Canadian Recommendations on the Prevention and Treatment of Zika Virus

Prepared by the Committee to Advise on Tropical Medicine and Travel (CATMAT)

Organization: Public Health Agency of Canada

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Key Points/Messages

- The Canadian recommendations for the prevention and treatment of Zika virus (ZIKV) were developed by a working group of the Committee to Advise on Tropical Medicine and Travel (CATMAT). Recommendations are based on a literature review and clinical judgement; they were not developed using an evidence-based medicine methodology.
- A large outbreak of ZIKV is occurring predominantly in the Americas. This outbreak has been associated with an increased rate of microcephaly in newborns in Brazil. The strength of the association between ZIKV infection and congenital abnormalities has previously been very poorly described. However, recent evidence suggests that ZIKV infection during pregnancy is frequently associated with serious neurologic consequences to the fetus.
- Infection with ZIKV also has also been associated with neurologic complications such as Guillain-Barré syndrome (GBS).
- Sexual transmission (male to female) of ZIKV has been documented, including in travellers.
- Much remains unknown about ZIKV. For example, the likelihood of infection among travellers to ZIKV-infected areas, the probability of vertical transmission from mother to fetus, the likelihood of sexual transmission (from symptomatic or asymptomatic partners), and the

likelihood of serious ZIKV-associated sequelae among travellers.

- CATMAT recommends that pregnant women avoid travel to areas of ongoing risk of ZIKV outbreak. Women planning a pregnancy should consult with their health care provider and consider postponing travel to risk areas.
- Other travellers, based on risk tolerance, values and preferences may wish to consider deferring travel to ZIKV-infected areas (e.g. males who are trying to impregnate their partner).
- Travellers should use personal protective measures against mosquito bites. These include skin repellents and protection of living areas against mosquito entry.
- Health care providers should take a travel history from their pregnant patients including relevant information related to the travel history of their partner(s). Any patient who indicates that they or their partner have recently travelled (i.e. during or just prior to the pregnancy) to a risk area should be further evaluated.
- Women should avoid becoming pregnant during travel and for two months after return from a risk area. After a male partner returns from an area of risk, it is reasonable to delay trying to become pregnant for six months.
- To minimize the risk of sexual transmission, CATMAT recommends abstinence or use of condoms for the duration of pregnancy by male partners who have travelled in areas of risk.

Introduction

Zika virus (ZIKV) infection is caused by a flavivirus transmitted through the bite of an infected Aedes mosquito, mainly *Aedes aegypti*. *Aedes albopictus* has also been associated with transmission of ZIKV (1). Although infections in humans were documented in the 1950s, ZIKV has only recently emerged as a disease of significant public health concern. At time of updating, a large outbreak in the Americas has affected more than 30 countries. Outbreaks have also recently occurred on some islands in the South Pacific and in Cabo Verde. Before these outbreaks, known areas of endemic transmission were limited to Asia and Africa. It is likely that the virus will continue to spread because the principal vectors are found in many tropical and subtropical regions as well as in some warmer temperate regions (2,3).

A particular concern with the current outbreak is the spatial and temporal clustering in Brazil of the ZIKV outbreak activity with an increase in the incidence of children born with microcephaly (4). The potential role of ZIKV in microcephaly is supported by detection of ZIKV viral genome in amniotic fluid, placenta and tissues of affected fetuses and neonates (5,6). In addition, although disease is usually mild in adults, ZIKV infection has been associated with Guillain-Barré syndrome (GBS) in a number of countries/regions (7). For example, a case control study done in French Polynesia suggested a 0.24 in 1000 risk for developing GBS in persons infected with ZIKV. This is comparable to the risk of 0.25 to 0.65/1000 observed following *C jejuni* infection. Finally, evidence of sexual transmission of ZIKV from male to female is accumulating (8-11), and suggests that this event is not as rare as previously believed.

The purposes of this statement are: to review the current understanding of ZIKV infection; and, to provide guidance for health care practitioners who provide advice to Canadians travelling to or living in affected areas and/or who manage travellers returning from these areas. Emphasis is placed on the sub-populations who appear to be at the greatest risk for ZIKV-associated harms, i.e. pregnant women and their developing fetuses.

