Since 2007, Zika virus infections have been reported in Africa, Asia and the Pacific Islands. From 2015, spread of the infection to the Americas led to large outbreaks across the region.\(^1\) The majority of people infected with Zika virus have no symptoms. For those with symptoms, Zika virus tends to cause a mild, short-lived (2 to 7 days) illness.\(^2\)

In November 2015, the Brazilian Ministry of Health declared a public health emergency following reports of a 20-fold increase in the number of babies born with microcephaly, suggesting a potential link with the ongoing outbreak of Zika virus infection in the region. On 1\(^{st}\) February 2016, it was declared that the recent cluster of microcephaly cases and other neurological disorders reported in Brazil constitutes a Public Health Emergency of International Concern (PHEIC). Based on a systematic review of the literature up to 30 May 2016, WHO has concluded that Zika virus infection during pregnancy is a cause of congenital brain abnormalities, including microcephaly; and that Zika virus is a trigger of Guillain-Barré syndrome.\(^3\)

On 18th November 2016, WHO declared the end of the PHEIC, although they stated that Zika virus and its associated consequences remained a significant and enduring public health challenge.\(^4\)

**Epidemiology**

The Zika virus was first discovered in a Rhesus monkey in Uganda in 1947 and in humans a few years later.\(^1\) The first outbreak reported outside of Africa and Asia occurred in Micronesia in 2007. This was followed by an outbreak of the same strain in French Polynesia in 2013; since then there have been outbreaks in other parts of the Pacific.\(^1\)

Brazil confirmed its first case of local Zika virus transmission in May 2015. Subsequently the virus spread rapidly, particularly in South America, Central America, and the Caribbean.\(^1\)
The rapid spread in 2015 and 2016 was mainly due to two factors: 5
1. An immunologically naïve population.
2. The distribution of Aedes aegypti mosquitoes, the primary vector for transmission.

Countries with current or past Zika virus transmission have been given one of three risk ratings (low, moderate, or high), based on the reporting of Zika cases and the risk to UK travellers. The greatest likelihood of acquiring Zika virus infection is from travelling to a country with moderate or high risk. A list of countries and their Zika virus risk can be found on Public Health England’s (PHE) website (https://www.gov.uk/guidance/zika-virus-country-specific-risk).

The Aedes aegypti mosquito is not present in the UK and is unlikely to establish in the near future as the UK temperature is not consistently high enough for it to breed. However, imported infections have been detected in travellers returning to the UK; further information is available on the PHE website (https://www.gov.uk/guidance/zika-virus).1

Transmission

Zika virus is transmitted by the bite of an infected female Aedes mosquito, most commonly Aedes aegypti. Other species of Aedes mosquito may also have the potential to transmit this virus.6 After an infected mosquito bites a human, the first symptoms can develop in 3 to 12 days but it can be shorter or longer in some people. Almost all cases of Zika virus are acquired via mosquito bites. However, a small number of cases of sexual transmission have been reported. Most cases have been male-to-female, but male-to-male and female to male transmission has occurred27. Potential routes of transmission include vaginal, anal, oral sex and the sharing of sex toys.28 Case reports suggest that sexual transmission can occur shortly before, during, and after symptoms but also when the infection causes no symptoms.7-9 The virus has been shown to be present in semen, vaginal secretions and menstrual blood.9-11,27,29 The virus persists longer in semen than in the female genital tract, but the viral RNA detected is not necessarily infectious.11 The risk of sexual transmission of Zika virus is considered to be low.
Zika virus can be transmitted by blood transfusion. In the UK, standard precautions for ensuring safe blood donations and transfusions are in place to prevent this (http://www.transfusionguidelines.org/document-library/change-notifications/change-notifications-issued-in-2016).

Cases of maternal fetal transmission have been confirmed. Whilst viable virus has been detected in breast milk there is currently no evidence that Zika virus can be transmitted to babies through breast milk and the advice to mothers to breastfeed remains unchanged.

**Symptoms**

The majority of people infected with Zika virus have no symptoms. For those with symptoms, it tends to cause a mild, short-lived (2 to 7 days) illness. Signs and symptoms suggestive of Zika virus infection may include a combination of the following: rash; itching/pruritus; fever; headache; arthralgia/arthritis; myalgia; conjunctivitis; lower back pain; retro-orbital pain. There is no evidence that pregnant women are more vulnerable to acquiring Zika virus infection or that this infection causes a more serious illness in pregnant women.

