



Zika Virus Infection: Laboratory Investigation of Symptomatic Individuals with Relevant Travel History

Background

Zika virus infection is an emerging viral threat that is currently circulating most prominently in the Americas and the Caribbean, with over 30 countries currently affected.

There is strong evidence that infection with Zika virus is the cause of a serious birth condition called microcephaly. Zika virus infection has also been linked with Guillain-Barré syndrome.

Zika virus is primarily spread through the bite of the *Aedes* genus of mosquito that is largely tropical and subtropical in distribution. It has also been recognised that Zika virus disease can be transmitted sexually. Finally, Zika virus disease can be transmitted vertically, from a pregnant woman to her developing foetus.

This guidance describes the recommended patient profile for laboratory investigations of Zika virus infection, along with the appropriate laboratory tests and specimens required.

The HPSC website also provides the following Zika virus resources:

- [Clinical guidelines for health professionals on Zika virus infection and pregnancy](#)
- [Interim Clinical Guidance for Primary Care](#)
- Frequently asked questions for the [general public](#)
- Frequently asked questions for [pregnant women and women who are planning a pregnancy](#)
- A list of [countries](#) reporting local transmission of confirmed Zika virus infection

Symptoms

An estimated three out of four people infected with Zika virus do not have symptoms at all. In symptomatic patients, Zika virus generally causes a mild illness that lasts from 2 to 7 days. The incubation period is between 3 and 12 days. Serious complications from Zika virus infection are uncommon. The most common symptoms include:

- Itching/pruritis (very common)
- non-purulent conjunctivitis
- muscle or joint pains (quite common)
- headache (in about half of cases)
- mild fever (in only a minority of cases)
- Lower back pain
- Retro-orbital pain

Suitable testing profile:

Zika virus infection should be considered in:

- individuals who develop symptoms consistent with Zika virus infection within 10 days of returning from an area with active transmission of virus
- symptomatic individuals who have had unprotected sex with a recently* returned traveller from an area with active transmission of virus
- **pregnant women** with **acute onset** of symptoms **NOT** consistent with Zika virus infection but who are within **10 days of return** from an affected area and **IF** the symptoms are **not explained** by other common infectious causes (e.g. URTI, UTI).

Diagnostic testing for men or non-pregnant women who have **never experienced symptoms** suggestive of Zika virus infection do **not** require laboratory investigation.

Zika virus laboratory testing:

Zika virus has been detected in whole blood (also serum and plasma), urine, cerebrospinal fluid, amniotic fluid, semen, vaginal fluids and saliva. There is accumulating evidence that Zika virus is present in urine and semen for longer periods than in whole blood or saliva. [Table 1](#) details the recommended Zika virus tests in relation to the time elapsed since symptom onset and the specimen types required.

Nucleic acid testing:

Within 0-7 days of onset of symptoms, Zika virus infection can often be diagnosed by detecting Zika virus RNA in blood by performing nucleic acid testing (NAT).

Within 0-10 days of onset of symptoms, urine should also be collected for Zika virus RNA testing using NAT.

Serological testing

Serological testing within 0-7 days of symptom onset could result in a “false negative” result as the antibody response may not yet have developed. As Zika virus-specific IgM and IgG typically develop toward the end of the first week of illness, blood samples are recommended to be collected between seven days and 12 weeks post-symptom onset for Zika virus-specific IgM and IgG serological testing.

Blood samples collected 12 weeks or more post onset of symptoms are suitable only for Zika-specific IgG testing.

Samples taken after seven days post-symptom onset should also be tested for other flaviviruses (e.g. Dengue virus and Yellow Fever virus) to out rule cross reactivity between Zika and serological assays

* Within 6 months of return from an affected area

for other flaviviruses. Chikungunya serological testing will be performed based upon relevant travel history, as the clinical presentation is similar to that of Zika virus infection.

Table 1: Recommended Zika virus tests in relation to time elapsed since symptom onset

Time elapsed since symptom onset	Appropriate tests to order	Specimen type required
0-7 days	<ul style="list-style-type: none"> • Zika RNA NAT • Zika RNA NAT 	<ul style="list-style-type: none"> • Blood (EDTA tube) • Urine without preservative
8-10 days	<ul style="list-style-type: none"> • Zika RNA NAT • Zika serology –IgM, IgG 	<ul style="list-style-type: none"> • Urine without preservative • Clotted blood (plain tube or serum separator tube)
10 days-12 weeks	<ul style="list-style-type: none"> • Zika serology –IgM, IgG 	<ul style="list-style-type: none"> • Clotted blood (plain tube or serum separator tube)
>12 weeks	<ul style="list-style-type: none"> • Zika serology – IgG 	<ul style="list-style-type: none"> • Clotted blood (plain tube or serum separator tube)

Specimen collection

1. Specimens for Zika virus RNA nucleic acid testing (NAT) testing:
 - Blood (EDTA tube) collected from patients presenting within 0-7 days of symptom onset
 - Urine (without preservative) collected from patients presenting within 0-10 days of symptom onset
2. Serology (IgM/IgG detection):
 - Clotted blood (plain tube or serum separator tube) collected from patients presenting after 7 days of symptom onset. Wherever possible, paired specimens should be collected at least 2-3 weeks apart, ideally with the first serum specimen collected after 7 days of illness. Samples collected greater than 12 weeks after onset of symptoms should be tested for Zika IgG only.

Laboratory test request forms must clearly indicate the following:

- whether the patient is pregnant (including the number of weeks gestation)
- travel history (countries visited and the dates of the outward and return journeys)
- clinical details (patient's symptoms, date of symptom onset).

If in doubt about the eligibility or requirements for testing the NVRL can be contacted for further advice.