

LABORATORY TRENDS



29 January, 2016

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Laboratory News

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Zika virus Guidelines

The Public Health Agency of Canada and CDC Atlanta have issued a travel notice regarding the Zika virus that has been associated with birth defects in Brazil and other countries. Zika virus infection is transmitted by infected mosquitoes (*Aedes aegypti* and *albopictus*). Zika is a flavivirus, closely related to West Nile virus and dengue virus, but had been associated with less severe clinical illness.

As of January 22, 2016, the US CDC recommends that pregnant women avoid travel to destinations that are known to have Zika virus outbreaks. These are: Barbados, Bolivia, Brazil, Cape Verde, Colombia, Dominican Republic, Ecuador, El Salvador, French Guiana, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Martinique, Mexico, Panama, Paraguay, Puerto Rico, Saint Martin, Samoa, Suriname, and Venezuela.

The BC Centre for Disease Control Public Health Laboratory (BCCDC PHL) has confirmed two BC cases that involved foreign travel: one from El Salvador and second from Columbia.

So far, there is growing evidence of an association between Zika virus infection and microcephaly in the fetuses/neonates of infected women as well as with Guillain-Barre syndrome. Only about 1 in 5 people infected with Zika develop symptoms. Symptoms can include fever, headache, conjunctivitis and rash, along with joint and muscle pain. The illness is typically mild and lasts only a few days.

Treatment is supportive and can include rest, fluids, and use of analgesics and antipyretics. Fever should be treated with acetaminophen. Severe disease requiring hospitalization is uncommon.

Laboratory testing:

Zika virus RNA may be present in a patient's blood for about a week after symptom onset. If symptoms have resolved, diagnosis is based on the detection of Zika specific antibodies. There are no commercial diagnostic tests for Zika antibody. In addition, infection with other flaviruses such as yellow fever virus, including yellow fever vaccination, dengue and West Nile virus can generate cross-reacting antibodies.

Testing is not recommended without a travel history to an area with Zika virus transmission. Pregnant women with a history of travel to an area with Zika virus transmission and who report two or more symptoms consistent with Zika virus infection (acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis) during or within 2 weeks of travel, or who have ultrasound findings of fetal microcephaly or intracranial calcifications, should be tested for Zika virus infection.

Sample collection instructions:

- 1) During acute symptomatic infection collect:
 - a. 5ml EDTA purple top blood tube
 - b. 5 ml gold top serum separator tube
- 2) If symptoms have resolved collect:
 - a. 5 ml gold top serum separator tube only

Please provide both the travel and clinical history, including the date of onset of symptoms. The onset date is extremely important to ensure appropriate testing.

Send samples with relevant history to the BCCDC PHL.

Advice to British Columbians:

Pregnant women travelling to South America should read travel health advisories released by the Public Health Agency of Canada. Precautions against mosquito bites such as use of mosquito repellents, nets, etc., are recommended (see URL below outlining mosquito repellents). As BC does not have the specific mosquito vector, local transmission is very unlikely and thus the local public health implications will be limited.

Further information:

<http://www.phac-aspc.gc.ca/phn-asp/2016/zika-eng.php>

http://www.cdc.gov/mmwr/volumes/65/wr/mm6503e1er.htm?s_cid=mm6503e1er_e

http://www.paho.org/hq/index.php?option=com_topics&view=article&id=427&Itemid=41484&lang=en

http://ecdc.europa.eu/en/healthtopics/zika_virus_infection/factsheet-health-professionals/Pages/factsheet_health_professionals.aspx

<http://www.cdc.gov/westnile/faq/repellent.html> (the US EPA does not recommend any additional precautions for repellent use by pregnant or nursing women)

http://www.paho.org/hq/index.php?option=com_content&view=article&id=11605%3A2016-paho-state-ment-on-zika-transmission-prevention-&catid=8424%3Acontent&lang=en

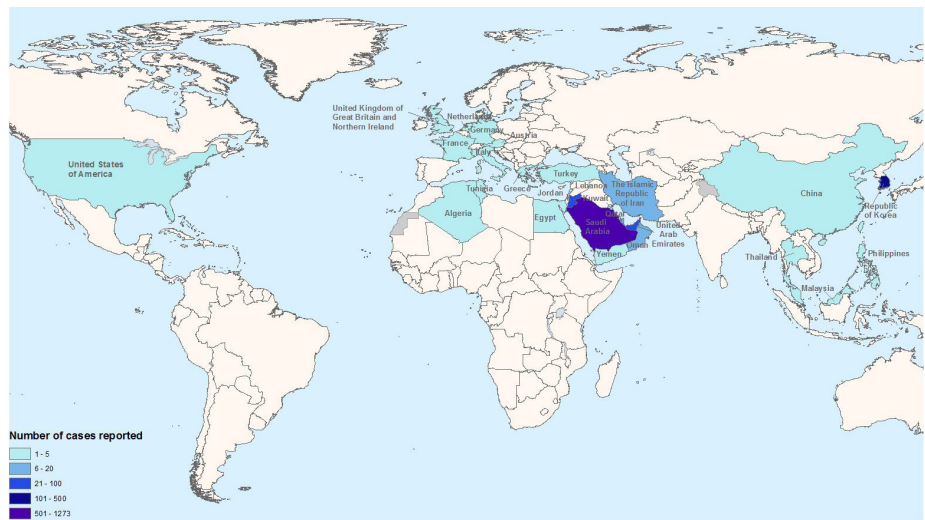
MERS-CoV Epidemiology Update and Specimen Sample Acquisition Guidelines

