



Zika virus infection: guidance for primary care

Introduction

There is currently an ongoing outbreak of Zika virus infections in South and Central America and the Caribbean, and increasing evidence that infection in pregnancy may be associated with fetal microcephaly and other central nervous system abnormalities. Zika virus infection has also been linked with Guillain-Barre syndrome. Symptomatic Zika virus infection is typically mild and short-lived in most individuals, but particular attention is required for travel-associated risks in women who are pregnant or who are planning a pregnancy.

This guidance summarises key advice for those working in primary care, since they may be consulted by patients, including pregnant women, who are travelling to or returning from countries that are part of this outbreak (ie those countries with active Zika transmission).

Scope

This guidance is intended for primary care clinicians in England. It has been produced by PHE in conjunction with the Royal College of General Practitioners and the British Medical Association.

Key messages

General travel advice for patients

Those working in primary care may be consulted by patients travelling to or returning from areas with active Zika transmission. Pregnant women may also request letters to justify suspension of travel to affected areas on medical grounds. In such cases, those working in primary care can refer to updated National Travel Health Network and Centre (NaTHNaC) advice, which has been produced in response to the ongoing Zika outbreak in South and Central America and the Caribbean (<http://travelhealthpro.org.uk/zika-virus-update-and-advice-for-travellers-including-pregnant-women/>).

- **All travellers** to areas with active Zika virus transmission should practise mosquito bite avoidance measures, both during daytime and night time hours (but especially during mid-morning and late afternoon to dusk, when the mosquito that transmits Zika virus is most active).

- **Pregnant women planning to travel** should consider avoiding travel to areas with active Zika transmission. If travel is unavoidable, or they live in areas where active Zika transmission is reported, they should take scrupulous insect bite avoidance measures, both during daytime and night time hours (but especially during mid-morning and late afternoon to dusk, when the mosquito that transmits Zika virus is most active).
- **All pregnant women who have recently travelled** to a country where active Zika transmission is reported should notify their primary care clinician, obstetrician or midwife.
- An application of **insect repellent containing 50% DEET** (N,N-diethyl-m-toluamide) will repel mosquitoes for approximately 12 hours. Repellents containing 50% DEET can be used by pregnant women, but higher concentrations should not be used. When both sunscreen and DEET are required, DEET should be applied *after* the sunscreen. Sunscreen with a 30 to 50 SPF rating should be applied to compensate for DEET-induced reduction in SPF. The use of DEET is not recommended for infants less than two months of age.

Preventing potential sexual transmission of Zika virus

The risk of sexual transmission of Zika virus is thought to be very low, but sexual transmission has been reported. If a female partner is at risk of getting pregnant, or is already pregnant, condom use is advised for a male partner arriving from an affected area for the following durations:

- 28 days after his return from a Zika virus transmission area *if* he has not had any symptoms compatible with Zika virus infection
- six months following recovery *if* a clinical illness compatible with Zika virus infection or laboratory-confirmed Zika virus infection was reported

This is a precautionary approach and may be revised as more information becomes available. 28 days represents an estimated 14 day incubation period plus an estimated 14 day period of viraemia.

Recommendations for women planning pregnancy who have travelled to or arrived from an area with active Zika virus transmission

After a woman leaves an area with active Zika virus transmission, it is recommended that she should not try to conceive for 28 days (this covers an estimated 14 day incubation period plus an estimated 14 day period of viraemia).

Recommendations for pregnant women who have travelled to or arrived from an area with active Zika virus transmission

Knowledge about Zika virus infection and pregnancy is limited and continues to evolve. Recommendations are based on current information and are likely to be updated periodically to reflect emerging evidence.