The symptoms of Zika virus infection may be similar to those of dengue fever (caused by a related flavivirus) and chikungunya (an alphavirus). These two infections are also transmitted by the *Aedes aegypti* mosquito and so are found in the same geographical areas. Differential diagnosis therefore requires laboratory testing (see Diagnosis below).

Serious complications from Zika virus infection are rare. WHO has concluded that Zika virus infection during pregnancy is a cause of congenital brain abnormalities, including microcephaly; and that Zika virus is a trigger of Guillain-Barré syndrome.

**Congenital Zika Virus Syndrome**

Congenital Zika Virus Syndrome is used to refer to the range of manifestations, in addition to congenital microcephaly, that have been reported following exposure to Zika virus in utero (see Table 1).
The risk of birth defects appears low compared with other viral infections such as CMV and rubella in some studies; however the incidence of Zika virus infection can be very high during outbreaks. There have been differing reports of the rates of adverse outcomes in offspring of women who test positive for Zika virus during pregnancy. A Brazilian study which followed women who presented with a rash during pregnancy found adverse outcomes for live births in 46% of Zika virus positive women versus 11.5% for Zika virus-negative women. A similar US study followed women with laboratory evidence of possible recent Zika virus infection and found adverse outcomes of 6% in fetuses or infants from symptomatic or asymptomatic mothers. Although the studies varied in terms of inclusion criteria, it is not clear why these differences exist.

The gestation at which the infection is acquired may be important. A fetus infected in early gestation is more likely to be affected compared to infection later in pregnancy (Cauchemez et al Lancet 2016, Johansson et al NEJM 2016). In one study of 35 cases of microcephaly in Brazil, 26 (74%) of the women reported having had a rash, 21 in the first trimester, 5 in the second trimester and none in the third trimester. However a single more recent report from Brazil also found CNS abnormalities in fetuses infected as late as 27 weeks of gestation.

Table 1: Fetal abnormalities reported in pregnancies complicated with Zika virus infection.\textsuperscript{14,23,25}

<table>
<thead>
<tr>
<th>Cranial abnormalities</th>
<th>Extra-cranial abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microcephaly</td>
<td>Fetal growth restriction</td>
</tr>
<tr>
<td>Cerebral and/or ocular calcifications</td>
<td>Oligohydramnios</td>
</tr>
<tr>
<td>Ventriculomegaly</td>
<td>Talipes</td>
</tr>
<tr>
<td>Periventricular cysts</td>
<td></td>
</tr>
<tr>
<td>Callosal abnormalities</td>
<td></td>
</tr>
<tr>
<td>Microphthalmia</td>
<td></td>
</tr>
<tr>
<td>Cerebellar atrophy (transverse diameter &lt;5th percentile)</td>
<td></td>
</tr>
<tr>
<td>Vermian agenesis</td>
<td></td>
</tr>
<tr>
<td>Blake’s cyst</td>
<td></td>
</tr>
<tr>
<td>Mega cisterna magna (&gt;95th percentile)</td>
<td></td>
</tr>
<tr>
<td>Choroid plexus cyst</td>
<td></td>
</tr>
<tr>
<td>Brain atrophy leading to micrencephaly (abnormally small brain)</td>
<td></td>
</tr>
<tr>
<td>Cortical and white matter abnormalities (e.g. agyria)</td>
<td></td>
</tr>
</tbody>
</table>
Prevention

There is currently no vaccine or drug available to prevent ZIKV infection. The *Aedes aegypti* mosquito, the primary vector for Zika virus, is active predominantly during daylight hours; bites are most common during mid-morning and late afternoon to dusk, when the mosquito is most active. This is in contrast to the *Anopheles* mosquito which transmits malaria and which is more active by night. Travellers to areas with moderate or high risk of Zika virus transmission should take all possible measures to minimise the chances of mosquito bites. This includes wearing light-coloured, loose-fitting clothes that cover as much exposed skin as possible, for example long trousers and long sleeves. Because the *Aedes* mosquito is active during daylight hours, it is important that travellers to these areas cover up during the daytime as much as possible. Clothing can be treated with an insecticide (e.g. permethrin) which kills insects, including mosquitoes, on contact.22

N, N-diethyl meta toluamide (DEET) based repellents are the most effective insect repellents widely available, and have been in use for over 50 years. Preparations with concentrations of DEET up to 50% are commonly available and are safe in pregnant and breastfeeding women (and in infants and children over the age of 2 months).22,26 Care should be taken to ensure that insect repellents are not ingested, and that they do not come in contact with the eyes or mouth.

