



SOGC recommendation on ZIKA virus exposure for clinicians caring for pregnant women and those who intend to get pregnant

Foreword

The rapid emergence of Zika virus as a potential causative agent for fetal neurological damage has left us with clinical questions for which there is only limited clinical evidence. The need for guidance for women who are potentially impacted is immediate. This update is largely based on expert opinion, a joint effort of the Infectious Disease, Diagnostic Imaging, Maternal Fetal Medicine and Reproductive Endocrine and Infertility Committees, working collaboratively with the College of Family Physicians of Canada (CFPC) and the Canadian Fertility and Andrology Society (CFAS). It is intended to be complementary to the Public Health Agency of Canada (PHAC) Guideline (1), in which the SOGC participated. As new evidence and information emerges, the recommendations may be updated to reflect changes in practice.

Introduction

The Zika virus is in the category of flaviviruses, first described in monkeys in 1947, and later reported in humans in Uganda in 1952. Zika transmission is now reported in over 30 countries, and an up to date map is maintained by the Center for Disease Control (CDC) (2). Congenital anomalies, including microcephaly in babies born to women who had a Zika infection, have now been reported in French Polynesia and in Brazil. Viral RNA has been isolated in the brain tissue of a microcephalic infant (3), and from the amniotic fluid in at least two cases where a microcephalic brain abnormality had been identified on ultrasound. This mosquito is not found in Canada, so the Canadian concern is restricted to travelers and their partners, returning from endemic areas. The mosquito vector for Zika is a common mosquito in warmer climates that bites both day and night. The viral illness is brief, and approximately 80% will be asymptomatic. Sexual transmission of the virus has now been documented by men returning from endemic areas. Persons who have had Zika appear to be at increased risk of developing Guillain-Barre syndrome. It is not known what other factors may contribute to the risk of neurologic damage.

Advice to women contemplating travel to endemic areas

There is insufficient data to be able to provide an accurate estimate of risk, and while microcephaly in infants born to Zika infected mothers has thus far only been reported in two countries, it is too early yet to know if this will be observed in countries that have only recently begun reporting Zika transmission. Women wishing to become pregnant should wait 2-3 months after their return from an affected area before trying to conceive. Women who are sexually active and travelling to an affected area may want to consider the use of consistent and effective contraception while in the affected region, as ZIKA virus is believed to be sexually transmitted.

Recommendation #1: A travel history and travel plans should be taken for all women who are pregnant, or planning a pregnancy

Recommendation #2: Women who are attempting to conceive, or who are pregnant should reconsider travel to areas in which there is active transmission of the Zika virus.

The list of countries with Zika transmission includes many popular holiday destinations (2).

Recommendation #3: Health care providers should provide women who wish to avoid travel to affected countries with a medical letter.

For those who are unable to avoid travel to endemic areas, personal protection measures against mosquito bites should be maintained throughout the duration of the stay. Protection includes physical barriers, such as long clothing to cover skin, bed nets, and use of insect repellents. DEET (diethyltoluamide) for personal use and permethrin to pre-treat clothing have both been tested and found safe for pregnant and breastfeeding women.

Recommendation #4: If travel is not postponed, women should be advised to take personal protection against mosquitoes, and be reassured that they can safely use insect repellants containing DEET.

Advice to men returning from endemic areas whose partner is attempting to conceive

Zika virus lasts only a few days in the blood, up to two weeks in the urine, and may last up to two or more months in the semen. The reported cases of sexual transmission have occurred within weeks of returning. Condom protection has been found to be effective against sexual transmission of other viruses found in semen.

Recommendation #5: Male partners of women who are planning a pregnancy should use condom protection for two to three months upon their return. It is reasonable to consider the use of condoms for the duration of the pregnancy by men in whom Zika was diagnosed, or a Zika-like illness occurred.

For couples who do not wish to wait the recommended two to three months (e.g., those in fertility treatment), sperm wash may be offered. There is no data to support the effectiveness of sperm washing to remove Zika virus, but it has been used effectively with other viral infections. Couples need to be made aware that there may still be a risk of transmission. Men contemplating sperm banking should be aware that Zika virus may not be destroyed by freezing.

Advice to women who have travelled to endemic areas

For other viruses that affect fetal CNS, the first trimester is a high risk period for neurological damage; however, in the case of the Zika virus, there is insufficient evidence to define a susceptible window.

Recommendation #6: Women who have travelled to high risk countries and who have developed viral symptoms, including fever, rash, conjunctivitis, myalgia or eye pain, and who are within 10 days of their symptom development, should be offered viral detection testing for Zika on a blood sample and serology. Psychological support should be offered.