Methods

This statement was developed by a working group of the Committee to Advise on Tropical Medicine and Travel (CATMAT). In addition to CATMAT members, the working group included representatives

from the Public Health Agency of Canada (the Agency) and the Society of Obstetricians and Gynaecologists of Canada. Each member was a volunteer, and none declared a relevant conflict of interest. This guideline complements existing CATMAT statements including the Statement on Personal Protective Measures to Prevent Arthropod bites (12) and the Statement on Pregnancy and Travel (13). A thorough literature search for relevant evidence related to ZIKV was conducted. Guidelines and reports from international and national public health organizations including, but not limited to, the Centers for Disease Control in the United States, the Pan American Health Organization and the World Health Organization were also reviewed.

Epidemiology of Zika Worldwide

ZIKV was first isolated from Ugandan monkeys in 1947. Soon after (1952), human infections were detected in Uganda and Tanzania (14,15). However, human infections were rarely reported until 2007, when the first major outbreak of ZIKV disease occurred on the island of Yap (Micronesia) in the southwestern Pacific Ocean (16). Between 2013 and 2015, additional outbreaks occurred on islands and archipelagos from the Pacific region including a large outbreak in French Polynesia (17,18). An outbreak was also reported in Cabo Verde (19). In 2014, the first report of local transmission in the Americas was reported on Easter Island (20). ZIKV has since spread to a wide region of the Americas including, at the time of updating, more than 30 countries and territories (21). In some situations transmission has been intense, for example the Brazilian Ministry of Health has estimated that 440,000 to 1,300,000 ZIKV infections occurred in Brazil in 2015 (7). It is anticipated that ZIKV will continue to spread through the Americas, in particular in tropical and subtropical regions (22-23).

Transmission

The mosquitoes associated with ZIKV can be active during the day and night, with biting activity often peaking in the morning and later in the afternoon. In vertebrate hosts, the incubation period is usually three to 12 days, with blood viremia (the period when ZIKV is present in the blood) usually lasting for three to five days. If bitten by a competent mosquito while viremic, the human (or other) host can infect the mosquito thereby completing the transmission cycle (23). Vertical transmission between mother and developing fetus also presumably occurs during this viremic period (24,25). Other routes of transmission include blood product transfusion (26) and sexual contact. Indeed, viral RNA has been detected in semen for up to 62 days after onset of febrile illness (27), and several cases of sexual transmission from men after symptomatic infection have been reported (8-11). Sexual transmission of ZIKV from infected women to their sex partners and from persons who are asymptomatically infected has not been reported; however there is insufficient evidence to exclude these as routes of transmission.

ZIKV RNA has been detected in breast milk; however, there have not been any documented reports of ZIKV being transmitted to infants through breastfeeding (19). At this time, the World Health Organization (WHO) considers that "*the benefits of breastfeeding for the infant and mother outweigh any potential risk of Zika virus transmission through breast milk*" (28). CATMAT shares this opinion.

Clinical Manifestations

Approximately 20-25% of persons infected with ZIKV will manifest symptoms, including fever, myalgia, eye pain, and maculopapular rash (16,29). Early clinical manifestations are generally similar to other arboviral infections including dengue and chikungunya, with considerable overlap in symptoms (29,30). Thus, the differential diagnosis of a febrile returned traveller from the Americas will likely include these arboviral entities, as well as malaria (31) and other viral infections (32,33).

Neurological complications, such as Guillan-Barré syndrome (GBS), have been reported from several

countries affected by ZIKV outbreaks (7, 34-36). They include French Polynesia where 42 GBS cases were associated with a ZIKV outbreak (37). A case-control study in this population estimated that the odds of positive ZIKV serology was substantially greater in cases compared to matched controls (OR 59.7; 95% CI 10.4 to ∞) (37). In this same study, and based on a ZIKV population seroprevalence of 0.66, the risk of GBS following ZIKV infection was estimated at approximately 1/4,000. Other neurological manifestations that have been recently reported include a case each of acute myelitis and meningoencephalitis, suggesting that the neurological spectrum of sequelae associated with ZIKV may be broader than previously thought (38,39).

