



## Zika virus congenital infection: Guidance for neonatologists and paediatricians

This guidance is intended for neonatologists and paediatricians in England. It has been produced by PHE and a Zika virus neonatal working group.

### Introduction and background information

Since 2007, Zika virus infections have been reported in the Americas, Africa, Asia and Oceania. Following a systematic review of the evidence up to 30 May 2016, WHO has concluded that Zika virus infection during pregnancy is a cause of congenital brain abnormalities, including microcephaly (also referred to as congenital Zika virus syndrome), and that Zika virus is a trigger of Guillain-Barré syndrome<sup>1</sup>.

Symptomatic Zika virus infection is typically mild and short-lived in most individuals, but particular attention is required for women who are pregnant or who are considering a pregnancy because of the risk to the developing fetus associated with Zika virus infection in pregnancy.

Almost all cases of Zika virus are acquired via mosquito bites; however, a small number of cases of sexual transmission have been reported.<sup>2</sup> Zika virus has been shown to be present in semen.<sup>3,4</sup> and vaginal secretions.<sup>5</sup> The virus persists longer in semen than in the female genital tract, but the viral RNA detected is not necessarily infectious.<sup>3,4</sup> The risk of sexual transmission of Zika virus is thought to be low. Therefore, if available, the travel history of both the mother and partner should be considered in the evaluation of a neonatal case.

Viable virus has been detected in breast milk and possible Zika virus infections have been identified in breastfeeding babies but Zika virus transmission through breast milk has not been confirmed.<sup>6</sup> Therefore, the benefits of breastfeeding are likely to outweigh the risks of Zika virus infection in infants.

Diagnostic laboratory testing is available from PHE's Rare and Imported Pathogens Laboratory (RIPL) Sample testing advice is regularly reviewed and updated accordingly:

[www.gov.uk/guidance/zika-virus-sample-testing-advice](http://www.gov.uk/guidance/zika-virus-sample-testing-advice)

## Zika virus and congenital Zika virus syndrome

Cases of maternal-fetal transmission of Zika virus have been confirmed<sup>7-10</sup> and a number of congenital abnormalities potentially associated with maternal Zika virus infection during pregnancy have been described<sup>9, 11-20</sup> (see Table 1).

**Table 1. Reported fetal and neonatal abnormalities potentially associated with Zika virus infection**

Imaging	On examination
Cerebral and cerebellar atrophy	Microcephaly
Cerebral calcifications	Craniofacial disproportion
Cortical and white matter abnormalities (eg agyria, pachygyria, lissencephaly)	Redundant scalp skin
Ventriculomegaly	Closed anterior fontanelle
Internal hydrocephalus	Exuberant external occipital protuberance
Periventricular cysts	Intrauterine growth restriction
Choroid plexus cyst	Contractures
Blakes's cyst	Talipes
Mega cisterna magna	Umbilical hernia
Vermian dys/agenesis	Hypertonia or spasticity
Callosal abnormalities	Hyperreflexia
Brain stem/spinal cord degeneration	Irritability
Ocular abnormalities (intraocular calcifications, cataracts, microphthalmia, macular alterations, optic nerve abnormalities)	Convulsions, tremors
	Hearing and visual abnormalities

Paediatricians should work closely with obstetric colleagues to identify confirmed and potentially infected infants born to parents who had travelled to areas with active Zika virus transmission. Guidance on the obstetric assessment of pregnant women with a history of travel during pregnancy can be found on the PHE website:

[www.gov.uk/government/publications/zika-virus-interim-algorithm-for-assessing-pregnant-women-with-a-history-of-travel](http://www.gov.uk/government/publications/zika-virus-interim-algorithm-for-assessing-pregnant-women-with-a-history-of-travel) Evidence of fetal infection should be sought as detailed below.

## Recommendations for the management of neonates of mothers with possible exposure to Zika virus during pregnancy or within 8 weeks before conception

Countries with current or past Zika virus transmission have been given 1 of 2 risk ratings (risk or very low risk) based on Zika virus epidemiology and risk to UK travellers. The greatest likelihood of acquiring Zika virus infection is in a country with risk, however the individual risk of infection may be lower especially if mosquito bite avoidance measures are followed:

[www.gov.uk/government/publications/mosquito-bite-avoidance-for-travellers](http://www.gov.uk/government/publications/mosquito-bite-avoidance-for-travellers)

A list of countries and their Zika virus risk can be found on the PHE website:  
[www.gov.uk/guidance/zika-virus-country-specific-risk](http://www.gov.uk/guidance/zika-virus-country-specific-risk)

Clinicians need to establish if the mother developed an illness compatible with Zika during pregnancy (including a combination of the following symptoms: rash; itching/pruritus; fever; headache; arthralgia/arthritis; myalgia; conjunctivitis; lower back pain; retro-orbital pain) and confirm if Zika virus testing and/or an antenatal USS has been done.