- A pregnant woman with a history of travel during pregnancy to an area with active Zika virus transmission who reports clinical illness that raises suspicion of Zika virus disease, during or within two weeks of travel, AND who is currently symptomatic, should be tested for Zika virus infection and have a baseline fetal ultrasound, via referral to a local antenatal ultrasound service.
- Symptoms of Zika virus infection may be mild and include a combination of the following: fever; joint pain; rash; conjunctivitis; headache; muscle pain; eye pain.
- Zika virus can be detected by PCR testing of blood during a seven day period following onset of typical symptoms. The following samples should be taken: **clotted 'red top' (plain) or 'yellow top' (serum separator) blood, EDTA 'purple top' blood, and a small volume of urine without preservative.** These should be sent to the local microbiology/virology laboratory. **Complete a standard, local laboratory request form, but also complete a Rare and Imported Pathogens Laboratory (RIPL) request form** (<https://www.gov.uk/government/publications/rare-and-imported-pathogens-testing-form-to-submit-sample>) and submit both forms with the samples. The RIPL form must clearly state both the travel history (ie which countries visited and the dates of the outward and return journeys) and the clinical details (ie the patient's symptoms, the date of illness onset, and details about the pregnancy); this is so that the appropriate investigations can be performed and results interpreted correctly, after the local laboratory has forwarded the sample to RIPL.
- All other pregnant women who have travelled to an area with active Zika virus transmission during pregnancy should be offered a baseline ultrasound scan (refer to 'further information' section, below)
- Practitioners should consider other causes of rash in pregnancy in the differential diagnosis, as appropriate (further guidance is available from PHE: <http://www.gov.uk/government/publications/viral-rash-in-pregnancy>)

For further information see: **interim algorithm for assessing pregnant women with a history of travel during pregnancy to areas with active Zika virus (ZIKV) transmission**, produced in association with the Royal College of Obstetricians and Gynaecologists, the Royal College of Midwives and Health Protection Scotland:

<http://www.gov.uk/government/publications/zika-virus-interim-algorithm-for-assessing-pregnant-women-with-a-history-of-travel> and **Interim clinical guidelines on Zika Virus Infection and Pregnancy** <https://www.rcog.org.uk/globalassets/documents/news/zika-virus-interim-guidelines.pdf>

Recommendations for all other (non-pregnant) patients who have travelled to or arrived from an area with active Zika virus transmission

Symptomatic Zika virus infection is typically a mild and self-limiting illness. In non-pregnant individuals who present **with active symptoms** suggestive of acute Zika virus infection (these may include a combination of the following: fever; joint pain; rash; conjunctivitis; headache; muscle pain; eye pain), it is recommended that the following samples are obtained: **clotted 'red top' (plain) or 'yellow top' (serum separator) blood and an EDTA 'purple top' blood** (urine only required for pregnant women). The samples should be sent to the local diagnostic microbiology/virology laboratory. **Complete a standard, local laboratory request form and also complete a Rare and Imported Pathogens Laboratory (RIPL) request form** (<https://www.gov.uk/government/publications/rare-and-imported-pathogens-testing-form-to-submit-sample>) and submit both forms with the samples. The RIPL form must clearly state both the travel history (ie which countries visited and the dates of the outward and return journeys) and the clinical details (ie the patient's symptoms and the date of illness onset); this is so that the appropriate investigations can be performed and results interpreted correctly, after the local laboratory has forwarded the sample to RIPL. Clinicians should also consider other travel-associated infections including dengue and chikungunya virus infections, common infections, and non-infectious diseases in the differential diagnosis.

Non-pregnant patients who were diagnosed elsewhere and who have since recovered from their infection do not require further investigation and can be reassured that Zika virus infection is typically short-lived and self-resolving. For male travellers diagnosed elsewhere, refer to advice about preventing potential sexual transmission (see above). If there are concerns about persistent symptoms beyond the expected recovery time for Zika virus infection, then discussion with a local infection specialist is recommended.

Queries about donating blood, tissues or semen

Individuals who have been diagnosed with Zika virus infection, or who report having experienced symptoms consistent with Zika virus infection, should not donate blood, tissues, or semen for six months following resolution of symptoms. All other individuals arriving from an area with active Zika virus transmission should not donate blood, tissues or semen for 28 days. Further information is available from the Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee: <http://www.transfusionguidelines.org/dsg/gdri/latest-updates>

Notifications and specialist advice

Zika virus infection is not a notifiable disease in England. Primary care clinicians do not need to inform Public Health England about suspected cases (unless seeking diagnostic testing), or cases diagnosed overseas. Additional clinical advice and information about diagnostic

testing can be obtained by contacting the Imported Fever Service (<https://www.gov.uk/guidance/imported-fever-service-ifs>).

