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The Canada Communicable Disease Report (CCDR) is a bilingual, peer-reviewed, open-access, online scientific journal published by the Public Health Agency of Canada (PHAC). It provides timely, authoritative and practical information on infectious diseases to clinicians, public-health professionals, and policy-makers to inform policy, program development and practice.

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CANADA
COMMUNICABLE
DISEASE REPORT

ZIKA VIRUS

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Canadian recommendations on the prevention and treatment of Zika virus: Update

Zika Working Group[1] on behalf of the Committee to Advise on Tropical Medicine and Travel (CATMAT)*

[1] **Note:** Members of the Zika Working Group are listed in the Acknowledgments section

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Abstract

Background: Zika virus (ZIKV) has recently emerged as a disease of significant public health concern. Currently, a large outbreak is occurring predominantly located in the Americas. ZIKV infection is a cause of microcephaly and other congenital abnormalities and can cause post-infectious neurologic complications such as Guillain-Barré syndrome.

Objective: To review current knowledge of ZIKV infection and to provide guidance to health care professionals who provide advice to Canadians who may be impacted by ZIKV infection.

Methods: This Statement was 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 judgment.

Results: All travellers should use personal protective measures against mosquito bites including insect repellents and protection of living areas against mosquito entry. Pregnant women should avoid travel to areas designated by the Public Health Agency of Canada as being of concern because of ongoing ZIKV transmission. Women planning a pregnancy should consult with their health care provider and consider postponing travel to these areas. All other travellers may wish to consider deferring travel to designated areas based on risk tolerance, values, and preferences.

Sexual transmission of ZIKV from male partners has been documented and couples should practise abstinence or use condoms for the duration of a pregnancy, while in a risk area, or until viral shedding has likely ceased. In the absence of clear data, we make the assumption that viral shedding is unlikely to persist beyond 6 months for men and two months for non-pregnant women.

Health care providers should take a travel history from their pregnant patients including relevant information related to the travel history of their partner(s). Screening and management recommendations are provided for all travellers including potentially contagious male partners, pregnant women (symptomatic and asymptomatic), and the fetus or infant of potentially infected women. There is no specific antiviral therapy for the treatment of ZIKV infection.

Conclusion: Robust quantitative assessments for the full spectrum of ZIKV-associated risks are not possible. This reflects, among other things, uncertainties related to the likelihood of infection among travellers to ZIKV-affected areas, vertical transmission from mother to fetus, sexual transmission (from symptomatic or asymptomatic partners), and serious ZIKV-associated sequelae among travellers. Given this uncertainty, as well as the potentially severe effects of ZIKV infection on the fetus, recommendations are conservative. CATMAT will update its recommendations as new information becomes available.

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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 (3). Although infections in humans were documented in the 1950s, ZIKV has only recently emerged as a disease of significant public health concern. Currently, there is a large outbreak underway (http://www.healthycanadians.gc.ca/diseases-conditions-maladies-affections/disease-maladie/zika-virus/risks-countries-pays-risques-eng.php) in the Americas with transmission also occurring in some other countries. Outbreaks have also recently occurred on islands in the South Pacific and in Cabo Verde. Before this, known areas of endemic transmission were limited to Asia and Africa, and transmission rates in these areas are generally low. It is likely that the virus will continue to spread because the mosquito vectors are found in many tropical and subtropical regions and in some warmer temperate regions (4,5).

A major concern with the current outbreak is the spatial and temporal clustering of ZIKV activity with an increase in the incidence of children born with microcephaly, defined as a head circumference measurement below the third percentile and disproportionate to the weight and length percentile measurements (6,7). A recent epidemiologic study also demonstrated a strong association of ZIKV and microcephaly in the population of French Polynesia, where an outbreak took place from 2013-2015 (8). The role of ZIKV in microcephaly is further supported by detection of ZIKV viral genome in amniotic fluid, placenta and tissues of affected fetuses and neonates (1,9), and the pattern of microcephaly associated with ZIKV appears to be within the context of a broader syndrome that may be distinct from that caused by other fetal insults (9). Based on the available evidence, a causal relationship between prenatal ZIKV infection and infant microcephaly or other severe brain anomalies has been acknowledged in the scientific community (10).

Although disease is usually mild in adults, ZIKV infection can cause neurologic sequelae such as Guillain-Barré syndrome (GBS) (7,11). A recent case control study done in French Polynesia estimates 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 *Campylobacter jejuni* infection. There are also reports of acute disseminated encephalomyelitis (ADEM) following ZIKV infection (12).

Finally, there are multiple reports of sexual transmission of ZIKV from infected males to their partner(s), including male-to-male (2,13-16), suggesting that this event is not a rare occurrence.

The purposes of this statement are to review our current knowledge of ZIKV infection and to provide guidelines for health care providers on prevention and management of ZIKV disease.

Methods

This statement was developed by a working group of the Committee to Advise on Tropical Medicine and Travel (CATMAT). Members of the working group were from CATMAT, 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 (17) and the Statement on Pregnancy and Travel (18). A literature search for 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 retrieved and reviewed.

Epidemiology

ZIKV was first isolated from monkeys in Uganda in 1947. Soon after (1952), human infections were detected in Uganda and Tanzania (19,20). 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 (21). Between 2013 and 2015, additional outbreaks occurred on islands and archipelagos from the Pacific region including a large outbreak in French Polynesia (22,23) and another in Cabo Verde (24). In 2014, local transmission in the Americas was reported for the first time on Easter Island (25). ZIKV has since spread to a wide region of the Americas (http://www.paho.org/hq/index.php?option=com_content&view=articl e&id=11603&Itemid=41696&lang=en) including, at the time of updating, more than 43 countries and territories. It is anticipated that ZIKV will continue to spread through the Americas, in particular in tropical and subtropical regions (27,28).

