Zika Virus

Revision Dates

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Case Definition

Confirmed Case\(^{(A)}\)

Laboratory confirmation of infection with or without clinical illness\(^{(B)}\) AND at least one epidemiological linkage\(^{(C)}\) identified:

- Detection of Zika virus (ZIKV) nucleic acid (e.g., by RT-PCR) or isolation from an appropriate clinical specimen (e.g., blood, CSF, urine);

OR

- Positive ZIKV IgM antibody with or without ZIKV IgG seroconversion AND a positive (≥1:20) ZIKV Plaque Reduction Neutralization Test (PRNT) where the DENV PRNT is negative (refer to Table 1 for more information);

Probable Case

Laboratory evidence of infection AND at least one epidemiological linkage\(^{(C)}\) identified:

- Positive ZIKV IgM antibody with or without ZIKV IgG and PRNT for ZIKV or DENV was not tested (refer to Table 1 for more information).

\(^{(A)}\) Due to the cross-reactivity of flaviviruses, Zika serology needs to be interpreted in conjunction with dengue serology, when available.

\(^{(B)}\) Clinical illness: refer to Clinical Presentation.

\(^{(C)}\) Epidemiological linkage:

- Resides in or recent travel to an area with known ZIKV transmission (See CDC Yellow Book webpage on ZIKV), OR
- Sexual contact with a confirmed or probable case within the infection transmission risk window of ZIKV infection or person with recent travel to an area with known ZIKV transmission, OR
- Vertical transmission where the mother has history of travel or residence in an area where Zika virus vectors were present during pregnancy, OR
- Receipt of blood or blood products within 30 days of symptom onset, OR
- Organ or tissue transplant recipient within 30 days of symptom onset, OR
- Association in time and place with a confirmed or probable case, OR
- Likely vector exposure in an area with suitable seasonal and ecological conditions for potential local vector borne transmission.
Table 1: Zika and Dengue Lab Result Interpretation(1)
(Highlighted columns of the most important when reviewing results)

<table>
<thead>
<tr>
<th>NAT/PCR Testing</th>
<th>Zika Testing</th>
<th>Dengue Testing</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZIKV IgM</td>
<td>ZIKV IgG</td>
<td>ZIKV PRNT</td>
<td>DENV IgM</td>
</tr>
<tr>
<td><strong>Positive</strong></td>
<td>Any result</td>
<td>Any result</td>
<td>Any result</td>
</tr>
<tr>
<td><strong>Negative</strong></td>
<td>Positive</td>
<td>Any result</td>
<td>≥20 (Positive)</td>
</tr>
<tr>
<td><strong>Negative</strong></td>
<td>Positive</td>
<td>Any result</td>
<td>Not tested</td>
</tr>
<tr>
<td><strong>DENV</strong></td>
<td>Any result</td>
<td>Any result</td>
<td>Any result</td>
</tr>
<tr>
<td><strong>Positive</strong></td>
<td>Negative,</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td><strong>Negative</strong></td>
<td>Negative,</td>
<td>Not tested</td>
<td>Negative,</td>
</tr>
<tr>
<td><strong>Negative</strong></td>
<td></td>
<td>≥20 (Positive)</td>
<td></td>
</tr>
<tr>
<td><strong>Negative</strong></td>
<td>Any result</td>
<td>Any result</td>
<td>≥20 (Positive)</td>
</tr>
</tbody>
</table>