The viral detection testing will be conducted at either a provincial/territorial laboratory or at the National Microbiology Laboratory using PCR. Zika may be present in the urine for a few days after the

viremia and urine can be sent within the first 10 days from onset of symptoms. Provincial testing protocols, where they have been developed, should be followed.

Recommendation #7: IgM serologic testing should be offered to women who have had symptoms but are no longer symptomatic; it should be discussed and may be offered to women who have travelled to endemic areas, and did not develop symptoms. IgM (non-specific) testing can be offered between ten days and twelve weeks after their return or symptom onset. Psychological support should be offered.

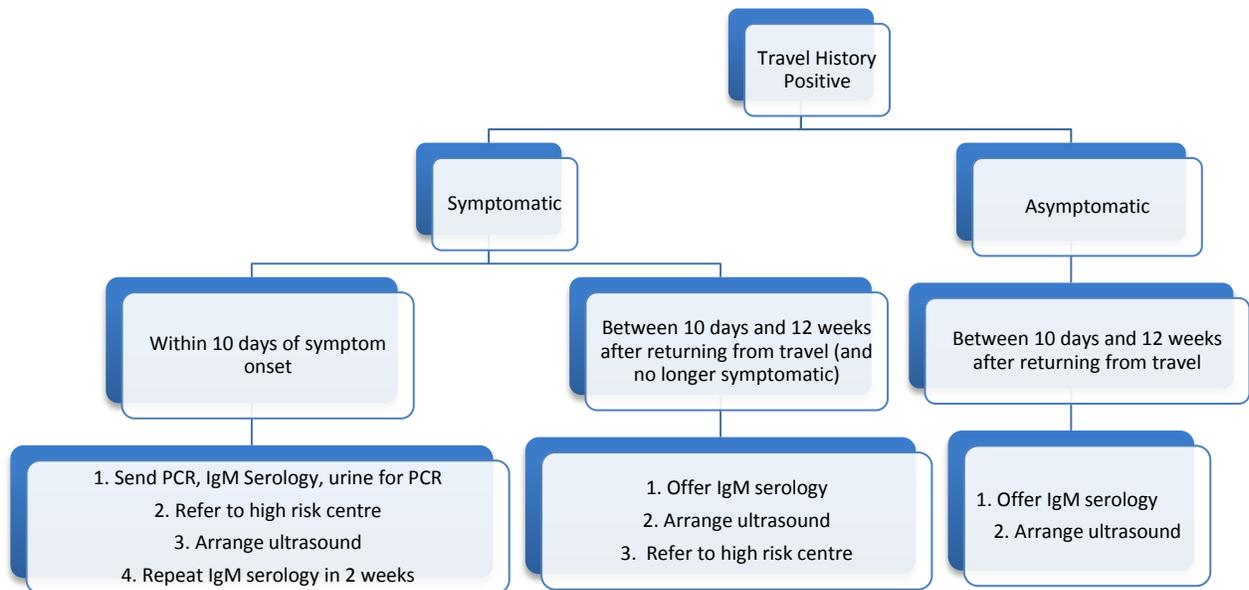
The available IgM assay may result in false positives and has potential cross-reactivity with other flaviviruses, such as dengue viruses which co-circulate in the same geographic areas as Zika virus. Previous flavivirus infection or vaccination (e.g. Yellow Fever) can also create difficulties interpreting the IgM. The negative predictive value of the IgM assay is currently unknown. A confirmatory IgG assay is labor intensive, and consequently has a long turn-around time.

Recommendation #8: Women who test positive for Zika in either viral or serologic testing should be offered referral to a high risk multidisciplinary centre. Consultation and consideration of amniocentesis for PCR testing of the amniotic fluid should be offered to assess for fetal infection depending on the clinical situation, in addition to a baseline detailed ultrasound. Consultation with the appropriate expert at a tertiary facility, if necessary, can then be undertaken. Counseling and management of this potential congenital infection should follow local procedures of referral such as Reproductive Infectious Diseases or Maternal Fetal Medicine.