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 (29,30). Viremia has typically been detected only during symptoms, although a case of prolonged viremia during pregnancy has been reported (31). It is uncertain whether viremia is detectable prior to symptoms, or during asymptomatic infection. If bitten by a competent mosquito while viremic, the human (or other) host can infect the mosquito thereby completing the transmission cycle (28). Vertical transmission between mother and developing fetus also presumably occurs during this viremic period (32,33). Other described routes of transmission include blood product transfusion (34) and sexual transmission from men after symptomatic infection (13-16). Viral RNA has been detected in the semen of males previously known to have symptomatic disease at very high levels; how long this persists, and whether it can occur in males who were infected but asymptomatic is not known. Viral RNA has also been detected in saliva (23) or urine (35,36) more than a week after clearance of blood viremia. Neutralizing antibodies for ZIKV are detectable after infection, and by extrapolation from other flaviviruses, post-infection immunity is presumed to be long lasting.

Sexual transmission of ZIKV from infected women to their sexual 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 transmission to infants through breastfeeding (19). At this time, the World Health Organization considers that "the benefits of breastfeeding for the infant and mother outweigh any potential risk of Zika virus transmission through breast milk" (37). CATMAT shares this opinion.

Clinical Manifestations

Approximately 20-25% of persons infected with ZIKV will manifest symptoms, including fever, myalgia, pruritis, eye pain, and maculopapular rash (21,38). Early clinical manifestations are generally similar to other arboviral infections including dengue and chikungunya (38,39). Thus, the differential diagnosis of a febrile returned traveller from the Americas will likely include these arboviral entities, as well as malaria (40) and other viral infections (41,42).

Post-infection neurologic complications, such as Guillain-Barré syndrome (GBS), have been reported from many of the countries affected by the current ZIKV outbreak (11,30,43,44). They include French Polynesia where a case-control study estimated that the odds of positive ZIKV serology was substantially greater in GBS cases compared to matched controls (OR 59.7; 95% CI 10.4 to ∞) (45). 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 have also been reported in association with ZIKV infection, e.g., acute myelitis, meningoencephalitis, and acute disseminated encephalomyelitis (12,46,47), suggesting that the neurological spectrum of sequelae associated with ZIKV may be broader than previously thought.

Clinically relevant thrombocytopenia and subcutaneous hematomas have been reported in a small number of cases (48,49). Deaths from other causes have also been reported (50,51).

Brazil, French Polynesia and several other affected countries (e.g., Colombia) (7) have reported infant microcephaly associated with ZIKV infection. Ocular abnormalities and other congenital malformations such as arthrogryposis and hydrops fetalis have also been described (52-54). Although the full impact of ZIKV infection during pregnancy remains to be described, there is now consensus that infection can cause fetal congenital anomalies (8,10). Although the likelihood of serious fetal harm following infection is unknown there is evidence to suggest that it is not a rare occurrence. For example, a recent case series from Brazil 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 ultrasonography was performed) (55). A retrospective study of patients in French Polynesia suggested that the impact of ZIKV was primarily through infections occurring during the first trimester (when it was estimated to result in an approximately 1% risk of microcephaly) (8).

Reviews of the epidemiology of ZIKV, as well as the causal association of ZIKV and microcephaly have been recently published (10).

Risk to travellers

The Agency has published an assessment of the risk of ZIKV to Canadians (56). It concludes:

- For most infected travellers, ZIKV will have little or no health impact (**Low** impact, with medium confidence).

However, severe outcomes (e.g., GBS) might occur in some affected individuals (**High** impact, medium confidence).

- There could be **Very High** impact (with medium confidence) to the unborn children of women who become infected with ZIKV while pregnant.

- Sexual transmission, from symptomatic male travellers to a sexual partner(s) who has(ve) not travelled, has been reported. Because the likelihood of infection with ZIKV is considered low, so too is the likelihood of transmission via this route (**Low** likelihood, medium confidence). However, if a man becomes infected with ZIKV, the likelihood of transmission to his sexual partner(s) is assessed as **Medium** (low confidence).

This assessment also considered factors that might affect the likelihood or impact of ZIKV infection. While evidence is very limited in this regard, several plausible relationships were identified:

- Conditions at higher elevations (≥ 2,000 m) are generally not supportive of viral replication in, or survival of, *Aedes aegypti* populations. Correspondingly, the relative likelihood of infection with ZIKV might be substantially lower for travellers (depending on how much time they spend at higher compared to lower elevations) to such areas.

- All else held equal, the likelihood of infection is higher in countries/areas that are reporting high levels of ZIKV activity compared to those that are not.

- The likelihood of infection is likely lower for shorter travel durations and/or when staying in protected environments (e.g., well screened and air-conditioned accommodations, transiting through an airport in a risk area). This might also apply to situations where the traveller is staying in an isolated location, i.e. where there are relatively few residents who might support sustained transmission.

CATMAT stresses that, at this time, robust quantitative assessments for the full spectrum of ZIKV-associated risks are not possible. This reflects, among other things, 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. Given this uncertainty, as well as the potentially severe effects of ZIKV infection on the fetus, our recommendations are conservative. However, we also realize that there might be circumstances where a patient is unable to or unsure about whether to adhere to our guidance. In this situation, we believe it is appropriate to consider factors such as those identified above to help inform the decision-making process (also see below, decision to travel to risk areas).

