 [22] and 18 328 notifications of pregnant women with confirmed and suspected Zika virus disease. Because many of these women remain pregnant, an increase in the incidence of congenital malformations is expected in September and October 2016.

In the Caribbean, several EU Outermost Regions (OMRs) and Overseas Countries and Territories (OCTs) still report vector-borne autochthonous Zika transmission. The epidemic has been decreasing in Martinique, Guadeloupe, Saint Martin and French Guiana since July 2016 [23]. The islands in the Dutch Antilles (Aruba, Bonaire, Curaçao, Saba and Sint Maarten) have all reported autochthonous transmission.

In North America, as of week 32 in 2016, new cases have exceeded one hundred confirmed cases per week for the past six weeks in Mexico with the highest incidence reported from the south-western part of the country [24]. The first locally acquired cases were reported in Florida on 29 July [25] and as of 19 August 2016, there have been 36 locally transmitted Zika virus cases. As of 19 August 2016, the focus of transmission is in the Miami-Dade County [25]. Investigations of cases without epidemiological links to the one square mile area in Miami-Dade are on-going in Florida state. There is an ongoing investigation of a case of Zika virus infection in a Utah resident who took care of a fatal Zika case in June 2016 [26]. Both infections have been laboratory confirmed. The secondary case had

not travelled to any affected area and had not had sex with anyone infected with Zika and there are no competent *Aedes* mosquitoes in the area.

On 17 August, WHO confirmed seven new cases of Zika virus infection in Guinea-Bissau in addition to the four cases on the island of Bubaque (Bijagós) in Guinea-Bissau previously reported [18,27,28]. Virus sequencing to determine the strain is pending and WHO experts are deployed to support preparedness and response activities [28].

As of 19 August 2016, no locally-acquired case by vector-borne transmission have been reported by EU/EEA countries in continental Europe. Since week 45/2015, 19 countries have reported 1 265 travel associated Zika virus infections through the European Surveillance System (TESSy). France reported 56% of the cases. Over the same period, six countries reported 69 Zika cases among pregnant women.

A weekly update gathering the latest information of the Zika virus epidemic is available through the ECDC Zika outbreak [webpage](#) [29] and a weekly update on the situation is available in [epidemiological update](#) [30] or in the [ECDC Communicable Disease Threats Report](#) by the European Centre for Disease Prevention and Control, #1001}. Countries and territories with reported confirmed autochthonous vector-borne transmission of Zika virus infection in the past three months are shown on ECDC's webpage [Countries and territories with local Zika transmission](#) [31].

Scientific developments

The main findings with regards to Zika virus research are:

- There is additional evidence indicating that microcephaly and other severe congenital malformations may represent the severe spectrum of Zika congenital syndrome that may include other congenital malformations (such as arthrogryposis) and neurological conditions with late clinical presentation[32].
- Findings from five pregnant women enrolled in the US Zika Pregnancy Registry indicate that pregnant women may have longer lasting viraemia than non-pregnant women [33,34]. Zika virus RNA could be detected with RT-PCR in the serum for up to 46 days after symptoms for symptomatic pregnant case and 53 days after exposure for asymptomatic pregnant women [34].
- Three potential Zika-associated fatal adult cases with co-morbidities were described in Suriname. The patients deteriorated rapidly and died despite intensive supportive care. This latest report of severe atypical presentations of Zika virus infection has similarities with a report from Colombia about four fatal cases [35].
- The potential role of *Culex* species in Zika virus transmission has been suspected. Brazilian scientists reported detecting Zika virus in salivary glands of *Culex quinquefasciatus* mosquitoes from the third day after artificial feeding of infected blood (unpublished data) [36,37]. However, Zika virus was not detected in *Cx. quinquefasciatus* mosquitoes collected during an outbreak in December 2015 in Chiapas, Mexico [38]. Experimental infections showed that *Cx. pipiens* mosquitoes from California do not transmit Zika virus [39].
- Experimental studies showed that dried droplets containing Zika virus remained infectious for more than three days. The virus lost its infectivity at temperature $\geq 60^{\circ}\text{C}$ and was destroyed by classical disinfectants and inactivation methods [40].
- Sexual transmission of Zika virus has been reported from men with symptomatic infection to both female and male sexual partners, from men with asymptomatic infection to female and from a female to male in one instance [41-43]. Zika virus might be transmitted to sexual partners of infected women through exposure to vaginal secretions or menstrual blood [44].
- A limited number of longitudinal studies report results from detection of Zika viral RNA in semen [45,46]. An in-depth longitudinal follow-up of a 40 years old-man with 40 semen samples between day 5 and 181 after onset of symptoms demonstrated a decreasing but persistent shedding of viral nucleic acid associated with the cellular component of semen for 181 days, while Zika RNA was not detected in the seminal plasma [47]. Another case report showed Zika virus RNA in semen at day 91, 134 and 188 after onset of symptoms [48].
- Recent studies showing protective efficacy of multiple vaccine platforms against Zika virus challenge in rhesus monkeys are supporting the rapid clinical development of Zika virus vaccine for humans [49]. The first phase I trials of two Zika virus DNA vaccine candidates to evaluate safety, tolerability and immunogenicity on healthy adult volunteers are starting in the US and Canada [50].