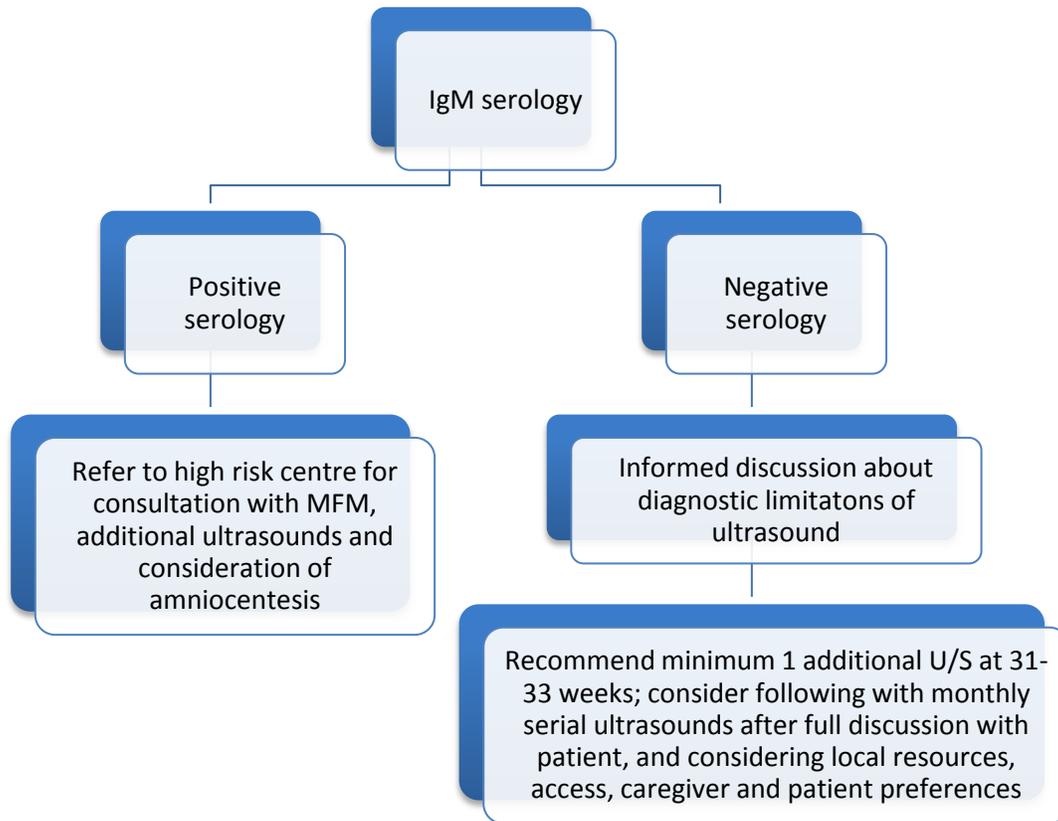
Recommendation #9: There is no consensus in the specific follow-up of IgM negative women using ultrasound. In this situation, in addition to the second trimester anatomy scan, at a minimum, a third trimester ultrasound (31-33 weeks) should be offered. Additional scans, such as on presentation and/or serial monthly ultrasound can be considered. Women should be advised of the limitations of ultrasonography to detect changes at an early stage.

While some guidelines advise serial ultrasound for women who are at potential risk of Zika exposure and who have had negative serology, women and their health care providers should be aware of the limitations of ultrasound to detect evidence of neurologic damage at an early stage in pregnancy. Experience from other perinatal infections known to cause microcephaly has been that the damage may only manifest on ultrasound in later pregnancy. Earlier and subtle changes, if present, may require a highly skilled diagnostic imaging unit to correctly interpret. Data demonstrating the evolution of Zika-associated neurologic injury is lacking, and badly needed, but the published literature to date suggests similar findings to CMV infection in utero with interference with migration and maturation of the brain, calcifications, limited growth and ventriculomegaly.

Algorithm 1. Screening and management of men and women of reproductive age at risk of Zika virus infection.



Algorithm 2. Screening and management of pregnant women at risk of Zika virus infection.



Reference List

- (1) Committee to Advise on Tropical Medicine and Travel. Canadian Recommendations on the Prevention and Treatment of Zika Virus. Public Health Agency of Canada 2016 [cited 2016 Feb 19]; Available from: URL: <http://www.healthycanadians.gc.ca/publications/diseases-conditions-maladies-affections/committee-statement-treatment-prevention-zika-declaration-comite-traitement-prevention/index-eng.php>
- (2) Areas with Zika. Centers for Disease Control and Prevention 2016 [cited 2016 Feb 19]; Available from: URL: <http://www.cdc.gov/zika/geo/index.html>
- (3) Mlakar J, Korva M, Tul N, Popovic M, Poljsak-Prijatelj M, Mraz J, et al. Zika Virus Associated with Microcephaly. N Engl J Med 2016 Feb 10.

Approved by the SOGC Board of Directors: February 22, 2016