Clinically relevant thrombocytopenia and subcutaneous hematomas has been reported in a small number of cases (40,41). One fatality has been reported in a case with sickle cell disease (42).

As noted above, Brazil has reported an association between ZIKV and microcephaly, defined as a head circumference measurement below the third percentile and disproportionate to the weight and length percentile measurements. Ocular abnormalities and other congenital malformations such as arthrogryposis and hydrops fetalis have also been described (43-45). Although the impact of ZIKV infection during pregnancy remains relatively poorly described, there is mounting evidence to suggest that congenital abnormalities are a frequent outcome. For example, a recent case series from Brazil (Footnote a) suggests that infection is associated with serious outcomes including fetal death, placental insufficiency, fetal growth restriction, and central nervous system (CNS) injury (12/42 ZIKV-infected females on whom Doppler ultrasonagraphy was performed) (46).

Blood viremia is estimated to last three to five days following symptom onset (34,37); however viral RNA has been detected in saliva (18) or urine (48,49) more than a week after clearance of blood viremia. Neutralizing antibodies for ZIKV are detectable after infection, and by extrapolation from other flaviviruses, immunity is presumed to be long-lasting.

Risk to Canadian travellers

The Agency has recently published the risk of ZIKV to Canadians travelling to affected areas in the Americas (50). Since it was published, additional information on sexual and congenital transmission, as well as risk of GBS has become available (36,37). Overall, currently available evidence suggests that:

- ZIKV will have modest to no health impact on the large majority of non-pregnant travellers, though infection might sometimes result in serious neurologic sequelae such as GBS;
- Although much uncertainty remains, ZIKV might have a very serious impact on the developing fetus in mothers infected during pregnancy;
- Sexual transmission from male to female partners has been documented and might not be an infrequent event. Such transmission could, if it occurred around the period of conception or during pregnancy, pose a risk to the developing fetus.

At this time, robust assessments of risks associated with ZIKV are not possible. This reflects, *inter alia*, uncertainties related to: the likelihood that travellers will be infected with ZIKV, the likelihood that travellers infected with ZIKV will manifest serious sequelae like GBS, and the probability that maternal infection during pregnancy will lead to fetal infection.

Areas of Risk

The areas of risk include regions currently considered to have suitable conditions for sustained and high levels of ZIKV transmission, even if ZIKV is not currently being reported. This includes Mexico and most areas of South and Central America, the Caribbean, but not temperate areas of Argentina or Chile. Altitude is a factor known to impact the spatial distribution of the mosquitoes associated

with transmission of ZIKV. Although risk of transmission remains at altitudes greater than 2000 metres, this risk is likely very low (3,51,52).

There are some areas of Africa and Asia where ZIKV transmission has been described in the past, and is likely to be endemic at a low level. The risk of transmission to travellers is considered very low, and these regions are not included in the definition of "areas of risk", nor are countries where ZIKV cases have been only travel-related or via sexual transmission.

The WHO provides updates on countries affected by ZIKV. The European Centre for Disease Control has a map of confirmed cases and the Pan American Health Organization has a list and map of countries and territories with confirmed cases in the Americas (53). The Agency has produced a list of countries with ongoing ZIKV outbreaks that will continue to be updated as the ZIKV outbreak evolves. The list includes countries that have reported autochthonous mosquito- associated outbreaks of ZIKV since 2015.

Prevention

There is no vaccine or immunoprophylaxis that protects against ZIKV infection. Health care practitioners who provide pre-travel consultations and those who care for pregnant women and women who intend to get pregnant should outline the potential risks associated with ZIKV infection to allow the traveller to make an informed choice about whether or not to travel to areas of risk. Those who choose to travel should be advised to strictly adhere to recommendations for the use of personal protective measures (PPM) against mosquito bites.

Recommendation to all Travellers

CATMAT recommends that all travellers to areas where ZIKV is circulating use PPM (see below) against mosquito bites.