Background information on Zika virus

Zika virus is part of the flavivirus family, which includes dengue virus and yellow fever virus. Zika virus infection is spread by the *Aedes aegypti* mosquito, which occurs predominantly in tropical and sub-tropical areas. This mosquito is most active during the day, especially during mid-morning and later afternoon to dusk, but it can also bite at night in well-lit areas. *Aedes aegypti* mosquitoes, and other proposed mosquito species that may be capable of transmitting Zika virus, are not found in the UK.

Zika virus was first identified in Uganda in 1947. Since 2007, an increasing number of Zika virus infection outbreaks have occurred across multiple regions, including South East Asia, Polynesia and other Pacific regions, certain Caribbean islands and most recently in over twenty countries and territories in the Americas. Locally-acquired transmission has also been reported by Cape Verde.

It is estimated that the majority of those infected with Zika virus do not develop symptoms or have subclinical illness. The estimated incubation period is up to 14 days. Infected individuals who do develop symptoms typically have a mild illness that is similar to uncomplicated dengue virus infection: a mild illness lasting two to seven days, consisting of a combination of fever, joint pain, rash, conjunctivitis/red eyes, headache, muscle pain and eye pain. No specific vaccine or specific anti-viral treatment is available for Zika virus infection, and most symptomatic cases are short-lived and will resolve spontaneously (see comments about infection in pregnancy, below).

A list of countries that have reported cases is available on the PHE website: <http://www.gov.uk/guidance/zika-virus>

Association of Zika virus infection with microcephaly and congenital malformations

In October 2015, the Brazilian Ministry of Health reported an unusual increase in the number of babies born with microcephaly and declared a public health emergency in November 2015. As of 30 January 2016, 4,783 suspected cases of microcephaly including 76 deaths have been reported across 21 states in Brazil. This exceeds significantly the expected annual incidence of microcephaly in Brazil (reported to be 150-200 cases per year, although this may be an underestimate).

It has been proposed that the marked increase in microcephaly cases in Brazil is *associated* with the ongoing Zika virus outbreak. There is increasing evidence to support this hypothesis, including detection of Zika virus in amniotic fluid, placenta or fetal tissue from babies of mothers suspected of having symptomatic Zika virus illness during pregnancy. In addition, an increase in central nervous system malformations in fetuses and new-borns was observed following a Zika virus outbreak in Polynesia in 2013-2014. However, *causation* has

not been demonstrated to date and investigational studies are ongoing. Additionally, an increase in cases of microcephaly and/or congenital malformations has yet to be reported from other countries where Zika virus outbreaks have occurred. If Zika virus infection does cause congenital malformations or microcephaly, then it is likely that the greatest risk is associated with infection acquired in early pregnancy, based on experience of other viral infections in pregnancy.

Potential association of Zika virus infection with Guillain-Barré Syndrome

A number of countries, including Brazil, French Polynesia and El Salvador have also reported cases of Guillain-Barré Syndrome in individuals with a history of symptoms consistent with Zika virus infection.

Risk of sexual transmission

It has been reported that Zika virus has been detected in semen from three infected men, and two cases of male-to-female sexual transmission has been reported. While it is not possible at the current time to quantify the risk of sexual transmission of Zika virus, the risk is considered to be very low.

Additional information about Zika virus for health professionals is available on the PHE website: <http://www.gov.uk/guidance/zika-virus>

Advice for patients and members of the public is available on the NHS Choices website: <http://www.nhs.uk/news/2016/01January/Pages/Zika-virus-your-questions-answered.aspx>

European Centre for Disease Prevention and Control (ECDC) list of countries with local Zika virus transmission: http://ecdc.europa.eu/en/healthtopics/zika_virus_infection/zika-outbreak/Pages/Zika-countries-with-transmission.aspx

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