Middle East respiratory syndrome (MERS) is a viral respiratory disease of humans caused by the recently discovered MERS-coronavirus (CoV). MERS-CoV is a zoonotic pathogen that is thought to have originated in bats with subsequent transmission to camels, the latter which are the major reservoir of the virus. Transmission occurs most frequently through close contact with an infected individual. Much like SARS-CoV, healthcare workers are at a greater risk of infection of MERS-CoV, highlighting the need for strict adherence to infection control guidelines. Furthermore, recent evidence suggests that environmental and medical device contamination of MERS-CoV may be found up to 96 hours after contact with an infected individual, suggesting these surfaces may be fomites for transmission (1). Symptoms of MERS are often

non-specific and include fever, cough, dyspnea, and pneumonia, but may progress to respiratory failure, shock, multi-organ system failure, and death (2-4). Cases have occurred in both women and men of all ages (range 0-99, median 50 years of age) but severity increases with age and in those with co-morbidity. MERS has a case fatality rate of around 36% (2,3). The virus was first identified in 2012 in Saudi Arabia and as of 4 January, 2016, the World Health Organization (WHO) was notified of 1,625 laboratory-confirmed cases of MERS-CoV infection (3). The majority of cases have been reported in or near the Arabian Peninsula where MERS-CoV is endemic, but imported cases have been confirmed in Africa, Europe, Asia, and North America related to travel to endemic regions. The largest outbreak occurring outside of Saudi Arabia

was in South Korea from May-December, 2015, with 186 confirmed cases and 38 deaths (5). So far, there have been no cases of MERS-CoV in Canada. Figure 1 below depicts a global map of countries with confirmed cases of MERS-CoV, current as of 18 December, 2015.

Figure 1
Confirmed cases of MERS-CoV, 2012-2015 (adapted from WHO, www.who.int/emergencies/mers-cov/en/)



In BC, MERS-CoV testing was implemented in late 2013. Detection of viral RNA is done through a real-time reverse-transcription PCR assay targeting the upE gene. This assay is based on the one published by Corman et al. in Eurosurveillance (6). Since testing began, the BCCDC PHL has tested eight samples in 2013, 33 samples in 2014 and 22 samples in 2015 (total = 63 tests performed), all of which were found to be negative. Excluding samples of unknown specimen type, 57% of the samples tested by the BCCDC PHL were nasopharyngeal or oropharyngeal swabs.

Specimens collected from the lower respiratory tract have been found to contain the largest viral load, likely because the receptor for MERS-CoV (dipeptidyl peptidase 4) is expressed in lower respiratory bronchiolar epithelium (7,8). Accordingly, the WHO recommends that **both lower respiratory samples (bronchoalveolar lavage, tracheal aspirate or sputum sample) and upper respiratory samples (nasopharyngeal and oropharyngeal swabs) be collected for investigation of MERS-CoV** to optimize the sensitivity of viral detection (9). We remind clinicians to supply both upper and lower samples if possible and to continue to comply with infection control guidelines when collecting samples.

Works Cited

1. Seo YB, Heo JY, Song M-S, Lee J, Kim E-H, Park S-J, et al. Environmental Contamination and Viral Shedding in MERS Patients during MERS-CoV Outbreak in South Korea. Clin Infect Dis. 2015;29.
2. WHO | Middle East respiratory syndrome coronavirus (MERS-CoV). World Health Organization; [cited 2016 Jan 5]; Available from: <http://www.who.int/mediacentre/factsheets/mers-cov/en/>
3. WHO | Middle East respiratory syndrome coronavirus (MERS-CoV) – Saudi Arabia. World Health Organization; [cited 2016 Jan 5]; Available from: <http://www.who.int/csr/don/4-january-2016-mers-saudi-arabia/en/>
4. Middle East Respiratory Syndrome (MERS): MERS Clinical Features. Atlanta, GA: Centers for Disease Control and Prevention; 2015.
5. WPRO | Middle East respiratory syndrome coronavirus (MERS-CoV). WPRO | WHO Western Pacific Region; [cited 2016 Jan 5]; Available from: http://www.wpro.who.int/outbreaks_emergencies/wpro_coronavirus/en/
6. Corman VM, Müller MA, Costabel U, Timm J, Binger T, Meyer B, et al. Assays for laboratory confirmation of novel human coronavirus (HCoV-EMC) infections. Eurosurveillance. 2012;17(49):20334.