Health care providers should discuss with travellers what is known and what is not known about ZIKV and its associated risks to help their patient make an informed choice about travel to areas of risk. The discussion should include the patient's values and preferences, and other factors such as:

- Concern about the risk of serious sequelae associated with ZIKV infection (e.g. GBS);
- Concern about ZIKV infection in pregnancy/unplanned pregnancy;
- The accumulating evidence for sexual transmission from men to women, which might be relevant to men who are actively trying to conceive with their partner;
- The patient's health history, e.g. immunosuppression, severe chronic illness.

Some travellers, for example based on their individual values and preferences, might wish to postpone travel to areas of ongoing risk of ZIKV outbreak.

Recommendation to Pregnant Women and those who are Planning a Pregnancy

CATMAT recommends that pregnant women avoid travel to areas of ongoing risk of ZIKV outbreak. Women planning a pregnancy should consult with their health care provider and consider postponing travel to risk areas as defined above.

For pregnant women and those planning a pregnancy who choose to travel to areas with ZIKV transmission or for whom travel cannot be avoided, use of PPM against insect bites is strongly advised (see below for more detail).

Based on current information on the incubation period and duration of viremia, and the unclear

duration of viral persistence in tissues, women wishing to become pregnant should wait at least two months after their return from an area currently considered to have suitable conditions for sustained and high levels of ZIKV transmission before trying to conceive.

ZIKV RNA has been detected in semen two months after acute illness (11.27). It is not known how long viral shedding in semen can last, how often this might happen when infection is asymptomatic, or how easily virus can be transmitted by sexual contact. The number of reports of sexual transmission has been increasing, suggesting this may not be a rare occurrence. Case detection is difficult and the true risk may be higher than recognized at present. It is reasonable to consider delaying trying to become pregnant for approximately six months if the male partner has travelled in an area currently considered to have suitable conditions for sustained and high levels of ZIKV transmission. Male partners should be tested for ZIKV infection if they have symptoms compatible with ZIKV disease. Negative serology in a male at two weeks or later post- onset of symptoms, or at least three weeks post-travel, makes infection with ZIKV unlikely. Infectious disease physicians, with asymptomatic male patients who are part of a couple trying to become pregnant, may want to consider consulting the local provincial lab to discuss serologic testing in scenarios where there is a medical need to pursue conception in advance of the recommended six-month deferral period. At this time, the sensitivity and negative predictive value of the test in this particular population is not sufficiently well-defined to be of practical use in clinical decision-making and therefore serology is not routinely available at the NML for asymptomatic individuals, other than pregnant women. This policy may be modified when sensitivity and specificity of available tests is better characterized. Patients and their physicians must be aware that the performance of ZIKV diagnostic testing has not been confirmed to accurately determine the absence of a current or past infection, and also that testing may take weeks before results are available.

When properly used, condoms should minimize the risk of sexual transmission. Such protection is especially important during pregnancy. Until more is known, and based on our experience with other viral infections where shedding in semen may be prolonged, it is reasonable to practice abstinence or use condoms for the duration of a pregnancy (while travelling and upon return to Canada).

Personal Protective Measures

PPM are recommended to protect all travellers to areas of risk. The mosquitoes that transmit ZIKV are often most active during daytime and evening hours (22). For this reason, PPM should be used through all hours of the day and night. Use of PPM will also provide protection against other vector-associated diseases such as malaria, dengue, and chikungunya. Recommendations for PPM can be found in CATMAT's *Statement on Personal Protective Measures to Prevent Arthropod Bites* (12). These are summarized in the table below.

Protect Yourself from Bites:

1. Cover up:
    - Wear light-coloured, long-sleeved, loose fitting, tucked-in shirts, long pants, shoes or boots (not sandals), and a hat.
2. Use insect repellent on exposed skin
    - It is recommended that adults use repellents that contain DEET (20-30%) or icaridin (20%).
    - It is recommended that children six months to twelve years of age use repellents that contain icaridin (20%). As a second choice, this age group can use repellents with age-appropriate DEET concentrations as per label.
    - If bites cannot be avoided using a physical barrier, consider use of up to 10% DEET or 10% icaridin for infants under six months of age.