In cases where maternal Zika virus infection, with or without fetal abnormality, was diagnosed prenatally OR where fetal abnormalities were diagnosed prenatally, neonatologists and obstetricians should collaborate prior to delivery to agree a plan for collection of samples for Zika testing and other investigations at birth.

Clinical assessment should include:

- physical examination: check for lymphadenopathy, hepatosplenomegaly, dysmorphic features, rash or other skin abnormalities, perform a complete neurological examination
- measure: head circumference, length, weight, assessment of gestational age
- if septic, follow local sepsis guidelines & consider testing for Zika virus
- ensure screening for hearing has been completed before hospital discharge

Following live birth of:

A. a normal baby, but maternal Zika serology or PCR tests were positive

Or

B. a baby with abnormalities of mothers with possible exposure to Zika virus during pregnancy or within 8 weeks of conception (regardless of maternal Zika virus test results, or presence or absence of maternal symptoms consistent with Zika virus infection).

In the UK, samples for testing for Zika virus should be sent to RIPL. Cases MUST be discussed with RIPL (usually by the local Infection specialist) prior to sample submission.

Investigations at birth:

- histopathological examination of the placenta and umbilical cord
- check that placental tissue and umbilical cord tissue have been taken for Zika Virus PCR

Investigations at birth or within 48 hours of birth:

1. ascertain whether there is a prenatally agreed Zika virus testing plan. If so, collect the neonatal samples for Zika virus testing according to the prenatally agreed plan. Confirm with the relevant local Infection specialist that they are liaising with RIPL to arrange testing of all the appropriate maternal and neonatal samples.
2. there may not be a prenatally agreed Zika virus testing plan if a neonatal abnormality has been identified only on *postnatal* examination of a baby born to a mother who, despite potential exposure, has had no Zika virus testing during pregnancy. If so, the case should be discussed urgently with the local Infection specialist in order to ensure that the appropriate neonatal and maternal samples are obtained and sent to RIPL for Zika virus testing.
3. in a baby with abnormalities, collect samples for testing for syphilis, toxoplasma, rubella, cytomegalovirus and herpes simplex virus infections
4. collect samples for full blood count, clotting, urea & electrolytes, liver function tests, C-reactive protein
5. perform cranial ultrasound; if microcephaly or intracranial abnormalities are present, perform an MRI of the brain
6. perform ophthalmological evaluation, including examination of the retina. If abnormal, repeat at appropriate intervals (as per ophthalmologist's decision)
7. if indicated, refer for more targeted hearing screening as outpatient
8. consider other evaluations specific to the infant's clinical presentation
9. consider investigations for differential diagnosis of microcephaly (eg chromosomal, genetic, metabolic, environmental exposure to toxins, radiation)
10. consider consultation with paediatric geneticist, infectious disease specialist, neurologist, endocrinologist according to test results
11. if abnormalities are present, please complete the BPSU reporting card

Follow up of a baby with abnormalities where Zika virus cannot be excluded OR a normal baby with laboratory evidence of Zika virus infection:

- follow up at 3 months, then 3 monthly up to 12 months if clinically stable, or more frequently if symptomatic (eg seizures)
- follow up Zika virus testing as advised by RIPL (Note that a normal baby whose mother tested positive for Zika virus by PCR or serology is likely to test positive for Zika IgG because of placental transfer. Serological follow up will be required until loss of maternal antibody is observed)
- perform hearing test at 3 to 6 months if initially normal; refer to audiologist for further evaluation if abnormal
- perform ophthalmology review at 6 months if initially normal, liaise with ophthalmologist about further follow-up if abnormal
- discuss with local neurologist and radiologist on best imaging and frequency of intracranial imaging
- consider performing an EEG if clinically indicated

- arrange early referral to community paediatric team for neuro-developmental assessment and long-term support
- follow-up should be continued into childhood to identify and monitor long-term adverse sequelae

Follow up of a normal baby whose mother had symptoms compatible with Zika virus infection whilst travelling or within 2 weeks of return and no Zika antibody test was performed 4 weeks or more after last possible exposure to Zika virus:

- appropriate samples for diagnostic testing will be advised by RIPL on a case-by-case basis
- if maternal Zika virus infection cannot be excluded, review infant at 3 months of age
- if any issues become apparent, tailor follow-up accordingly
- if the baby remains well, refer to primary care/health visitor with advice to refer back to secondary care early if any concerns arise
- review at 12 months by a neonatologist or paediatrician
- further guidance will follow as more evidence becomes available

Follow up of a normal baby whose mother was symptomatic whilst travelling or within 2 weeks after return and maternal Zika antibody testing was negative 4 weeks or more after her last possible exposure to Zika virus OR whose mother was previously asymptomatic:

- record and inform primary care provider of maternal history
- provide routine care
- if concerns arise during routine investigations (eg hearing test), follow up accordingly

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