7. Raj VS, Mou H, Smits SL, Dekkers DHW, Müller M a, Dijkman R, et al. Dipeptidyl peptidase 4 is a functional receptor for the emerging human coronavirus-EMC. *Nature* [Internet]. 2013;495(7440):251–4. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23486063>
8. Memish Z a, Al-Tawfiq J a, Makhdoom HQ, Assiri A, Alhakeem RF, Albarak A, et al. Respiratory Tract Samples, Viral Load, and Genome Fraction Yield in Patients With Middle East Respiratory Syndrome. *J Infect Dis* [Internet]. 2014;1–5. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24837403>
9. Laboratory testing for Middle East respiratory syndrome coronavirus (MERS CoV): Interim guidance [Internet]. Geneva: WHO Press; 2015. p. 6. Available from: http://apps.who.int/iris/bitstream/10665/176982/1/WHO_MERS_LAB_15.1_eng.pdf?ua=1

Introduction of a Test for Simultaneous Detection of Respiratory Viruses and Atypical Bacterial Agents

The BCCDC PHL currently screens respiratory virus samples first for Influenza A/B/RSV by a very sensitive in-house developed PCR. In the past, specimens were tested for a broader array of viruses using the Luminex 200 xTAG Respiratory Viral Panel (RVP) fast assay when they were Influenza A/B/RSV negative and (i) <5 years old, (ii) part of an outbreak, or (iii) from a hospitalized patient (per request).

Samples where testing was requested for atypical bacterial agents (*Chlamydomphila pneumoniae*, *Legionella pneumophila*, and *Mycoplasma pneumoniae*) would be tested by an in-house PCR assay.

We recently evaluated the performance of the new MAGPIX NxTAG Respiratory Pathogen Panel (RPP) assay for simultaneous detection of respiratory viruses and atypical bacteria (*C. pneumoniae*, *L. pneumophila*, and *M. pneumoniae*). As of mid-February, 2016 the NxTAG RPP assay will replace the older Luminex assay. Therefore, all respiratory specimens submitted for viral testing will be simultaneously tested for atypical bacterial agents.

For a period of time, a head-to-head, prospective analysis of the in-house atypical bacterial PCR and the new MAGPIX NxTAG RPP will be performed. As a result specimens tested for atypical bacteria will also be tested for respiratory viruses. Results will be provided based on the combination of results obtained from the in-house PCR and the MAGPIX NxTAG RPP assay.

We hope to use this process to determine the validity of using nasopharyngeal or other upper respiratory samples to detect atypical bacteria. Lower respiratory specimens are currently considered to be optimal for detection of atypical bacteria.

Influenza Surveillance

After an initial early start and rise in incidence of influenza A in September a steady decline was noted in October, as previously reported. November saw sporadic incidence of influenza A detection between 0-10%. In December there was a rise of influenza A from 0% to between 4-8% with an increase to 16% by the second week of January. In December and the beginning of January, rates of influenza B display a steady increase from 0.5% to 13% in week 2 of January (Figure 3). Influenza A(H3) remains the dominant subtype detected so far with 21 detections of influenza A(H1N1)pdm09 during November to current.

Figure 3
Respiratory testing volumes and influenza detection rates, Virology Program, BCCDC PHL.