3. Protect living areas from mosquito entry:
    - Stay in a well-screened or completely enclosed air-conditioned room.
    - Reduce your risk in work and accommodation areas by closing eaves, eliminating holes in roofs and walls and closing any other gaps.
4. If mosquito entry into living quarters cannot be otherwise prevented (e.g. by screening):
    - Use a bed net (e.g. for sleeping or resting inside), preferably treated with insecticide.
    - Netting can also be used to protect children in playpens, cribs, or strollers.
    - Bed nets will also provide protection against diseases like malaria.
5. Apply a permethrin insecticide to clothing and other travel gear for greater protection
    - Although permethrin clothing treatments are not widely available in Canada, travel health clinics can advise you how to purchase permethrin and pre-treated gear before or during your trip.
    - Permethrin-treated clothing is effective through several washes. Always follow label
    - instructions when using permethrin.
    - Do not use permethrin directly on skin.

Source: CATMAT's *Statement on Personal Protective Measures to Prevent Arthropod Bites*Footnote (12)

Insect repellents, insecticide treated bed nets and permethrin treated clothing/clothing treatments have been reviewed for safety in Canada and/or the United States. They are considered safe for children, pregnant and breastfeeding women if used in accordance with label directions.

Laboratory Diagnosis

Molecular testing using reverse-transcriptase PCR (RT-PCR) is conducted by some provincial laboratories in Canada. The National Microbiology Laboratory (NML) provides provincial support, along with confirmatory testing. Sensitivity is unknown, but presumed to be high, at least in the initial few days of illness, since ZIKV appears to circulate in the blood for the first three to five days after onset of symptoms (22). ZIKV RNA may be present in urine for a few days after it is no longer detectable in blood (22,54). Specificity is presumed to be high. Information about NML's guidelines and testing recommendations are available for health care professionals on the Government of Canada's website.

Serologic testing is currently performed at the NML using a CDC based in-house IgM enzyme linked immunosorbent assay (ELISA) and a confirmatory ZIKV plaque reduction neutralization test (PRNT) (36). Antibodies appear approximately five to six days after onset of symptoms (34). For the acutely unwell patient with less than 10 days of symptoms, both RT-PCR and serology should be requested. For the convalescent patient with symptom onset over 10 days ago, only serology should be requested. Appropriate diagnostic specimens for RT-PCR testing include plasma/serum, urine, cerebrospinal fluid (CSF), amniotic fluid and placental tissue. Serology is usually only performed on serum; however, viral antibodies may also be detected in CSF in some cases of neurological disease.

As ZIKV is a member of the flaviviridae, serologic tests, including the IgM ELISA assay performed by the CDC, may be cross-reactive with other flaviviruses such as dengue, West Nile, and Yellow Fever (including vaccine recipients) (2). Confirmation of ZIKV therefore rests on amplification of viral RNA by RT-PCR, or by confirmatory PRNT serologic testing which is laborious and time consuming. Confirmatory testing generally requires neutralizing IgG production, which may appear later than IgM. The specificity of the IgM ELISA is limited particularly during secondary flavivirus infections, and the sensitivity is ill-defined at this time, although it is presumed to be high. Patients whose serum samples are IgM positive and are also shown to harbour ZIKV specific antibodies by a PRNT assay are confirmed cases of viral infection. However, it is also recommended for suspect cases that acute and convalescent sera be collected 2-3 weeks apart to document a seroconversion or a diagnostic increase (four-fold or greater) in virus specific neutralizing antibodies. Individuals previously infected

with or vaccinated against flaviviruses may exhibit cross reactivity in PRNT tests as well and the test results may be difficult to interpret. Since dengue virus and ZIKV are transmitted by the same types of mosquitoes, co-infections with these viruses are possible. As noted above, if antibody is present against both of these viruses or other related flaviviruses, it may be difficult to determine the virus responsible for current versus past infections.