Detailed report about the relevant scientific literature published since the [latest rapid risk assessment \(7th Update - 12 Jul 2016\)](#) is available at in [Zika epidemic scientific advance](#) [51].

International guidance, response and preparedness plans update

Since the last rapid risk assessment, WHO/PAHO published a revised Zika strategic response plan for July 2016 to December 2017 [52]. The US Centers for Disease Control and Prevention updated the following documents:

- Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States, July 2016 [53];
- Interim Guidance for Prevention of Sexual Transmission of Zika Virus — United States, July 2016 [44].
- Operational risk communication plan and community engagement plan [54].

- Update: Interim Guidance for the Evaluation and Management of Infants with Possible Congenital Zika Virus Infection — United States, August 2016 [55].

ECDC has published a [preparedness planning guide for diseases transmitted by *Aedes aegypti* and *Aedes albopictus*](#). The guide focuses on the main components that should be considered when developing preparedness plans [56].

ECDC threat assessment for the EU

The Zika epidemic remains a significant concern for public health. The third meeting of the International Health Regulations Emergency Committee on 14 June 2016, 'concurred with the international scientific consensus... that Zika virus is a cause of microcephaly and GBS, and, consequently, that Zika virus infection and its associated congenital and other neurological disorders is a Public Health Emergency of International Concern (PHEIC)' [57].

Vector-borne transmission is expected to continue during the summer months in northern hemisphere countries, notably in Central American countries, Mexico, the southern part of the US and the Caribbean, as weather conditions favour a seasonal increase of vector activity. The report of locally-acquired cases in Florida is not unexpected as small outbreaks of local transmission of dengue and chikungunya have been reported in Florida in the past and the area is receptive for *Aedes* transmitted diseases [58,59].

There is consensus that Zika virus infection during the first and second trimester of pregnancy is associated with increased risk for CNS malformations and microcephaly. The risk of CNS malformations when the infection occurs during the third trimester of pregnancy is unknown, hence Zika virus infection should be considered as a risk throughout the duration of pregnancy. To date, there is insufficient data to provide a robust estimate of the risks of adverse pregnancy outcomes by gestational age and the role of potential co-factors. It is likely that the clinical spectrum of congenital abnormalities associated with Zika virus infection in utero will not be limited to CNS and could include other organ systems such as genitourinary, cardiac and digestive systems [60]. Prospective epidemiological studies of Zika virus affected populations should provide a clearer picture of the clinical spectrum of diseases caused by Zika virus.

It is conceivable that co-factors, such as the mother's age, nutritional status, genetic pre-disposition, socio-economic status, environmental exposures, immune status, and concomitant infections, influence the probability of Zika transplacental transmission and congenital malformations. New investigations are on-going to clarify the high incidence of Zika congenital syndrome in the northeast region of Brazil [61].

Vector-borne transmission remains the primary route of transmission. Sexual transmission does occur but its role in spreading the epidemic remains to be determined. Comprehensive data on the presence and duration of Zika virus in bodily fluids, especially in semen, is required to assess the risk of sexual transmission at population level.

The outbreak is unprecedented in terms of size and public health impact and constitutes a significant development in the epidemiology of this emerging vector-borne disease. The evolution of the Zika epidemic in the Americas and other world regions demands close monitoring as it has a direct impact on the risk of importation and possible occurrence of local transmission in the European Union. The viral circulation in affected countries coincides with the summer holiday period in Europe and it is expected that Zika viraemic travellers will continue to return to the EU during the entire 2016 European mosquito season. This will create the possibility of onward transmission of Zika virus in receptive areas in Europe.