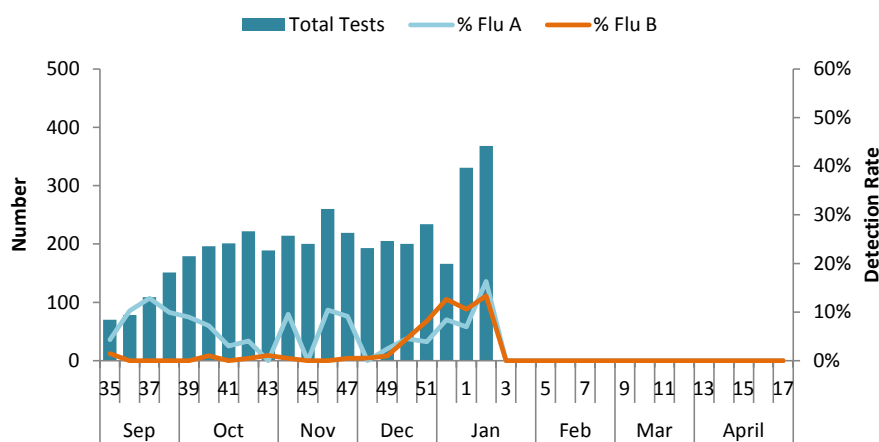
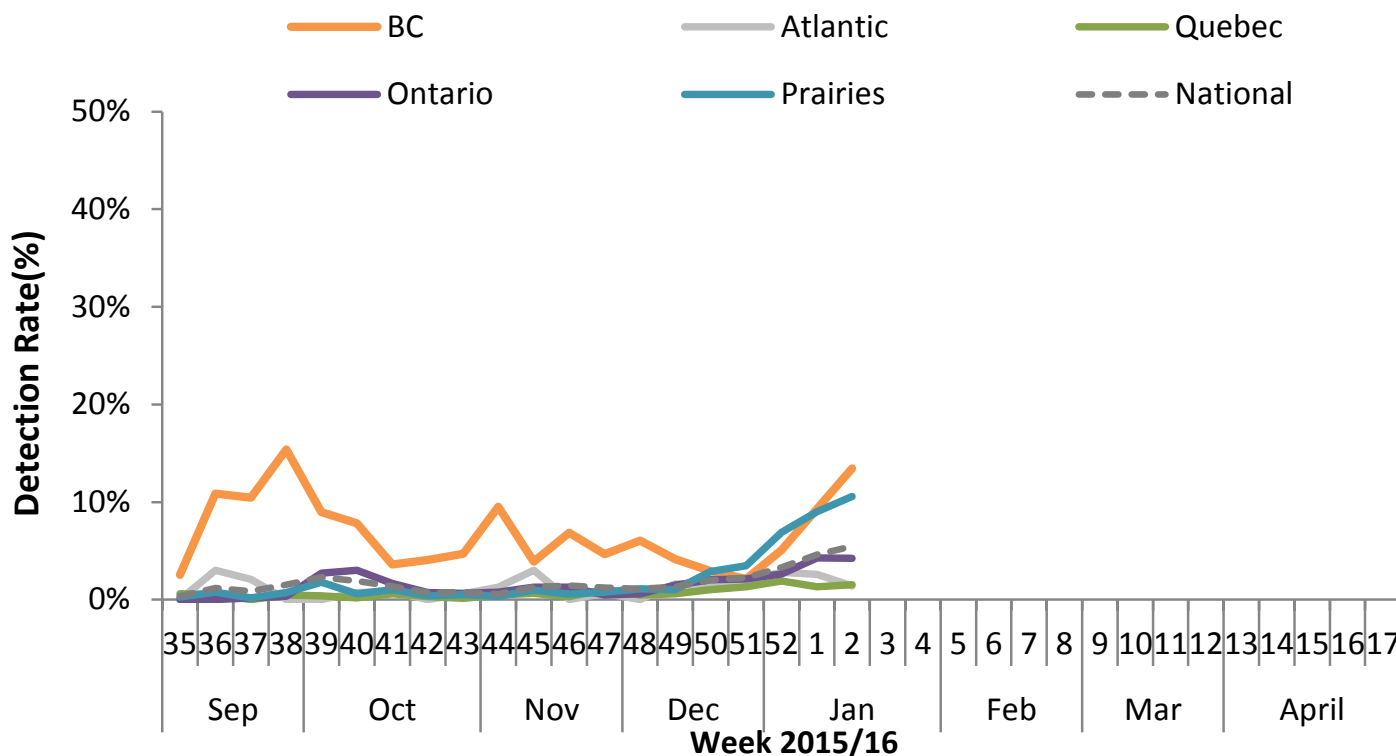