Areas of risk

There is widespread transmission over much of South and Central America, the Caribbean, but not temperate areas of Argentina and Chile. An up to date list of countries (http://www.healthycanadians.gc.ca/diseases-conditions-maladies-affections/ disease-maladie/zika-virus/risks-countries-pays-risques-eng. php) to which our recommendations apply is maintained by the Agency.

There are areas of Africa and Asia where ZIKV transmission has previously occurred, or is considered endemic with very low potential for transmission to travellers. These are not currently designated as risk areas by the Agency, nor are countries/ territories where ZIKV has been reported, but only in travellers and/or as a result of sexual transmission.

Prevention

Decision to travel to areas of risk

All travellers

Health care providers should discuss with travellers what is known and what is not known about ZIKV to help their patients make an informed choice about travel based on this guideline and the ZIKV information on the Government of Canada's ZIKV webpage (http://www.healthycanadians.gc.ca/diseases-condition s-maladies-affections/disease-maladie/zika-virus/index-eng.php). Factors to consider include:

- The possibility of serious sequelae such as post-infection neurologic complications (e.g., GBS, ADEM).

- The potential for ZIKV infection during pregnancy to have a severe impact of the fetus.

- The potential for sexual transmission from men to their sexual partners, which is particularly relevant to couples who are actively trying to conceive.

- The potential for co-morbidities to predispose to more serious outcomes (there is little specific evidence in this regard, though it is reasonable to expect such impacts).

- Patients' values and preferences (including risk perception and risk tolerance).

- The potential impacts of following the recommendation on a couple's reproductive plans.

- The large uncertainties that continue to hamper the development of robust risk assessments for Canadians.

- Itinerary- specific factors (see section on risk to Canadian travellers) that might affect the likelihood of being exposed to ZIKV.

Pregnant women and women who are planning a pregnancy

CATMAT recommends that pregnant women **avoid** travel to areas of risk (http://www.healthycanadians.gc.ca/diseases-conditions-maladies-affections/disease-maladie/zika-virus/risks-countries-pays-risques-eng.php). Women planning a pregnancy should consult with their health care provider and consider postponing travel to areas of risk as defined above. Pregnant women and those planning a pregnancy who choose to travel to areas of risk or for whom travel cannot be avoided are strongly advised to use Personal Protective Measures (PPM) against insect bites (see below for more detail). As for travellers generally (see previous section), health care providers should help their patients make an informed decision regarding travel or other aspects of ZIKV prevention. The risk of severe adverse outcomes of pregnancy deserves particular emphasis.

RECOMMENDATIONS

Prevention of mosquito-borne transmission

There is no vaccine or immunoprophylaxis that protects against ZIKV infection. CATMAT recommends that all travellers to areas of risk should be advised to strictly adhere to recommendations for the use of personal protective measures against mosquito bites (see below). Because the mosquitoes that transmit ZIKV can bite at any time (including during daylight hours), PPM should be used through all hours of the day and night. In addition to ZIKV, PPM 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* (17). These are summarized below:

Personal protective measures to prevent athropod 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. Since publication of the PPM guidelines, p-Menthane-3,8-diol 20% has become available in Canada and is an option.
•	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.

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, including for children, pregnant and breastfeeding women if used in accordance with label directions.

Prevention of sexual transmission

ZIKV RNA has been detected in semen two months after acute illness (16,57). 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. When properly used, condoms should minimize the risk of sexual transmission.

Pregnant women and their male partner

If travel to a risk area (http://www.healthycanadians.gc.ca/diseases-conditions-maladies-affections/disease-maladie/zika-virus/risks-countries-pays-risques-eng.php) is unavoidable, pregnant woman and male partners should practise abstinence or use condoms until more is known about the prolonged viral shedding of ZIKV in semen. If the male partner of pregnant female has been in a risk area the couple should practise abstinence or use condoms for the full duration of the pregnancy (including after return).

Couples planning a pregnancy

Based on current information on the incubation period and duration of viremia, and the unclear duration of viral persistence in tissues, women planning a pregnancy should wait at least *two months* after their return from an area of risk before trying to conceive. For couples where the male partner has travelled in an area of risk, it is reasonable to delay trying to conceive for *six months*.

Couples outside the context of current or planned pregnancy

Men who have returned from a risk area and who wish to reduce the possibility of sexual transmission to their partner (outside of the context of pregnancy) can do so through appropriate use of condoms. Although transmission has so far only been reported after symptomatic infection, and it is plausible that the risk after asymptomatic infection is lower, there are no data to support making different recommendations for symptomatic or asymptomatic men. Use of condoms likely provides the greatest protection in the first weeks following illness, but given the potential for long-term persistence in semen, condom use should be considered for six months after return from a risk area.

Role of laboratory testing in transmission prevention or monitoring of pregnant women

Laboratory testing for ZIKV infection is fully described below. In theory, based on information from other similar viral infections, the absence of ZIKV-specific antibodies two weeks or more after the last possible exposure implies that the individual has never been infected, and is not contagious to sexual partners or to the fetus. Such seronegative individuals could consider discontinuing measures to intensively follow the pregnancy for ZIKV-related complications, as well as measures to prevent sexual transmission. The absence of ZIKV RNA in a semen sample might indicate absence of contagiousness, but there are no data to support this practice at this time, and there remains the theoretical risk of poor test sensitivity for some ZIKV strains. However, at this time, serology and RNA testing in Canada is only available for symptomatic individuals and pregnant women. Testing of asymptomatic individuals (men or non-pregnant women) is not routinely offered.