**NOTIFIABLE** – For information only to assist with case management and classification

<table>
<thead>
<tr>
<th>ZIKV IgM</th>
<th>ZIKV IgG</th>
<th>ZIKV PRNT</th>
<th>DENV IgM</th>
<th>DENV IgG</th>
<th>DENV PRNT</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive, Negative, Equivocal</td>
<td>Positive or Negative</td>
<td>Pending</td>
<td>Positive or Negative</td>
<td>Any result</td>
<td>Pending</td>
<td>SUSPECT CASE: zika or dengue, pending</td>
</tr>
<tr>
<td>Any result</td>
<td>Positive or Negative</td>
<td>Negative</td>
<td>Positive or Negative</td>
<td>Any result</td>
<td>Negative</td>
<td>NOT A CASE: No evidence of zika or dengue, however if a specimen was collected &lt;5 days after onset the PRNT results may be negative. Convalescent specimens are recommended in 14 days.</td>
</tr>
<tr>
<td>Equivocal, Negative or Not tested</td>
<td>Positive or Negative</td>
<td>≥20 (Positive)</td>
<td>Negative</td>
<td>Any result</td>
<td>Negative</td>
<td>NOT A CASE: Evidence of zika infection; likely remote infection &gt; 3months (Not an acute case)</td>
</tr>
<tr>
<td>Equivocal, Negative or Not tested</td>
<td>Positive or Negative</td>
<td>Negative</td>
<td>Negative or Not tested</td>
<td>Any result</td>
<td>≥20 (Positive)</td>
<td>NOT A CASE: Evidence of dengue infection; likely remote infection &gt; 3months (Not an acute case)</td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>PRNT Testing not indicated</td>
<td>Negative, Positive</td>
<td>PRNT Testing not indicated</td>
<td>Negative</td>
<td>NOT A CASE: No evidence of acute zika or dengue</td>
</tr>
</tbody>
</table>

(1) “Any result” includes “Not tested”. Applicable where ever this phrase is used in the table.
(2) For the purposes of lab result interpretation, a negative PRNT is any value less than 20.
(3) Equivocal, indeterminate and inconclusive ZIKV results are indicative of laboratory samples that could not be interpreted for various reasons (e.g., borderline positive or non-specific binding) in order to give a result of positive or negative. If clinically indicated, new specimens should be collected for these individuals. Applicable where ever this phrase is used in the table.
(4) Individuals tested >3 months after exposure will almost always test IgM negative. If clinically indicated (e.g., pregnancy) samples may be forwarded to NML for PRNT testing with incomplete serology.
Reporting Requirements

1. **Physicians, Health Practitioners and others**
   Physicians, health practitioners or others shall notify the Medical Officer of Health (MOH) (or designate) of the zone, of all confirmed and probable cases in the prescribed form by mail, fax or electronic transfer within 48 hours (two business days).

2. **Laboratories**
   All laboratories shall report all positive laboratory results by mail, fax or electronic transfer within 48 hours (two business days) to the MOH (or designate) of the zone and the Chief Medical Officer of Health (CMOH) (or designate).

3. **Alberta Health Services and First Nations Inuit Health Branch (FNIHB)**
   - The MOH (or designate) of the zone where the case currently resides shall forward the initial Notifiable Disease Report (NDR) of all confirmed and probable cases to the CMOH (or designate) within two weeks of notification and the final NDR (amendment) within four weeks of notification.
   - For out-of-province and out-of-country reports, the following information should be forwarded to the CMOH (or designate) by phone, fax or electronic transfer within 48 hours (two business days):
     - name,
     - date of birth,
     - out-of-province health care number,
     - out-of-province address and phone number,
     - positive laboratory report and
     - other relevant clinical/ epidemiological information.
Etiology
Zika virus (ZIKV) is a member of the *Flaviviridae* family.\(^2\)

Clinical Presentation
The majority of individuals infected with ZIKV will have no symptoms; however, approximately 20–25% will develop symptoms.\(^2\) Symptoms are usually mild and can include fever, rash, conjunctivitis, myalgia, arthralgia and headache lasting from 2 – 7 days.\(^3\) Most people recover without incident or hospitalization.

Complications of ZIKV include Guillain-Barré syndrome or other neurological manifestations such as acute myelitis, meningoencephalitis and acute disseminated encephalomyelitis.\(^4\) – \(^6\) ZIKV has been linked to microcephaly and other congenital anomalies in infants infected with ZIKV during pregnancy.\(^7\)

Reservoir
Non-human and human primates are likely the main reservoirs of the virus with anthropoontic (human-to-vector-to-human) transmission occurring during outbreaks.\(^8\) ZIKV virus is transmitted to humans primarily through the bite of an infected *Aedes* species mosquito (*Ae. aegypti* and *Ae. albopictus*). There is no significant evidence that the *Culex* species are able to transmit the virus.