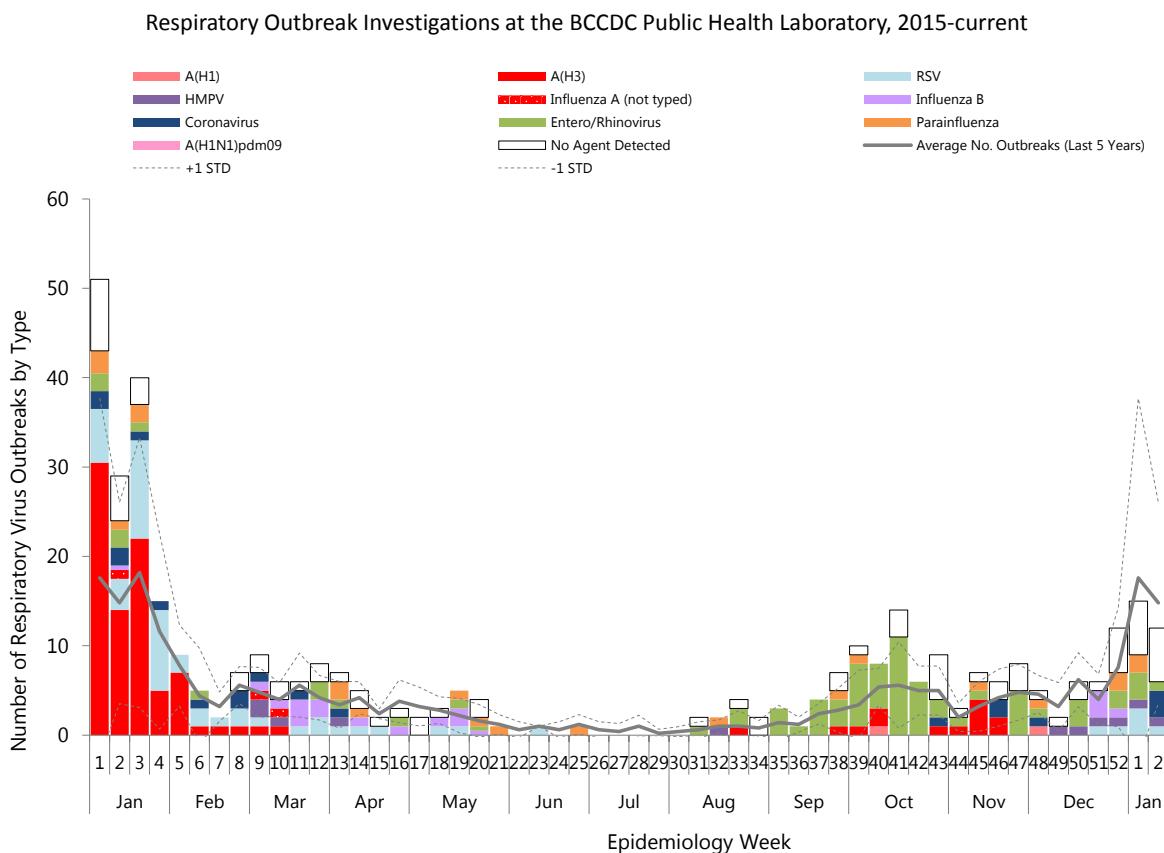
Figure 4
Influenza A detection rates across Canada, September 2015 to present. Data derived from FluWatch reports. Note: Reported detection rates may be different from actual detection rates (Figure 3) if subtyping is completed in subsequent weeks.



Influenza-Like Illness Outbreaks

In November there were 24 influenza-like illness outbreaks investigated by the Virology Program which is slightly above the expected trend (Figure 5). There were seven (29%) detections of entero/rhinovirus, one (4%) detection of parainfluenza, two (8%) detections of coronavirus, and seven (29%) detections of influenza A(H3). In December there were 29 influenza-like illness outbreaks investigated with three (10%) detections of human metapneumovirus, six (21%) detections of entero/rhinovirus, three (10%) detections of parainfluenza, one (3%) detection of respiratory syncytial virus, one (3%) detection of coronavirus, one (3%) detection of influenza A(H1), and four (14%) detections of influenza B. Of the 85 ILI outbreaks reported to the BCCDC PHL during November to current, 78 (92%) were reported from longterm care facilities, four (5%) from hospitals, one (1%) from a community setting, and two (2%) from other settings.

Figure 5
Influenza-like illness outbreaks investigated* in 2015, Virology Program, BCCDC PHL.