Laboratory Diagnosis

Molecular testing using reverse-transcriptase PCR (RT-PCR) is conducted by some provincial laboratories in Canada. The National Microbiology Laboratory provides provincial support, along with confirmatory testing. Sensitivity and specificity are 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 (27). ZIKV RNA may be present in urine for a few days after it is no longer detectable in blood (27,58). Information about National Microbiology Laboratory's guidelines and testing recommendations are available on the Government of Canada's website (http://healthycanadians.gc.ca/diseases-conditions-maladies-affections/disease-maladie/zika-virus/index-eng.php).

At the National Microbiology Laboratory, serologic testing is currently performed using a Centers for Disease Control in the United States based in-house IgM enzyme linked immunosorbent assay (ELISA) followed by a confirmatory ZIKV plaque reduction neutralization test (PRNT) (36). Antibodies appear approximately five to six days after onset of symptoms (30). For the acutely unwell patient with less than 10 days of symptoms, both RT-PCR and serology should be requested to maximize sensitivity. 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 be detected in CSF in some cases of neurological disease.

As ZIKV is a member of the flaviviridae, serologic tests, including the IgM ELISA, may be cross-reactive with other flaviviruses such as dengue, West Nile, and Yellow Fever (including among vaccine recipients) (4). Confirmation of ZIKV therefore rests on amplification of viral RNA by RT-PCR, or by confirmatory PRNT serologic testing. 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. Patients whose serum samples are IgM positive and have ZIKV-specific antibodies confirmed through PRNT are confirmed cases of viral infection. However, it is also recommended for equivocal 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. This is because individuals previously infected with or vaccinated against flaviviruses may exhibit cross reactivity in PRNT tests making them difficult to interpret.

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 clinical utility of this test result. A negative PCR result likely means that the fetus is not currently infected, but would not eliminate the possibility of previous infection. 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 (59).

For postnatal diagnosis of congenital infection, PCR for ZIKV can be performed on placental tissue, umbilical cord blood or infant blood, and CSF for confirmation of congenital infection. It is possible, 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 (PCR) 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 an area of risk. Testing for other similar viral infections and for malaria should also be done as appropriate.

Serologic testing may be considered for male returned travellers whose clinically compatible illness has resolved, and are at least two weeks post exposure, in order to assess for potential contagiousness to sexual partners. The same would theoretically apply to males who have travelled and remain asymptomatic but testing is not currently being offered to this group in Canada. Testing an asymptomatic individual simply out of curiosity concerning their serostatus would not be a prudent use of limited resources. Given that neurologic disorders like GBS have occurred 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 for the patient and any male sexual partners should be elicited. If ZIKV infection is thought to be potentially associated with the illness, a specialist should be consulted.

Evaluation in the context of pregnancy

Evaluation of pregnant women with a travel history to an area of risk

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 an area of risk should be further evaluated.

Screening of asymptomatic pregnant women should be discussed on a case-by-case basis between the woman and her health care provider. Screening would consist of serology at least two weeks after the last potential exposure, as well as fetal ultrasounds, at a frequency to be determined in consultation with the woman's obstetrician, at least until serology is shown to be negative. The usefulness of serology will depend partly on the turn-around time for results, which can be discussed with the local laboratory. 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 risk of vertical infection (with clinical sequelae) in the setting of symptomatic or asymptomatic maternal infection in a given trimester of pregnancy is unknown, but appears highest in the first trimester (8). However severe sequelae have been reported after infection at all stages of pregnancy (55). 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.

Evaluation of pregnant women with symptoms compatible with ZIKV infection

Testing (including PCR) should be offered to pregnant women with acute signs and symptoms compatible with ZIKV. As described above, for the acutely unwell patient with less than 10 days of symptoms, both RT-PCR and serology should be requested to maximize sensitivity. For the convalescent patient with symptom onset over 10 days ago, only serology should be requested. Repeated ultrasound monitoring is indicated, unless the woman is found to be negative on laboratory testing. A woman whose fetus is suspected of having a congenital anomaly should also be offered testing if she or her partner has travelled to any location where ZIKV transmission may be occurring (http://www.healthycanadians.gc.ca/diseases-conditions-maladies-affections/disease-maladie/zika-virus/risks-countries-pays-risques-eng.php), even at a low level.

The risk of microcephaly or other adverse pregnancy outcomes 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 of risk while awaiting diagnosis, 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 of the fetus (e.g., amniocentesis) should be considered 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 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) (32). 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 cytomegalovirus and toxoplasma.

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 (60). 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 specialist familiar with Reproductive Infectious Diseases 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 (http://healthycanadians.gc.ca/diseases-conditions-maladies-affections/disease-maladie/zika-virus/professionals-professionnels-eng.php?id=health_prof).

Government of Canada – Countries with reported locally acquired Zika virus infection (http://www.healthycanadians.gc.ca/diseases-conditions-maladies-affections/disease-maladie/zika-virus/risks-countries-pays-risques-eng.php?_ga=1.47407591.1129954220.1460575439).

Government of Canada – Travel health notice: Zika virus infection: Global Update (http://travel.gc.ca/travelling/health-safety/travel-health-notices/143?_ga=1.101883841.1113463633.1435244057).

Pan American Health Organization – Zika Virus Infection (http://www.paho.org/hq/index.php?option=com_content&view=article&id=11585&Itemid=41688&lang=en).