PCR for ZIKV can be performed on amniotic fluid (when amniocentesis is technically feasible) to confirm infection of the fetus. At this time, the risk of adverse outcomes of pregnancy if the fetus is infected with ZIKV is unknown, so the risk of the procedure must be weighed against the benefits of this test result. A negative PCR result likely means that the fetus is not actively infected at that moment, but would not eliminate the possibility of prior infection and potential injury to the fetus. It is not known when ZIKV RNA would be expected to appear in amniotic fluid after infection, or how long it is likely to be detectable. There is some evidence that viral RNA may persist in amniotic fluid for months (55).

For postnatal diagnosis of congenital infection, PCR for ZIKV can be performed on placental tissue, umbilical cord blood or infant blood sample, and CSF for confirmation of congenital infection. It is likely, however, that infants or fetuses infected weeks prior to specimen sampling will no longer have detectable viral RNA.

Screening and Management

Evaluation of non-pregnant travellers returning from endemic countries

Testing for ZIKV infection should be considered in the diagnosis of any ill traveller with compatible epidemiologic and clinical history, when symptom onset is within three days after arrival in, to 14 days after departing from, a country where ZIKV transmission is ongoing or widespread. Testing for other similar viral infections and for malaria should also be done as appropriate.

Testing is generally not a routine recommendation for returned travellers whose clinically compatible illness has resolved, or for those who have travelled and remain asymptomatic, because of the uncertain benefit of such testing. Given that neurologic disorders, including GBS have been reported following ZIKV infection, returning travellers should be counselled to report any neurologic symptoms to their doctor. In the event of the diagnosis of GBS or other unusual neurologic syndrome, a travel history should be elicited. If ZIKV infection is thought to be potentially associated with the illness, a specialist should be consulted.

Screening in the context of pregnancy

Evaluation of pregnant women with a travel history to a country with ongoing or widespread transmission of ZIKV

Health care providers should take a travel history from their pregnant patients including relevant information related to the travel history of their partner(s). Any patient who indicates that they or their partner have recently travelled to a country with ongoing or widespread transmission of ZIKV should be further evaluated.

Screening of pregnant women should be discussed on a case-by-case basis between the woman and her health care provider. In these discussions, it is important to consider the problems with sensitivity and specificity of currently available diagnostic testing, overall test result interpretation, as well as the prolonged turnaround time of up to two weeks after receipt in a reference lab for the available tests, which may be problematic in some cases. The decision to test should include consideration of how the results of the screening tests would be used to inform subsequent decisions. Diagnosis and

identification of poor fetal outcomes will allow for appropriate counselling.

Pregnant women and their partners may be justifiably concerned about the risk of ZIKV infection to their fetus and may want to receive counselling to decide the best course of action, including the question of termination. The actual risks of ZIKV infection in pregnancy are currently unclear. Specifically, the risk of symptomatic vertical infection (with microcephaly/intracranial calcification) with maternal infection in a given trimester of pregnancy is entirely unknown although severe sequelae have been reported after infection at all stages of pregnancy (46). This uncertainty makes pregnancy counselling a difficult prospect. Regardless, discussion and informed decision making regarding options for management of ZIKV infection in pregnancy (much like any other congenital infection or congenital anomaly) requires thorough consultation with a Maternal Fetal Medicine Specialist or another specialist familiar with reproductive infectious diseases. As understanding of the risks of ZIKV infection in pregnancy becomes clearer, so too will the related counselling messages, which in turn will allow each patient to make her own individual decision about her pregnancy.

Testing (including PCR) should be offered to pregnant women with acute signs and symptoms compatible with ZIKV. Likewise, a pregnant woman who has a clinical history of a compatible ZIKV-like illness either during or after travel to an area with ZIKV transmission, or whose fetus is suspected of having a congenital anomaly should also be offered testing.

Asymptomatic pregnant women with a history of travel to a country where ongoing or widespread ZIKV transmission is known or suspected should be evaluated and counselled appropriately. A detailed travel history should be taken in order to assess risk of exposure to ZIKV (e.g. date, duration, type of travel, exposure to mosquito bites). Testing should be considered; however, the decision to test should include consideration of how the results would be used. Serologic testing risks false positive results on the initial IgM testing and there is a subsequent delay in completion of confirmatory testing to detect ZIKV specific antibodies. Screening by ultrasound cannot reliably detect microcephaly until late in the second trimester.