Insect repellents should be used as per the manufacturer’s instructions and re-applied regularly, particularly after swimming and in hot humid conditions when they may be removed by perspiration. When both sunscreen and insect repellents are required, the insect repellent should be applied over the sunscreen. DEET based repellents can reduce the sun protection factor (SPF) of sunscreen so pregnant women should consider wearing a higher factor sun cream (SPF 30-50) when also using DEET based repellents.22

The following cannot be recommended as insect repellents: citronella oil-based repellents (these have a very short duration of action); vitamin B12 complex; vitamin B1; tea tree oil.26

Travellers staying in accommodation without screening should sleep under a mosquito net, particularly in malaria risk areas. Those sleeping or resting during the
day in an area with Zika virus should sleep/rest under a mosquito net (if in accommodation without screening). Ideally, nets should be impregnated with permethrin or another contact insecticide. Retreatment after six months of use is necessary. A Leaflet entitled “Mosquito Bite Avoidance for Travellers” is available on the PHE Website (https://www.gov.uk/government/publications/mosquito-bite-avoidance-for-travellers).

**Travel Advice for Pregnant Women and Couples Planning Pregnancy**

In the UK, the National Travel Health Network and Centre (NaTHNaC), and Health Protection Scotland (via TRAVAX and fitfortravel) provide advice for pregnant women regarding potential travel to areas with high or moderate risk of Zika virus transmission. For further information see: NaTHNaC (http://travelhealthpro.org.uk/zika-virus-update-and-advice-for-pregnant-women/), TRAVAX (www.travax.nhs.uk) and fitfortravel (www.fitfortravel.nhs.uk).

It is recommended that:

- Pregnant women should postpone non-essential travel to areas with high risk of Zika virus transmission until after pregnancy.
- Pregnant women should consider postponing non-essential travel to areas with moderate risk of Zika virus transmission until after pregnancy.

Pregnant women who must travel (or choose to travel) to an area with high or moderate risk of Zika virus transmission should take all necessary precautions to minimise the chances of a mosquito bite, as described above. Pregnant women recently returned to the UK from areas with high or moderate risk of Zika virus transmission should inform their obstetrician, midwife or GP that they may have been exposed to the virus so that they can be monitored and/or tested.

It is recommended that couples planning pregnancy should check the Zika risk for their destination before travel and consider any travel advisories. Couples planning pregnancy who are travelling to an area with high or moderate risk of Zika virus transmission should delay conception to reduce the risk of the developing fetus being exposed to Zika virus, by consistently using effective contraception and barrier methods during and after travel. These measures should be followed for 8 weeks after return (or the last possible Zika virus exposure) if only the female partner
travelled. If both partners, or just the male partner, travelled the measures should be followed for 6 months after return or the last possible Zika virus exposure.

**Diagnosis**

The diagnosis of Zika virus infection should be considered among individuals who experience symptoms suggestive of acute Zika virus infection within 2 weeks of leaving an area with high or moderate risk of Zika virus transmission OR within 2 weeks of sexual contact with a male sexual partner who has recently travelled to an area with high or moderate risk of Zika virus transmission. Healthcare providers should ask all pregnant women and their partners about recent and planned travel.

Diagnostic laboratory testing is available from PHE’s Rare and Imported Pathogens Laboratory (RIPL), a specialist centre for advice and diagnosis for a wide range of unusual viral and bacterial infections including Zika virus. The recommended sample types for testing will depend on whether the patient has current symptoms or previous symptoms that have now resolved. Patients presenting to their healthcare provider with current or previous symptoms of Zika virus that began within 2 weeks of return to the UK, can be tested. Clinicians should refer to PHE’s sample testing advice webpage for information on sample types required and the tests available for different patient groups. Sample testing advice will be regularly reviewed and updated accordingly. [https://www.gov.uk/guidance/zika-virus-sample-testing-advice](https://www.gov.uk/guidance/zika-virus-sample-testing-advice)

Zika virus PCR can be performed on amniotic fluid although it is currently not known how sensitive this test is for congenital infection or the likelihood of an infected fetus being affected, i.e. subsequently developing a fetal abnormality.

If a health professional suspects Zika virus infection, advice can be sought from their local Infectious Disease, Microbiology or Virology Consultant in the first instance. In the UK, samples for testing for Zika virus should be sent to RIPL, accompanied by the appropriate RIPL request form clearly stating symptoms, date of symptom onset, areas visited, dates of travel and the stage of pregnancy (weeks of gestation).
For more information regarding testing, please refer to: https://www.gov.uk/guidance/zika-virus-sample-testing-advice. This web page details exactly which samples to send on which patients and which RIPL request form to use.