Recommendations for ZIKV

Action	Group	Recommendation
Decision to travel to areas of risk	All travellers	Health care providers should discuss current knowledge about ZIKV, associated risks, and preferences and values with patients. Some travellers may wish to postpone travel to areas of risk.
	Pregnant women	Pregnant women should avoid travel to areas of risk.
	Women planning a pregnancy	Women planning a pregnancy should consider postponing travel to areas of risk.
Prevention of mosquito borne transmission	All travellers	All travellers to areas of risk should strictly adhere to recommendations for the use of personal protective measures against mosquito bites through all hours of the day and night.
Prevention of sexual transmission	Pregnant women and their male partner	Couples should practise abstinence or use condoms while in a risk area and for the duration of the pregnancy.
	Couples planning a pregnancy	Women planning a pregnancy should wait *at least two months* after their return from an area of risk before trying to conceive. Male partners who have travelled in an area of risk should delay trying to conceive for *six months* after their return.
	Couples outside the context of current or planned pregnancy	Male partners who have travelled in an area of risk should consider using condoms for *six months* after their return.
Screening and management	All travellers	Testing should be considered for 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 an area of risk. Serology and RNA testing in Canada is only available for symptomatic individuals and pregnant women. Testing of asymptomatic individuals (men or non-pregnant women) is not routinely offered *Acutely unwell patient* with less than 10 days of symptoms, both RT-PCR and serology should be requested to maximize sensitivity. *Convalescent patient* with symptom onset over 10 days ago, only serology should be requested.
	Male partners	Serologic testing may be considered for male returned travellers whose clinically compatible illness has resolved, and are at least two weeks post exposure, in order to assess for potential contagiousness to sexual partners.
	All pregnant women	All pregnant patients with a travel history to an area of risk should have further evaluation.
	Asymptomatic pregnant women	Asymptomatic pregnant women should consider testing; this would consist of serology at least two weeks after the last potential exposure and fetal ultrasounds, (unless found to be seronegative) at a frequency to be determined in consultation with the woman's obstetrician.
	Symptomatic pregnant women	*Acutely unwell patient* with less than 10 days of symptoms, both RT-PCR and serology should be requested to maximize sensitivity. *Convalescent patient* with symptom onset over 10 days ago, only serology should be requested. Repeated ultrasound monitoring is indicated, unless the woman is found to be negative on laboratory testing.
	Fetus of pregnant women with confirmed or suspected ZIKV infection	Pregnant women with confirmed or suspected ZIKV infection in pregnancy should receive serial ultrasounds (every 3-4 weeks).
	Infant born to a woman with confirmed or suspected 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 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.

Screening and management	Infants with suspected or confirmed congenital ZIKV infection	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. Those with confirmed infection should have neurodevelopmental monitoring throughout infancy to assess the potential for long term sequelae.
Treatment	Pregnant cases	Acetaminophen, hydration, and rest. Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided until dengue can be ruled out. Urgent medical care is recommended for any symptoms associated with GBS or other neurologic syndromes. Referral to a maternal fetal medicine specialist or infectious diseases specialist should be made. If fetal abnormalities are identified, appropriate counselling should be offered.
	Non-pregnant cases	Antipyretics, hydration, and rest. Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided until dengue can be ruled out. Urgent medical care is recommended for any symptoms associated with GBS or other neurologic syndromes.

Acknowledgements

Conflict of interest

None.

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Investigation and management of psittacosis in a public aviary: A One Health approach

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Abstract

Background: *Chlamydophila psittaci* is a zoonotic bacterium that causes avian chlamydiosis in birds and psittacosis in people. Public aviaries provide a setting for occupational and recreational exposure to ill birds.

Objective: To describe the investigation and management of avian chlamydiosis in a public aviary in Canada using a One Health approach.

Methods: In June 2013, a previously healthy lorikeet died. Post-mortem examination showed fungal air sacculitis and hepatitis with RT-PCR testing positive for *C. psittaci*. Provincial veterinarians along with provincial and local public health officials investigated the avian and worker health at the aviary.

Outcome: A One Health approach to prevention, detection and response was applied to the people and birds potentially exposed to *C. psittaci*. The aviary was closed pending investigation and response measures. No further cases of avian or human disease were found. Birds were treated with antibiotics in the event the dead bird was infectious prior to death. The aviary was appropriately cleaned and disinfected and then re-opened to the public.

Conclusions: The *C. psittaci* death likely represented latent infection and/or a low virulence strain given the lack of spread to other birds or people. A coordinated, multiagency approach using a One Health framework was successfully used during the first *C. psittaci* investigation at a public aviary in Canada.

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Introduction

On June 20, 2013, a previously healthy rainbow lorikeet (*Trichoglossus haematodus*) died in a public aviary in Ontario, Canada. Indoor aviaries are large enclosures that allow birds to fly and interact within a controlled environment. Public aviaries allow the public to enter the birds' habitat to view or interact with them. As per protocol, all bird deaths in the facility undergo post-mortem examination and testing. The bird's carcass was submitted to the Animal Health Laboratory, University of Guelph by the aviary's attending veterinarian. The samples sent for real-time polymerase chain reaction (RT-PCR) testing were found to be positive for *Chlamydophila psittaci*, suggesting active or latent infection.

Background

Avian chlamydiosis and psittacosis

Avian chlamydiosis in birds and psittacosis (ornithosis) in people are bacterial infections caused by *C. psittaci* (1-3). Although psittacine (parrot-type) birds, especially cockatiels and budgerigars, are most commonly infected, *C. psittaci* bacteria have been identified in over 460 bird species (2,4). The people most at risk are bird owners or those who work with birds, although infection can occur with passing or seemingly minimal exposure (1-3). Birds with latent or clinical disease are infectious (the former intermittently), and those with clinical disease exhibit non-specific signs of lethargy, anorexia, ruffled feathers, sleepiness, shivering, weight loss, respiratory distress, serous or mucopurulent ocular or nasal discharge, conjunctivitis, diarrhea and excretion of green to yellow-green urates (2,5). People with psittacosis generally present with mild flu-like symptoms, but they can develop more severe disease, including pneumonia, encephalitis and myocarditis (1,3). The incubation period may be long: 3 days to several weeks in birds and 1 to 4 weeks in people (2,6). Shedding of high virulence strains in birds, in particular, can lead to outbreaks (2,3). The combination of asymptomatic shedding and a long incubation period makes outbreak prevention challenging (2).