Populations of *Aedes* (*aegypti* or *albopictus*) mosquitoes are not established in Canada at this time. The likelihood that *Aedes* mosquitoes will become established in Canada is considered very low as they are limited by the lack of environmental and climate suitability here.\(^2\)

Transmission
ZIKV is most commonly transmitted to humans by the bite of an infected mosquito.\(^9\) Other less common modes of transmission include:\(^10\) – \(^11\)
- sexual,
- vertical,
- blood and organ donation, and
- laboratory-acquired.

In addition, non-sexual person-to-person transmission has been reported in the setting of an immunocompromised contact.\(^12\)

Similar to other flaviviruses, ZIKV is susceptible to common disinfectants and various methods of inactivation, such as ultra-violet light and heat.\(^13\)

Incubation Period
The incubation period ranges from 3 – 12 days.\(^3\)

Period of Communicability
ZIKV is thought to be communicable, via blood (viremia) from 3 – 7 days after the onset of symptoms.\(^2\) However, ZIKV has been detected in urine 2 – 3 weeks after the onset of symptoms\(^14\), in vaginal fluid 11 days after the onset of symptoms\(^15\) and in semen up to 6 months after the onset of symptoms.\(^16\) – \(^18\)

In Canada, there is a very low risk of ZIKV transmission to mosquitoes from humans during the viremic period mainly because the mosquitoes that are capable of reproducing the virus are not endemic to Canada. For more information see Reservoir.
Host Susceptibility
Susceptibility is universal. Individuals with co-morbidities may be at increased risk for more serious ZIKV-associated complications (see Clinical Presentation). Fetuses are susceptible in utero via vertical transmission from an infected mother.

Incidence in Alberta
ZIKV is not endemic in Alberta and case are like to be acquired through international travel. ZIKA was first reported in Alberta in a female who had travelled to Thailand. Since December 2015, Alberta has seen additional cases related to the increase in global ZIKV disease incidence and international travel of Albertans. For more information on the occurrence of ZIKV worldwide refer to the CDC Yellow Book webpage on ZIKV.

Public Health Management

Diagnosis
PCR testing by ProvLab should be performed on plasma (blood in EDTA) collected during the first two weeks after symptom onset. ZIKV has been detected by PCR in urine for 2 – 3 weeks and in semen up to 6 months.

Antibody detection should be performed on whole blood in SST tubes. IgM antibodies are usually detectable 6 – 7 days after the onset of illness and generally indicate a current or recent infection. Flavivirus antibodies can cross-react in the existing serological tests, especially those for IgM, resulting in some uncertainty in IgM results between ZIKV and DENV. Currently the two most frequently acquired flaviviruses in returning travelers are ZIKV and DENV, and they do show cross-reactivity. Because of these cross-reacting antibodies with other flaviviruses, especially ZIKV at this time, cases with positive (or equivocal) serology are sent to the National Microbiology Laboratory (NML) in Winnipeg to be confirmed using (PRNT).

A serum specimen should be collected for acute phase ZIKV IgM antibody testing at least 5 days and up to 12 weeks after the onset of clinical illness. A convalescent phase serum should be obtained at least 2 weeks after the first sample has been collected. As is the case for DENV virus, ZIKV IgM antibodies will likely not be detected beyond 3 months after exposure.

PRNT is not always able to provide a definitive determination of the specific flavivirus causing a recent infection, especially if the person has a prior history of flavivirus infection (e.g., previous DENV or West Nile virus), is immunized against a flavivirus (e.g., yellow fever or Japanese encephalitis) or is currently co-infected with another flavivirus. These cases may have test results such as DENV IgM negative with positive PRNT results or positive PRNT results for both DENV and ZIKV, making it difficult to determine which virus is causing the illness (i.e., probable flavivirus).

(Due to the novelty of this virus and changing evidence, refer to the ProvLab website for the latest information regarding diagnosis and testing).
Key Investigation

- Confirm the diagnosis, if possible. Other arboviral diseases such as chikungunya, DENV, West Nile virus and rash illnesses such as measles, rubella, parvovirus, enterovirus, or febrile illnesses such as malaria should be ruled out.\(^{(22)}\)
- Determine where the case may have been exposed, taking into consideration the incubation period, reservoir, and mode of transmission, including a history of:\(^{(23)}\)
  - Recent travel to or residence in an area with known ZIKV transmission (See CDC Yellow Book webpage on ZIKV), OR
  - Sexual contact with a confirmed or probable case within the infection transmission risk window of ZIKV infection or person with recent travel to an area with known ZIKV transmission, OR
  - Vertical transmission where the mother has history of travel or residence in an area where Zika virus vectors were present during pregnancy, OR
  - Receipt of blood or blood products within 30 days of symptom onset, OR
  - Organ or tissue transplant recipient within 30 days of symptom onset, OR
  - Association in time and place with a confirmed or probable case, OR
  - Likely vector exposure in an area with suitable seasonal and ecological conditions for potential local vector borne transmission.