Options for prevention and response are presented above (see Conclusions and options for response). ECDC will continue to monitor new scientific evidence and update of the assessment of the risk of transmission and option for prevention and control accordingly.

Travel-related risk for EU citizens

Travellers to affected areas are at risk of becoming infected through mosquito bites and sexual transmission. Due to the link between Zika virus infection and severe congenital anomalies, pregnant women and women who may become pregnant constitute a high-risk group for serious adverse outcomes of Zika virus infection.

Risk of importation and transmission in EU Outermost Regions and Overseas Countries and Territories

Residents in EU Outermost Regions (OMR) and Overseas Countries and Territories (OCT) with competent and active vectors are at risk of exposure to Zika virus. *Aedes aegypti* mosquitoes are present in the EU OCTs and OMRs in the Americas and the Caribbean, and most of them have reported autochthonous transmission (see [Countries and territories with local Zika transmission](#)) [31].

EU OMRs and OCTs outside of the Caribbean where mosquito vectors are present, such as Madeira and Mayotte with *Aedes aegypti* or La Réunion with *Aedes albopictus*, are at risk of local transmission should the virus be introduced [62].

Madeira is of particular concern because of the presence of *Aedes aegypti*. The probability of vector-borne pathogen transmission is considered high during late summer and fall period because the previous dengue outbreak lasting between September and January 2012 demonstrated the favourable conditions for mosquito-borne outbreaks during the summer and fall months. There is an increased frequency of travel between Madeira and Brazil as well as other countries where Zika virus is currently circulating, thus increasing the risk of the virus being imported [63]. The *Aedes aegypti* vector surveillance program in place since 2008 demonstrates an increase of the vector activity in Madeira since late June 2016 which remains to date. The *Aedes aegypti* vector surveillance program in place since 2008 demonstrates an increase of the vector activity in Madeira since late June 2016 that remains to date. It is expected to observe a high vector activity in August and September based on seasonal pattern [64].

According to the Interim Risk Assessment issued by WHO Regional Office for Europe, the capacity to contain Zika virus transmission at an early stage is good for the countries of the WHO European Region overall [65].

Risk of importation and transmission within the continental EU

The outbreak in the Americas and the Caribbean has considerably increased the risk of Zika virus importation into the EU through infected returning travellers and visitors from the affected areas. Cases of Zika virus infection arriving from countries with autochthonous transmission continue to be reported in the EU and it is expected that this will continue.

The likelihood of mosquito-borne transmission of Zika virus infection in the EU is considered plausible only for receptive areas: those areas where mosquitoes capable of transmitting the virus are present and active. The transmission depends on several factors related to the mosquito, the virus and the environment [66,67]:

- The introduction of the virus by a viraemic traveller during the summer season where *Aedes albopictus* is established can be expected (see situation in the EU/EEA and EU Outermost Regions and Overseas Countries and Territories) [68]. *Aedes albopictus* is established around the Mediterranean basin. As part of the VectorNet project, ECDC shows the current known distribution of invasive mosquito species in Europe at regional administrative level (NUTS 3) [69].
- The suitable conditions for *Aedes albopictus* activity increased progressively during the spring (April to June), especially in southern Europe. By analogy with other mosquito-borne disease transmission, the conditions for autochthonous Zika virus transmission will remain favourable in continental Europe during summer and autumn [70].
- A study investigating the impact of mosquito-borne and sexual transmission estimated a basic reproduction number of 2.05 (95% CI: 0.52–6.30) [71]. Incidence data from Brazil, Colombia, and El Salvador were used to calibrate the deterministic model. The percentage contribution of sexual transmission is estimated at 3.04% (95% CI: 0.13–45.7). The sensitivity analyses of R0 showed that the biting rate and mortality rate of mosquitoes are key parameters influencing the reproductive number. Factors such as the mosquito survival, density, and biting behaviour for humans of the vector species are known to determine the final transmission potential of the vector species (so-called vector capacity). Local vector-borne transmission in the EU therefore cannot be excluded.

Given the low vector competence of the studied European populations of *Aedes albopictus* [72-74], the likelihood of local vector-borne transmission in the EU is considered to be low to moderate. As of 24 August 2016, no cases of locally acquired mosquito-borne Zika transmission have been reported to ECDC in continental Europe.

Risk of sexual transmission

While Zika virus is considered a mild disease for the general population, the severity of foetal impairment in pregnant women infected by Zika virus implies the need to reduce the risk of infection in pregnant women and women of childbearing age through vector-borne and/or sexual transmission and to adapt gamete donation and preconception counselling recommendations.