In Canada, because avian chlamydiosis surveillance is not conducted nationally, the incidence is not known. In Ontario, one to two cases were diagnosed each year over the previous five at the Animal Health Laboratory, Guelph, Ontario

Human psittacosis is a mandatory reportable disease in Ontario (7). Between 2003 and 2007, fewer than five cases were reported yearly (6).

One Health

"One Health" is an approach to diseases that considers the interactions between people, animals and the environment (8) [**Figure 1**]. One Health promotes interdisciplinary work, recognizes the complementary skill sets of various disciplines (e.g., veterinary medicine, public health, human medicine, environmental health) [9] and can be used to support prevention, detection and response to public health risks (10).

Rationale and objective

A public aviary can potentially expose workers and the public to zoonoses such as psittacosis. Even a single case requires prevention of an outbreak. A framework to support a comprehensive, multiagency approach is needed. In this article, we describe the first known report of an integrated avian and human chlamydiosis/psittacosis investigation in Canada and highlight the use of One Health to describe the multiagency approach to the investigation.

Methods

The investigation of the outbreak commenced on September 18, 2013, when the lorikeet tested positive for *C. psittaci*, and was declared over on November 6, 2013, 44 days after the bird population in the aviary tested negative for the bacteria following antibiotic treatment. The investigation completion date was determined based on more than one maximum incubation period having passed with no further cases detected in birds or people.

Aviary investigation

The aviary was a large facility open to the public. It consisted of several areas, separated by walls and doors, with separate ventilation systems. The lorikeet that died was from the main aviary, which contained approximately 150 mostly free-flying birds. The lorikeets in this main aviary had their own cage and did not come in direct contact with other birds.

As required under the *Animal Health Act* (11), the Animal Health Laboratory reported the positive *C. psittaci* result in the dead lorikeet to the Ontario Ministry of Agriculture, Food and Rural Affairs (OMAFRA) who in turn notified the local public health unit, and the Ontario Ministry of Health and Long-Term Care (MOHLTC). The various agencies began working with the aviary to investigate and limit the possible spread of *C. psittaci*

Figure 1: Summary of One Health and its roles in the *Chlamydophila psittaci* investigation
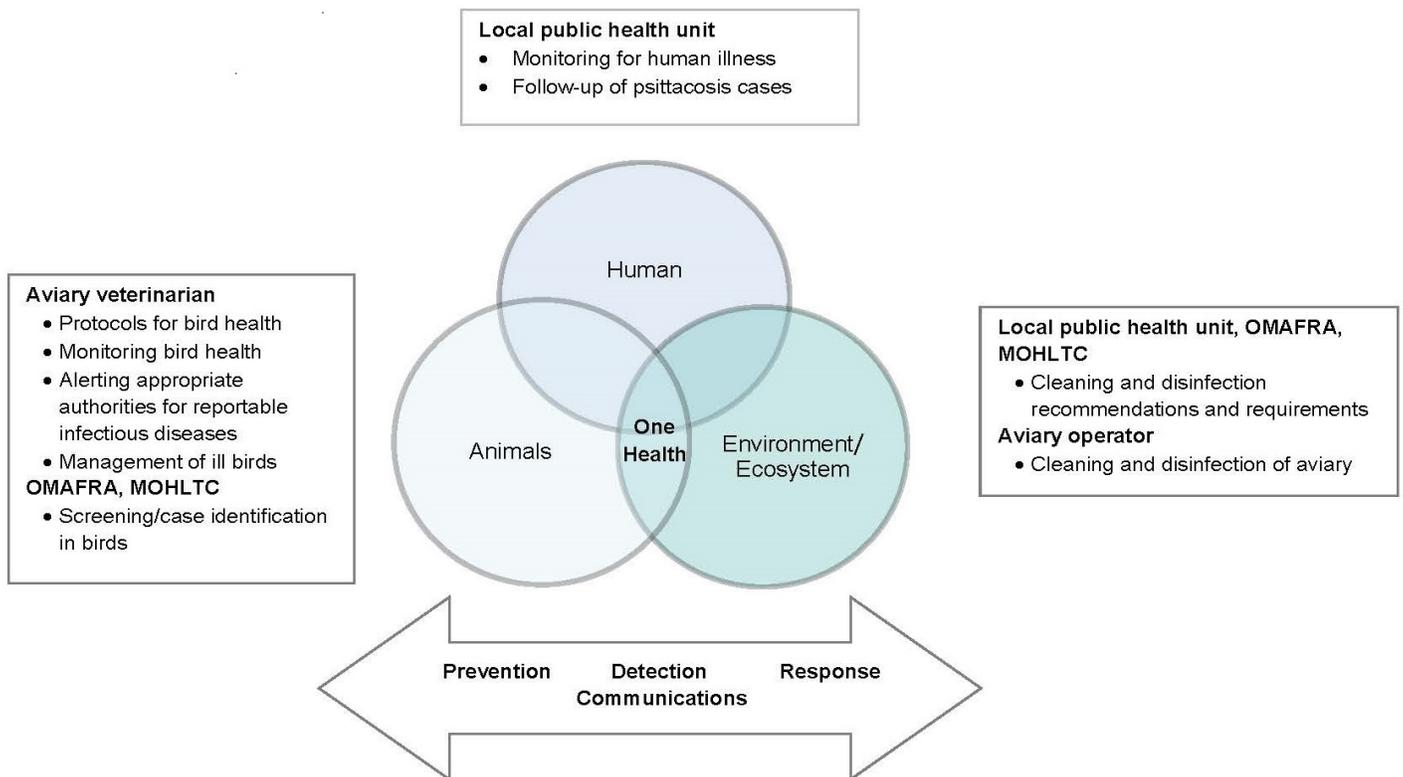
Abbreviations: MOHLTC, Ministry of Health and Long-Term Care; OMAFRA, Ontario Ministry of Agriculture, Food and Rural Affairs