Zika virus testing is not available for individuals who do not have symptoms consistent with Zika virus infection.

**Treatment**

There is no specific antiviral treatment available. However, as Zika virus infection is usually mild and short-lived, no specific treatment is required. Supportive nursing care and relief of symptoms are the standard treatment. If symptoms are troublesome, an individual should be advised to get plenty of rest, drink adequate fluids and manage pain and fever with regular paracetamol and other cooling measures. In the unlikely event that symptoms become more severe, particularly if pregnant, they should seek medical advice.

**Recommendations for pregnant women and those planning pregnancy**


The following four scenarios outline the appropriate management for women PLANNING pregnancy, pregnant women with CURRENT symptoms, PREVIOUS symptoms or NO symptoms at all.

**Couples planning pregnancy:**

It is recommended that women should avoid becoming pregnant while travelling in an area with high or moderate risk of Zika virus transmission.

The Faculty of Sexual and Reproductive Healthcare’s (FSRH) advice is that effective contraception should commence in advance of travel to an area with high or
moderate Zika virus transmission. The FSRH’s statement on the different contraceptive methods available to women can be found here: https://www.fsrh.org/documents/contraception-advice-for-women-and-the-female-partners-of-men/.

If a couple are planning pregnancy, consistent use of effective contraception is advised to prevent pregnancy and barrier methods (e.g. condom use) are advised during vaginal, anal and oral sex to reduce the risk of sexual transmission which could result in a developing fetus being exposed to Zika virus. These measures should be followed while travelling and for:

- six months after return from an area with moderate or high risk of Zika virus transmission, or last possible Zika virus exposure, if both partners travelled
- six months after return from an area with moderate or high risk of Zika virus transmission, or last possible Zika virus exposure, if just the male partner travelled
- eight weeks after return from an area with moderate or high risk of Zika virus transmission, or last possible Zika virus exposure if only the female partner travelled

If a woman develops symptoms compatible with Zika infection on her return to the UK, it is recommended that she avoids becoming pregnant for 8 weeks following recovery.

**Pregnant women whose partner has been to an area with high or moderate risk of Zika virus transmission:**

Almost all cases of Zika virus infection are acquired via mosquito bites. However a small number of cases of sexual transmission of Zika virus have been reported. The risk of sexual transmission of Zika virus is thought to be low.

If a female partner is pregnant, condom use is advised for a male traveller during vaginal, anal and oral sex for the duration of the pregnancy to reduce the risk of sexual transmission.

Note that the testing of male returning travellers who had previous Zika-like symptoms and whose partners are currently pregnant should be discussed individually with a local Infection specialist. Please refer to the Zika virus sample
testing advice web page which will be kept updated with test availability (https://www.gov.uk/guidance/zika-virus-sample-testing-advice).

**Pregnant women reporting CURRENT or PREVIOUS symptoms suggestive of Zika virus disease:**
Healthcare providers should regularly ask all pregnant women about their own and their partners’ recent travel. Pregnant women with a history of travel to an area with high or moderate risk of Zika virus transmission and who have or have had symptoms consistent with Zika virus disease during or within two weeks of travel OR within 2 weeks of sexual contact with a male partner who has recently travelled to an area with high or moderate risk of Zika virus transmission (regardless of her own travel history due to the possibility of sexual transmission) should be tested for Zika virus infection by submitting appropriate samples to RIPL (https://www.gov.uk/guidance/zika-virus-sample-testing-advice).

If they are significantly unwell, and particularly if they require hospitalisation, other travel associated infections, including malaria, must be considered. For pregnant women with a rash, clinicians should also consider other causes of rash in pregnancy (https://www.gov.uk/government/publications/viral-rash-in-pregnancy).

If laboratory testing shows evidence of Zika virus infection, the woman should receive a baseline fetal ultrasound, if this has not already been performed, and be referred to a fetal medicine service for further assessment.