Several occurrences of sexual transmission from symptomatic cases in the early phase of infection have been described, with the longest interval of 44 days reported between the onset of symptoms in a man and in his female partner [75]. In addition, there has been one probable transmission between asymptomatic partners (male to female) [41] and one likely transmission from an asymptomatic traveller male to his non traveller female partner who developed symptoms [76]. This would support a higher probability of sexual transmission of Zika virus during this early period. However, possible sexual transmission has been described in scientific literature up to 34 to 41 days after the index case [75].

A recent report describes the detection of Zika virus RNA from a woman's cervical mucus, genital swab, and endocervical swab at day 3 after symptoms and up to 11 days after onset of symptoms in cervical mucus which substantiates the possibility of female-to-male Zika virus transmission [77].

Longitudinal sampling of two male patients showed continuous shedding of Zika virus RNA in semen up to days 181 and 188 after onset of symptoms, although Zika RNA viral detection in a bodily fluid does not necessarily imply the presence of infectious viral particles [47,48]. While late transmission cannot be ruled-out, likelihood of sexual

transmission from partners with low level of Zika virus RNA in semen remains to be defined as the relationship between the viral load of Zika virus RNA in semen and infective virus in genital fluids remains unknown. Isolation of replicative Zika virus particles in semen is reported in only two patients – at day 22 and at day 24 post symptoms – currently supporting Zika virus infectiousness in semen in the early aftermath of acute phase of infection [78,79]. Systematic investigation of infectiousness of a patient with long term shedding of Zika virus RNA is warranted through further viral isolation studies.

Limited data about the presence of viable virus, viral load or kinetics in saliva are available through case reports. Hence, the effective role of saliva for Zika transmission cannot be established and the risk of transmission via saliva cannot currently be assessed.

There are limited case reports of Zika virus detections in oral and genital secretions do not allow for inferring the timing of the presence of viable Zika virus among the population of Zika virus cases. Standardised data from longitudinal cohorts on the frequency of presence and duration of Zika virus in bodily fluids are urgently required to establish the risk of transmission at population level.

Risk of Zika virus transmission via substances of human origin

Zika virus RNA has been detected in blood, urine, saliva, semen, female genital secretions and breast milk [78,80-83] [77].

People with asymptomatic infections and those who are viraemic during the incubation period of Zika virus disease could potentially donate contaminated substances of human origin (SoHO) without their infections being recognised at the time of donation. The virus could also be transmitted by SoHO from donors after clinical recovery from Zika virus disease due to possible prolonged viraemia or a persistence of the virus in semen after viraemia has cleared. There are no data available on the survival of Zika virus in processed and stored SoHO.

One publication from Brazil describes two cases of likely Zika virus transmission by blood transfusion from one person who donated platelets by apheresis in January 2016 and reported two days later a febrile illness compatible with Zika virus infection [84]. This investigation provides some evidence that Zika virus can be transmitted through donated cells due to the confirmed presence of the virus in human blood and bodily fluids. Cases of Zika virus transmission through tissues and organs have not been reported, but this possibility cannot be excluded due to the confirmed presence of the virus in human blood and bodily fluids. Several reported cases of sexual transmission from males to their partners (see 'Risk of sexual transmission' below) strongly support a possibility of Zika transmission through donated sperm.

There are no documented transmissions of the virus via saliva, urine or breastfeeding. The presence of Zika virus in placenta and amniotic fluid of infected pregnant woman/foetus implies a possibility of Zika virus transmission through donated gestational tissues and cord blood [85,86].

Zika virus RNA has been detected in brain, liver, spleen, kidney, lung and heart samples from a fatal case in an adult with underlying chronic health conditions [87]. Yet, it is unknown whether organs, infected with Zika virus, could transmit a disease.

The limited set of data indicates that there is a potential risk of Zika virus transmission through SoHO that may cause serious consequences to the health of recipients. However, a scarcity of reported cases of donor-derived Zika virus infection precludes a more accurate risk assessment. The evidence of association between Zika virus infection and congenital malformations and GBS justifies preventive measures to reduce the risk of transmission via SoHO supply [88].

Considering the recent scientific and epidemiological information, the US Food and Drug Administration (FDA) issued on 26 August 2016 a revised guidance recommending universal testing of donated whole blood and blood components for Zika virus in the USA and its territories. This is a change from the previous guidance which recommended testing for Zika virus only in areas with active Zika virus transmission [89,90].

References

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