among the bird population and to people using the One Health approach of prevention, detection and response.

In order to detect *C. psittaci* in birds, veterinarians from OMAFRA and the aviary veterinarian assessed them for signs of chlamydiosis. They collected fecal samples and pharyngeal swabs from the lorikeet population and pooled fecal samples from all other species in the same air space as the lorikeets. All samples were tested for *C. psittaci* by RT-PCR (Animal Health Laboratory, Guelph, ON).

Interventions

Public health inspectors assessed the facility to determine the potential risk of psittacosis to visitors and to workers at the aviary and to determine the best actions to minimize or eliminate the risk of transmission from birds to people.

Three main approaches were used: 1) treating of potentially infected birds; 2) environmental cleaning of the aviary for bird secretions; and 3) restricting human contact until all birds were treated.

Birds in the aviary were treated with doxycycline for 24 days (with drug delivery in nectar for lorikeets and in water for the other birds).

Wood shavings were removed from all the cages and incinerated. A disinfectant with bactericidal, virucidal and fungicidal properties was used for the environmental cleaning of the birdcages and the parts of the exhibit open to the public. Because there are no clear guidelines, there was much discussion about disinfecting the plant life, soil, porous and irregular surfaces. Given that the lorikeets were caged and did not come in direct contact with the public, other bird species, plant life or soil, we elected to leave the plants intact, disinfect surfaces where possible and monitor for signs of human or animal illness.

Under the *Animal Health Act* (11), a detention order was issued stopping any movement of birds off the premises and conditions were set to incinerate all waste.

Surveillance data for respiratory syndromes in people were reviewed for signals that may have been attributable to *C. psittaci*. A risk assessment identified the aviary workers as having the greatest exposure and highest risk of contracting psittacosis, the public having no direct contact with birds or their cages, and so the investigation focussed on worker health. Aviary workers were educated and asked to monitor for symptoms and signs during the incubation period and report to their local public health unit if these developed.

Results

The rainbow lorikeet (*Trichoglossus haematodus*) that died was at least nine years old although its exact age was unknown. It was asymptomatic, and trauma was the suspected cause of death because of the observed bruising. Findings on necropsy (localized fungal air sacculitis and hepatitis) led to testing of the liver, spleen and kidney for *C. psittaci* and *Coxiella burnetii*, and the samples were positive for *C. psittaci*. No other avian deaths were reported in the facility in the month prior to notification.

The main aviary contained over 150 birds (32 lorikeets), none of which had any signs of disease. The pooled pharyngeal and fecal samples of all lorikeets were negative for *C. psittaci* by RT-PCR. Five pooled fecal samples taken from other bird species were also negative for *C. psittaci*. The aviary remained closed for eight days while it was cleaned and disinfected and the birds given antibiotic treatment for 48 hours. The detention order was lifted on day 44, after negative post-treatment laboratory results were received.

Human investigation

Emergency department syndromic surveillance systems did not report any activity suggestive of increased pneumonia or respiratory syndromes during the observation period. Ten workers were identified as having had direct contact with the lorikeets or their cage and contents. No staff members were ill in the month prior to or following the death of the lorikeet and, specifically, there were no cases of significant respiratory illness. The local public health unit sent letters to all employees asking them to report any psittacosis-like illness to public health and to seek medical attention for appropriate testing and treatment. No potential cases were identified.

Coordinated multiagency approach for communications

Extensive communications took place between the provincial government ministries (OMAFRA and MOHLTC), the local public health unit, and the aviary operators and veterinarian. As this was the first known case of a possible *C. psittaci* outbreak in an indoor public aviary in Canada, we consulted with the Centers for Disease Control and Prevention and the National Association of Public Health Veterinarians in the United States to gain insight into their experiences with similar investigations. Given the absence of *C. psittaci* spread and lack of active or latent infection in any other birds, veterinarians and public health officials agreed that *C. psittaci* probably did not cause the bird's death and that appropriate steps had been taken to minimize the risk of spread in the event the bird was shedding prior to death.

Discussion

To our knowledge, this is the first report of an avian chlamydiosis outbreak investigation in a public aviary in Canada. A review of the literature found only a small number of published outbreak investigation reports worldwide. Matsui and colleagues (12) reported an outbreak of psittacosis associated with an indoor bird park in Japan, resulting in 17 human cases. Schlossberg and colleagues (13) described 13 human cases of psittacosis attributed to an aviary in a church basement. Small outbreaks have also been reported following bird shows, such as the 18 people who developed psittacosis after visiting a bird show in the Netherlands (14) and 2 confirmed (along with 46 probable and possible) cases following a bird fair in France (15). Outbreaks have also been reported in outdoor aviary settings, such as in Megellanic penguins at the San Francisco Zoo, with no human cases reported (16). These outbreaks have demonstrated that birds without clinical signs may be infectious. However, unlike the outbreaks described in previous reports, the incident we investigated did not result in an outbreak for a number of possible reasons: the bird had minimal shedding or was infected

with a low virulence strain; the public did not have direct contact with the lorikeet; the building ventilation was adequate; and/or practices to maintain a clean aviary environment were in place.