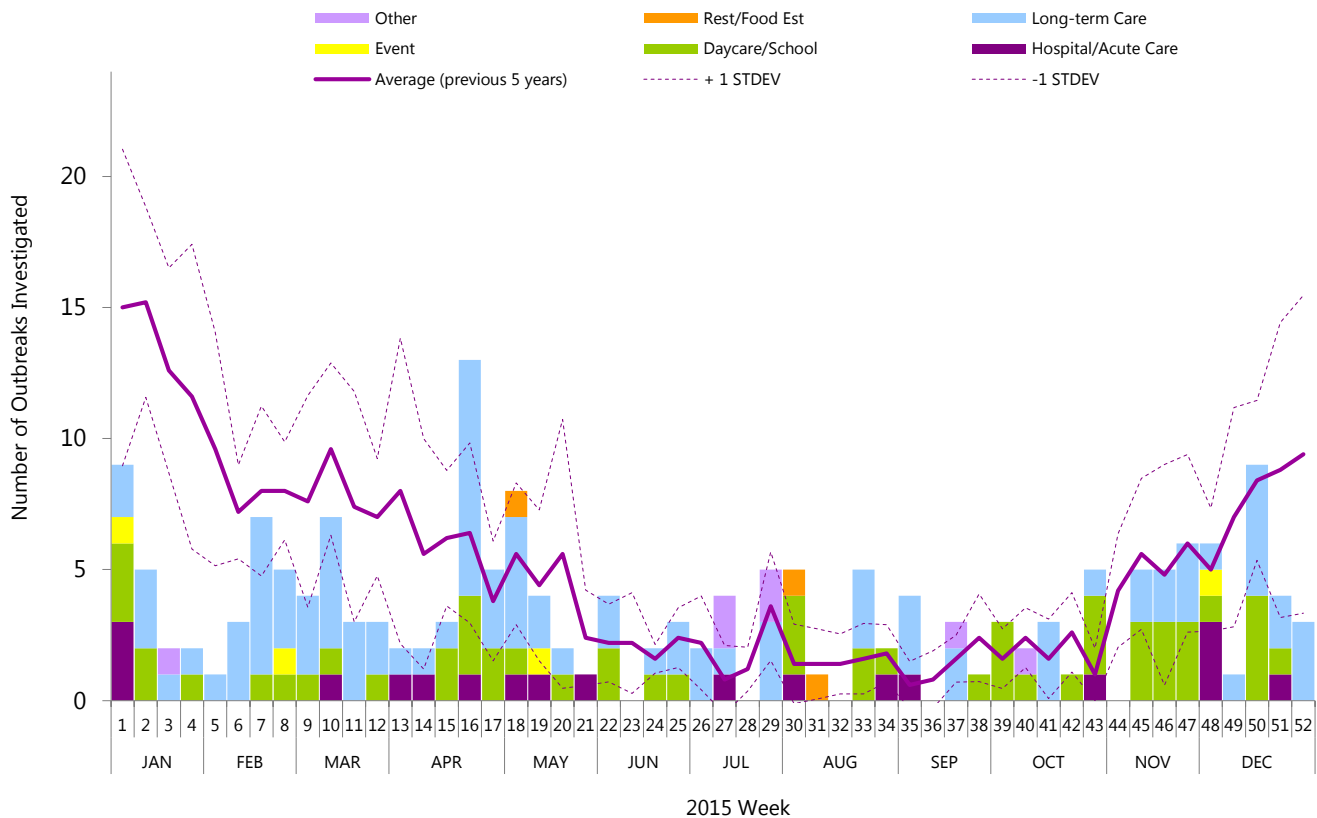


* The data available are from outbreaks in which the BCCDC PHL has been notified. Some acute care microbiology laboratories are also testing for influenza in the province.

Gastrointestinal Outbreaks

In November and December, there were 39 gastrointestinal outbreaks investigated by the BCCDC PHL (Figure 6), within the expected historical trend. Outbreaks were investigated from 19 (48%) LTC facilities, 15 (38%) daycares/schools, four (10%) hospitals, and one (3%) event type. Samples were received from 26 (67%) of these outbreaks with norovirus detected in 16 (41%) outbreaks (12 LTC facilities, three hospitals and one event facility type) and sapovirus detected at two daycares/schools.

Figure 6
Gastrointestinal outbreaks investigated* in 2015, Environmental Microbiology, Public Health
Advanced Bacteriology & Mycology, Parasitology and Virology Programs, BCCDC PHL.



* The data available are from outbreaks in which the BCCDC PHL has been notified. Some acute care microbiology laboratories are also testing for norovirus in the province and these data may not include outbreaks from all Health Authorities. Given the nature of GI outbreaks, samples are not always available for testing.

Invasive Group A *Streptococcus* Surveillance

Invasive Group A *Streptococcus* (GAS) is a bacterium capable of causing mild skin and upper respiratory infections to severe, life threatening infections such as bacteremia, toxic shock syndrome or necrotizing fasciitis. In 2015 there were 187 GAS isolates tested for serology at the BCCDC PHL.

Figure 7 shows the number of GAS isolates sent to the BCCDC PHL for serology with the 6 year historical trend and +/- one standard deviations provided for reference. Test volumes were above the expected trend for all months except for March and December (although data to the end of December were not available at the time of analysis which may make the results from December spurious). Test volumes peaked in May and July with 23 isolates per month and were lowest in March (excluding December) with 10 isolates per month. Of note is that 2015 test volumes were only within the +/- one standard deviation expected margin during September and October (excluding December), meaning during the remaining months, test volumes were either above or below this average.

Figure 7
Invasive Group A *Streptococcus* serology test volumes, 01 Jan-22 December, 2015