The risk of microcephaly or other adverse outcome of pregnancy for a woman known to be infected with ZIKV cannot be estimated from currently available data. Although measurements of head circumference and biparietal diameter may occur as early as 15 weeks, there is no defined gestational age by which microcephaly can be ruled out. Serial monitoring by ultrasound with close attention to measurement trends over time is recommended. It is possible that changes in intracranial anatomy may not be elucidated until well into the third trimester or later.

Evaluation of the Fetus among Pregnant women diagnosed with ZIKV infection

Serial ultrasounds (every 3-4 weeks) are recommended in pregnant women with confirmed or suspected (if testing results are pending) ZIKV infection in pregnancy, and for asymptomatic pregnant travellers returning from areas currently considered to have suitable conditions for sustained and high levels of ZIKV transmission, to help define risk and counsel the mother. Should CNS calcifications or fetal microcephaly be noted at ultrasonography of the asymptomatic pregnant returned traveller, then specific ZIKV testing (along with other routine testing) should be undertaken to help define the likely cause of the anomaly.

Evaluation of the Infant born to a Woman diagnosed with ZIKV infection or with Suspected Congenital ZIKV infection

Infants born to women with confirmed or suspected ZIKV infection in pregnancy, or those with microcephaly, intracranial calcifications or other symptoms of congenital ZIKV infection in whom the mother had potential geographic exposure to the virus, should be tested. This testing should include

serology, PCR of serum (umbilical cord or infant sample), and PCR of placenta; if CSF is sampled, this can also be sent for PCR and serology. Infants with suspected or confirmed congenital ZIKV infection should also undergo further work-up including: routine lab tests (CBC and liver enzymes), head ultrasound, ophthalmologic examination, and hearing evaluation. Infants with confirmed congenital ZIKV infection should have neurodevelopmental monitoring throughout infancy to assess the potential for long term sequelae.

Infants born to women with symptoms of active ZIKV infection around the time of delivery are at risk for perinatal transmission of the disease. In the limited number of reported cases to date, perinatally infected infants have exhibited either no or mild symptoms and laboratory findings (rash, thrombocytopenia) (24). Regardless, such infants should be monitored closely given the unclear spectrum of potential illness in this emerging infection. Testing with serology and serum PCR during acute illness is recommended. In such cases, care should be taken to ensure a thorough work up for other important and treatable causes of congenital infections, such as CMV and toxoplasma infection.

Treatment

Currently there is no specific antiviral therapy for the treatment of ZIKV infection. Treatment is supportive with antipyretics (acetaminophen in pregnancy), hydration and rest. Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided until dengue can be ruled out to reduce the risk of hemorrhage (56). Symptomatic disease typically lasts for up to seven days. Urgent medical care is recommended for any symptoms associated with GBS, and treating health care providers should be made aware of recent travel to area with ZIKV circulation and/or symptoms of ZIKV infection.

If ZIKV infection is confirmed in the setting of pregnancy, referral to a Maternal Fetal Medicine Specialist or Infectious Disease Specialist should be made. If microcephaly, intracranial calcifications or other abnormalities are identified, appropriate counselling by a Neonatologist and Pediatric Infectious Diseases Specialist on potential neurodevelopmental outcome should be offered to parents.

Additional Resources and Useful Links

Government of Canada - For health professionals: Zika Virus

Government of Canada - Travel health notice: Zika virus infection: Global Update

Pan American Health Organization - Zika Virus Infection

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CATMAT members: McCarthy A (Chair), Acharya, A, Boggild A, Brophy J, Bui Y, Crockett M, Greenaway C, Libman M, Teitelbaum P and Vaughan S.

Liaison members: Audcent T (Canadian Paediatric Society), Gershman M (United States Centers for Disease Control and Prevention) and Pernica J (Association of Medical Microbiology and Infectious Disease Canada). Ex officio members: Marion D (Canadian Forces Health Services Centre,

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Footnote a

88 women with a recently manifested rash were enrolled of which 72 (82%) tested positive for ZIKV.