As with any complex investigation, multiple challenges occurred and questions remained. Evidence of the survival of *C. psittaci* in the environment and the role of plant vegetation as a fomite was lacking. The aviary had significant amounts of live vegetation that regularly comes in contact with bird feces and discharges, but which visitors do not contact. In addition, the lorikeets remained in their cage and did not come in direct contact with the vegetation or the public. As mentioned previously, we elected to focus on cleaning the cages and changing the shaving materials in the lorikeet cage and left the vegetation in place suspecting its role in transmission to the public would be minimal given the lack of direct contact. We were fortunate that no further bird or human cases presented. Had this occurred, it may have been more difficult to differentiate between ongoing spread in the bird population and the role of fomites.

A full treatment course for avian chlamydiosis is usually 30 to 45 days (5). Given that this investigation focussed on a public aviary, significant business would have been lost if the aviary had remained closed for the entire duration of treatment. Economics are an important consideration in a One Health approach and, after researching the literature and consulting with an expert, we elected to allow the aviary to re-open after the birds had been treated for 48 hours, as significant organism shedding decreases after this time (*5; Personal communication. Beaufrère H., Ontario Veterinary College; 2013*).

Lastly, whether the dead lorikeet had active or latent infection, with implications for shedding, and the lack of experience in managing avian chlamydiosis in public aviaries led to resources being devoted to an investigation where it was likely the dead bird had latent infection that may never have led to an outbreak. Further research to understand risk factors for outbreaks of *C. psittaci* and most effective interventions to prevent and manage cases of *C. psittaci* would help target prevention measures and allocate resources appropriate to the response.

This investigation was strengthened by multiple jurisdictions working together using a One Health approach (**Figure 1**). Veterinarians detected the potential for a psittacosis outbreak and informed public health. A coordinated response to limit the spread of disease between birds and to people was initiated, which included antibiotics for birds with latent infection, infection control measures at the aviary, and surveillance for avian and human cases of infection. Finally, measures to prevent future outbreaks were considered, including ongoing surveillance in the aviary, biosecurity and ongoing quarantine procedures for birds introduced to the aviary, and improved access to alcohol-based hand rub for staff and visitors to the aviary.

By considering the animals, people and environment/ecosystem involved, One Health can provide a framework for risk minimization whereby multiple threat pathways are considered and managed, leading to a potentially more rapid or effective public health response. However, this also has a downside. Significant resources were used to investigate a single case of *C. psittaci* that was likely latent infection with minimal outbreak potential.

Future outbreak investigations and successful collaborations will benefit from motivated owners/operators/veterinarians working with various public officials representing human and animal health; a clear understanding of roles and responsibilities within a One Health framework; pre-existing communications protocols or channels to support collaboration; access to centralized expertise given the rarity of psittacosis outbreaks; and incorporation of further scientific evidence to support decision making as it becomes available. The use of the One Health approach, while useful in this outbreak investigation, would also benefit from analysis over time of use, and possibly the development of response protocols that may be more proportionate to assessed level of risk.

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Preparing for local mosquito-borne transmission of Zika virus in the United States

Source: **Vital Signs: Preparing for Local Mosquito-Borne Transmission of Zika Virus — United States, 2016**. MMWR Morb Mortal Wkly Rep 2016;65:352. DOI: http://dx.doi.org/10.15585/mmwr.mm6513e1.

On April 1, 2016, CDC hosted a 1-day Zika Action Plan Summit, which focused on awareness and planning for U.S. state and local jurisdictions most likely to face mosquito-borne transmission of Zika virus in the coming months. The Commonwealth of Puerto Rico, U.S. Virgin Islands, and American Samoa are already experiencing active mosquito-borne Zika virus transmission at varying levels. The U.S. government convened this summit to provide senior state and local government officials with information, plans, and tools to improve Zika preparedness, and an opportunity for them to develop effective response plans for their jurisdictions.

Persons who are planning travel should visit CDC's Travelers' Health site (http://wwwnc.cdc.gov/travel/page/zika-travel-information) for the most up-to-date travel information. Areas with active Zika virus transmission are likely to change over time and might include locations not yet listed. CDC has published interim guidelines and additional updates on Zika virus disease and will continue sharing information as more is learned.

Yellow fever in Angola

Source: Public Health Agency of Canada. Travel Health Notice: **Yellow fever in Angola**. http://www.phac-aspc.gc.ca/tmp-pmv/notices-avis/notices-avis-eng.php?id=159

The Ministry of Health of Angola is reporting an ongoing outbreak of yellow fever, primarily in Luanda province. The outbreak started in December 2015 in the municipality of Viana and has since spread to other provinces.

Yellow fever is a serious and occasionally fatal disease. It is caused by a virus which is spread to humans by infected mosquitoes. Symptoms can include fever, chills, headache, muscle pain (mostly back pain), yellowing of the skin and eyes (jaundice), loss of appetite, nausea and vomiting.

Yellow fever transmission occurs in Africa and South America. The government of Angola requires that travellers over 9 months of age show proof of yellow fever vaccination to enter the country.

The Public Health Agency of Canada recommends that travellers get vaccinated against yellow fever 6 weeks before travel and protect themselves from mosquito bites if travelling to Angola.

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