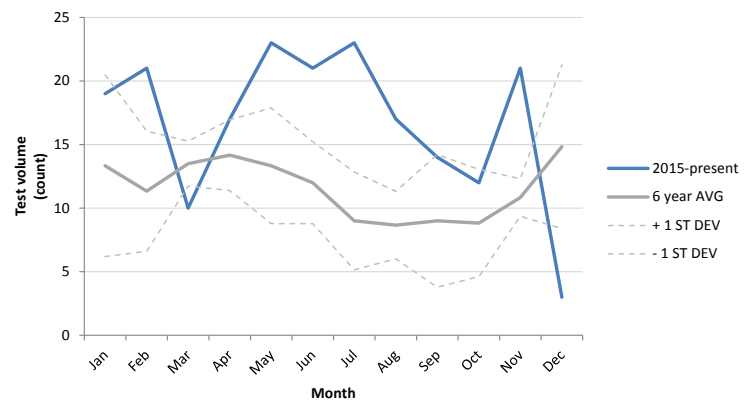
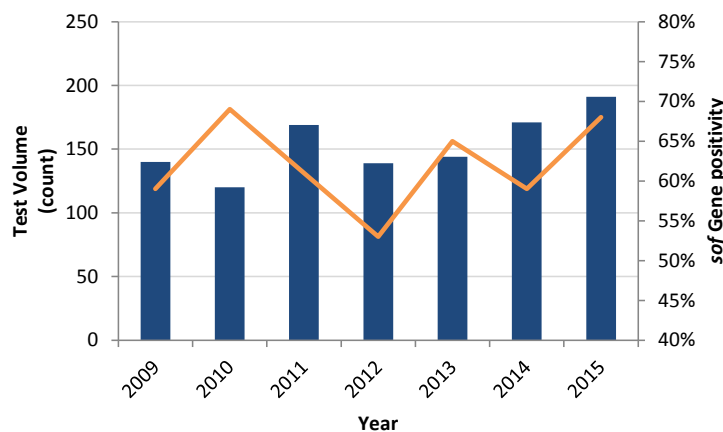


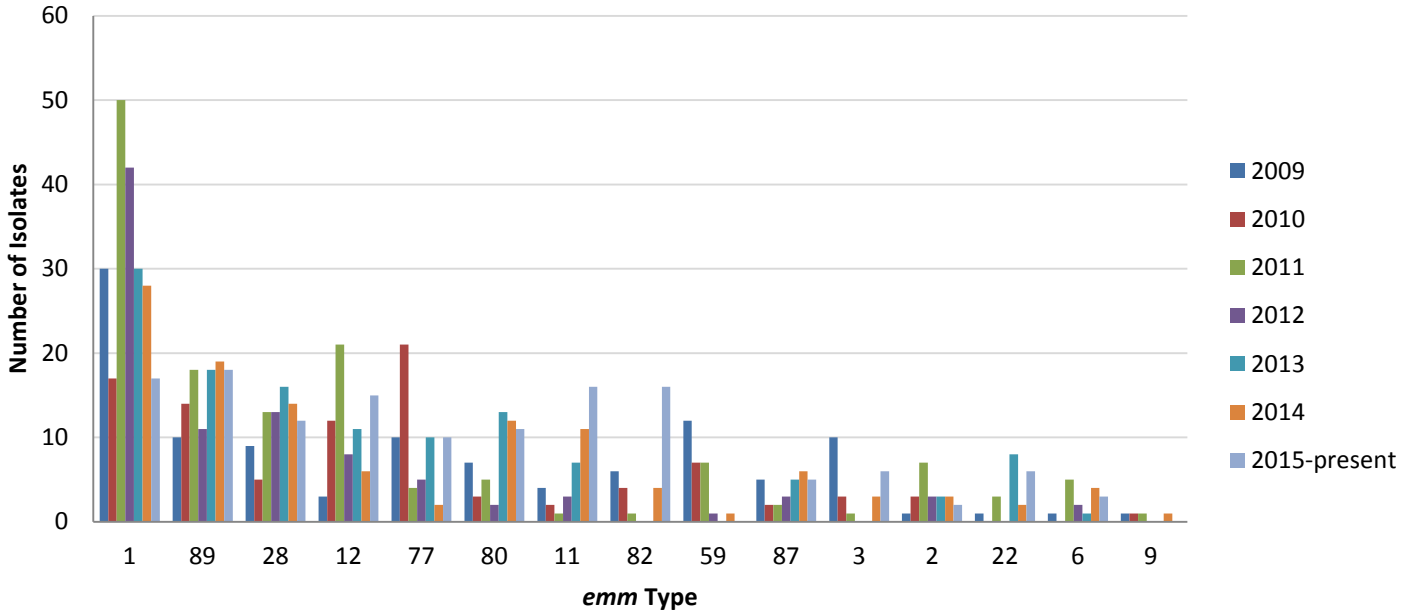
Figure 8
GAS isolate *sof* positivity, 2009-22 Dec, 2015



The GAS *sof* gene encodes the virulent serum opacity factor protein, a cell surface-bound and release protein capable of opacification of mammalian serum. Figure 8 shows the *sof* gene prevalence in GAS isolates tested for serology at the BCCDC PHL during 2009-22Dec, 2015 (GAS test volumes provided as reference). GAS *sof* positivity prevalence varied between 53% (2012) and 69% (2010) during the observed period. The GAS *sof* gene has been found to predict another gene encoding a virulent factor that is useful in serologic identification of GAS, the M gene.