Case Management

- The following information should be provided to cases as appropriate:
  - In general, ZIKV cases should use condoms during sex to prevent disease transmission during the period of communicability, which can be up to 6 months for males.
  - If planning pregnancy, women with ZIKV should wait at least 8 weeks after symptom onset, and men testing positive should wait at least 6 months after symptom onset.
  - ZIKV cases with pregnant partners should use condoms for the duration of the pregnancy or 6 months, whichever is longer.
  - Pregnant women with ZIKV should be referred to a maternal fetal medicine specialist and/or an infectious diseases specialist.\(^{(24)}\)
  - ZIKV cases should defer donating blood for 56 days after the onset of symptoms.\(^{(25)}\)

Treatment of a Case

- There is no effective therapy for ZIKV. Supportive care only.
- ZIKV infections have not shown the same bleeding risks as DENV but should be managed the same way until DENV is ruled out. Acetylsalicylic acid (ASA) and other non-steroidal anti-inflammatory drugs (NSAIDs) should not be used, if possible, due to anticoagulant effects that may aggravate the bleeding tendency associated with some DENV infections.\(^{(24)}\)

Management of Contacts

- Generally, contact follow-up is not required as the risk of person-to-person transmission is low.
- If made aware of any pregnant sexual contacts, ensure they are educated about:
  - the importance of using condoms during sex for the duration of pregnancy to prevent the transmission of infection,
  - the signs and symptoms of ZIKV, and
  - consulting their healthcare provider if symptoms do occur.
- Infants born to ZIKV-infected mothers may undergo further evaluation as per their health care provider.
Preventive Measures
- There are currently no vaccines to prevent the acquisition of ZIKV. Research is underway.

Travellers going to ZIKV-Affected Areas
- Provide the following recommendations:
  o Consult a health care professional or visit a travel health clinic preferably six weeks before you travel.
  o Pregnant women and those planning pregnancy should consider avoiding, or postponing, travel to ZIKV-affected areas.\(^{(28)}\)
  o Protect yourself from mosquito bites:\(^{(27)}\)
    ▪ remain in well-screened or completely enclosed, air-conditioned areas whenever possible,
    ▪ wear light-colored clothing and cover up as much as possible with long pants, long-sleeved loose fitting shirts, shoes/boots (not sandals) and a hat.
    ▪ sleep under a bed net, preferably treated with insecticide, and
    ▪ use insect repellent (containing DEET or Icaridin), 15 minutes after sunscreen, on exposed skin and on clothing.
  o Protect yourself from sexually transmitted ZIKV by using a condom when having sex.

All Travellers returning from ZIKV-Affected Areas\(^{(24,26)}\)
- Men should use condoms during sex, wait to conceive and defer all semen donations for 6 months after their return, even if no symptoms occur.
- If the returning traveller has a pregnant partner, condoms (male or female) should be used during sex for the duration of the pregnancy. Further studies are required to determine if other barrier methods (e.g., cervical cap, diaphragm) are adequate protection against ZIKV transmission.\(^{(21)}\)
- Women should use condoms during sex and delay conception for 2 months after their return, even if no symptoms occur.
- Blood and tissue donations should be deferred for a period of 21 days following travel to ZIKV outbreak countries.\(^{(2)}\)

Pregnant Travellers returning from ZIKV-Affected Areas\(^{(28)}\)
- Pregnant women should seek medical attention if the signs and symptoms compatible with acute ZIKV occur while travelling or upon return home.
- Pregnant women may under-go further evaluation as per their health-care provider.
- The decision to test for ZIKV without the presence of symptoms should be discussed between the pregnant woman and her health care provider.
References