**If Zika virus antibodies are NOT detected in a serum sample collected 4 or more weeks after the last possible travel-associated or sexual exposure, then recent Zika virus infection is highly unlikely.** Pregnant women with negative antibody results for such samples do not require extra fetal ultrasound follow-up, unless there are additional concerns

**Pregnant women who have visited a county with high or moderate risk of Zika virus transmission but had NO symptoms of Zika Virus:**
Healthcare providers should regularly ask all pregnant women about their own and their partners’ recent travel. Routine testing of asymptomatic women (those who remained asymptomatic while travelling and for two weeks after their return from areas with high or moderate risk of Zika virus transmission) is not available. However,
as many people with Zika virus do not have symptoms, baseline fetal ultrasound should be offered and repeated at 18-20 weeks and a repeat considered at 28-30 weeks in line with WHO guidance.32

**Any woman with possible exposure to Zika virus, presenting with fetal ultrasound findings consistent with microcephaly:**

Any woman in whom a small fetal head (Head Circumference more than 2 Standard Deviations below the mean for gestational age, i.e. below the 2.5th centile) or brain abnormality (such as intracranial calcifications) is diagnosed on ultrasound, and who has previously visited during pregnancy an area with risk of Zika virus transmission, should be referred to a maternal fetal medicine service for further assessment. Although the majority of babies with a Head Circumference more than 2 SD below the mean will be normal and will not have microcephaly, referral to a specialist fetal medicine service is recommended. Microcephaly is usually diagnosed when the baby’s Head Circumference is even smaller than this, and usually together with structural abnormalities of the brain that can be diagnosed with specialist imaging (Table 1). Women with a diagnosis of fetal microcephaly or intracranial calcifications but who have not travelled to an area with risk of Zika virus transmission during pregnancy do not need to be assessed for Zika virus infection.

If fetal microcephaly or brain abnormality, such as intracranial calcification (see table), is diagnosed, consideration should be given to performing an amniocentesis to test for the virus using RT-PCR. This decision should be taken only after careful counselling. Amniocentesis is associated with a small risk of miscarriage or preterm birth and in general should not be performed before 15 weeks of gestation. However, for the purpose of identifying Zika virus, amniocentesis should not be performed before 20 weeks of gestation as fetal urination is not well-established until then (and this is the source of the virus in the amniotic fluid). As discussed above, even if positive, it is not known how sensitive this test is for congenital infection, nor the likelihood of an infected fetus being affected. Nevertheless, if there is fetal abnormality on ultrasound and Zika virus PCR on amniocentesis is positive, then it is highly likely that the abnormality is Zika virus associated and that the outcome is likely to be poor. When brain abnormalities are identified on ultrasound scan, consideration should be given to performing fetal brain MRI which may detect further abnormalities that have not been detected on ultrasound. When a significant brain abnormality or microcephaly is confirmed in the presence of Zika virus infection, the
option of termination of pregnancy should be discussed with the woman, regardless of gestation.

**Perinatal outcome**

**Women with laboratory diagnosed Zika virus infection:**
For any woman with positive laboratory diagnosis, spontaneous abortion/stillbirth or anticipated TOP or livebirth should be discussed with a local Infection Specialist and then with RIPL before sending samples ([https://www.gov.uk/guidance/zika-virus-sample-testing-advice](https://www.gov.uk/guidance/zika-virus-sample-testing-advice)).


Surveillance for congenital anomalies potentially associated with Zika virus infection has been established in the UK. Further information is available on the PHE website [https://www.gov.uk/government/publications/zika-virus#surveillance-for-congenital-zika-syndrome](https://www.gov.uk/government/publications/zika-virus#surveillance-for-congenital-zika-syndrome).

**Pregnancy advice leaflet**
An advice leaflet for pregnant women who have travelled to areas with high or moderate risk of Zika transmission is available at: [https://www.gov.uk/government/publications/zika-virus-advice-for-women-returning-from-areas-with-active-zika-virus-transmission](https://www.gov.uk/government/publications/zika-virus-advice-for-women-returning-from-areas-with-active-zika-virus-transmission)

This new version of the guidelines takes into account the current epidemiology of Zika virus infection globally, changes to the Zika virus country specific risks, and revised guidance for travel and sexual transmission of Zika virus for pregnant women, their partners and couples planning pregnancy.

**References**


29. CDC, Morbidity and Mortality Weekly Report (MMWR) Suspected Female-to-Male Sexual Transmission of Zika Virus — New York City, July 15, 2016 / 65(28);716–717 http://www.cdc.gov/mmwr/volumes/65/wr/mm6528e2.htm

30. CDC, Update: Interim Guidance for Prevention of Sexual Transmission of Zika Virus — United States, July 2016 http://www.cdc.gov/mmwr/volumes/65/wr/mm6529e2.htm?s_cid=mm6529e2_e


This document was last updated on 24/07/2017