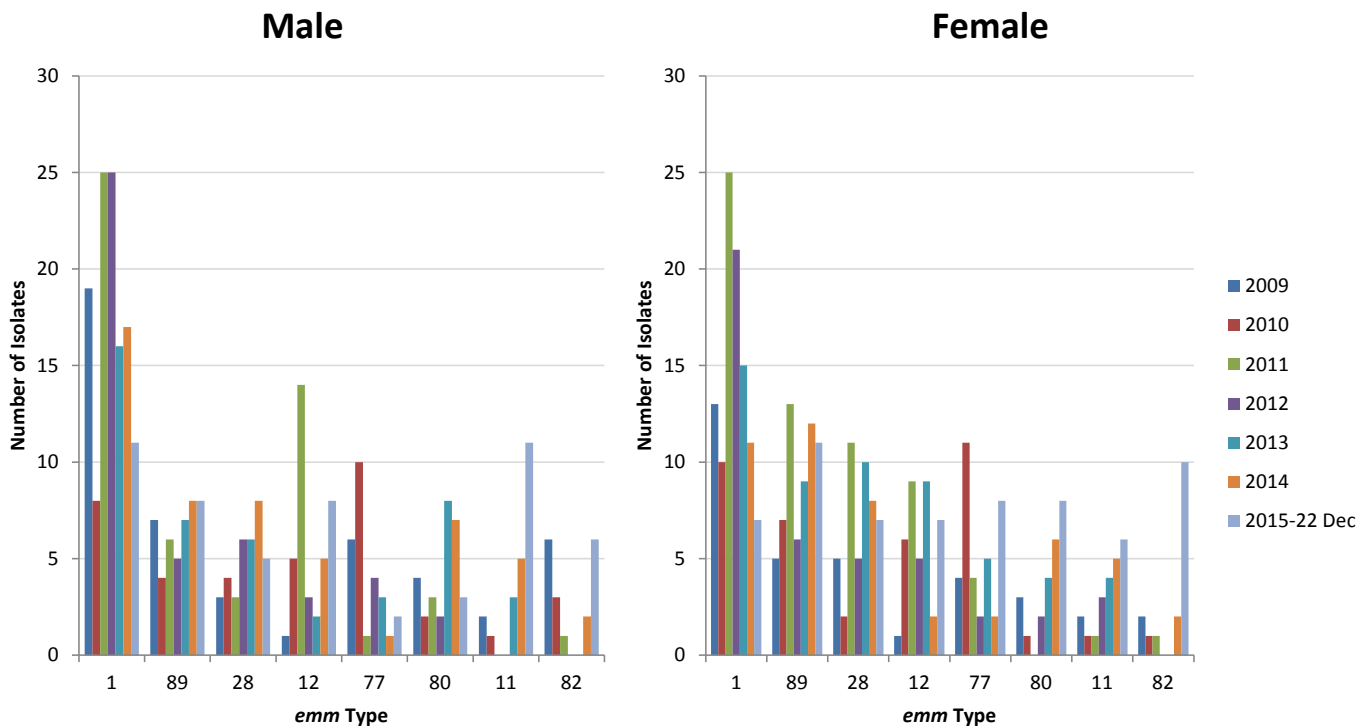
There are around 100 serospecificities of GAS based on the cell surface M virulence protein and *emm* typing utilizes the *emm* gene that encodes for this protein for serotyping. Figure 9 shows the distribution of the 15 most common GAS *emm* types during 2009-22 Dec, 2015. In 2015, *emm* type 89 was most prominent while in previous years *emm* type 1 was most common. Also of note is that *emm* type 11 and 82 were more prevalent when compared to previous year's isolate types.

Figure 9
Most common Invasive Group A *Streptococcus emm* types, 2009-22 Dec, 2015



When stratified by gender we find that *emm* type 89 was most prevalent among females in 2015 and types 1 and 11 were most prevalent among males. Between the observed years, *emm* type 1 was most common among males for years 2009, 2011, 2012-2015 (with type 11, as noted) and type 77 and 12 were most common during years 2010 and 2011, respectively. Observed *emm* types among females show type 77 to be most prevalent during year 2010, type 89 during year 2014 and type 1 most common during all remaining years (Figure 10).

Figure 10
Eight most common Group A *Streptococcus emm* types, 2009-22 Dec 2015, gender stratified



A Report of the BCCDC Public Health Laboratory,

Vancouver, BC

The BCCDC Public Health Laboratory at the BCCDC site provides consultative, interpretative testing and analyses for clinical and environmental infectious diseases in partnership with other microbiology labs and public health workers across the province and nationally. The BCCDC Public Health Laboratory is the provincial communicable disease detection, fingerprinting and molecular epidemiology centre providing advanced and specialized services along with international defined laboratory core functions province-wide.

This report may be freely distributed to your colleagues. If you would like more specific information or would like to include any figures for other reporting purposes, please contact us.

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