November 2016

LABORATORY TRENDS

A Report from the BCCDC Public Health Laboratory

Highlights

Enterovirus-D68 detections in BC

Respiratory pathogen panel testing

***Neisseria gonorrhoeae* susceptibility trends**

Tuberculosis susceptibility trends

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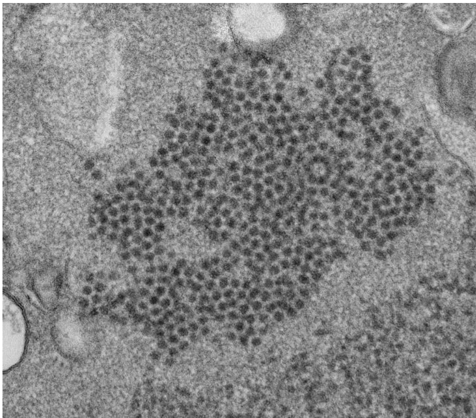
LAB NEWS

Enterovirus-D68 detections in BC



CDC/Cynthia Goldman, Yiting Zhang

During epidemiology week 34 – 42 (21 Aug – 22 Oct, 2016) there have been 38 Enterovirus-D68 (EV-D68) cases (13% positivity based on 290 enterovirus/rhinovirus isolates tested) detected in BC based on laboratory result date. As planned, the BCCDC Public Health Laboratory (BCCDC PHL) began enhanced laboratory testing of EV-D68 in epidemiology week 34 (21-27 August, 2016). All enterovirus/rhinovirus positive specimens identified by the MAGPIX NxTag respiratory pathogen panel, as well as all respiratory specimens collected from pediatric patients <20 years old, are screened by polymerase chain reaction for EV-D68.

Enteroviruses are major causes of respiratory infections each year. Analysis of EV-D68 outbreaks in North America and Europe in 2014 found an association between EV-D68 infection and acute flaccid myelitis in rare cases. EV-D68 infection in children with asthma or reactive airway disease has also been associated with severe respiratory disease requiring intensive case and ventilator support.[1-3] In 2014, 129 EV-D68 cases were reported in the comparable period, including 4 cases with neurologic symptoms and 2 deaths.[4] By contrast, despite systematic testing of all inpatient and outpatient respiratory samples for EV-D68 in August and September, 2015, no cases were found.[4]

Of the 38 laboratory positive EV-D68 cases by week 42 this year, 66% are male (n=25). Age range is <1 to 68 years old, 29 (76%) were detected in children < 10 years old, and 16 (44%) were < 2 years old, compared to 18% during the 2014 outbreak. Cases have been detected in all BC Health Authorities. One infant/toddler presented with neurological symptoms.

By implementing enhanced surveillance of EV-D86 we hope to improve detection and assessment of the burden of this infection among children in BC. Further information on EV-D68 can be found online at the BCCDC website.

Cases have been detected in all BC Health Authorities...one infant/toddler presented with neurological symptoms

References

1. Midgley CM, Watson JT, Nix WA, Curns AT, Rogers SL, Brown B a, et al. Severe respiratory illness associated with a nationwide outbreak of enterovirus D68 in the USA (2014): a descriptive epidemiological investigation. Lancet Respir Med [Internet]. Elsevier Ltd; 2015;2600(2014):1–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26482320

2. Aliabadi N, Messacar K, Pastula DM, Robinson CC, Leshem E, Sejvar JJ, et al. Enterovirus D68 infection in children with acute flaccid Myelitis, Colorado, USA, 2014. Emerg Infect Dis. Centers for Disease Control and Prevention (CDC); 2016 Aug 1;22(8):1387–94.

3. Leshem E. Acute Flaccid Myelitis Among Persons Aged ≤21 Years — United States, August 1–November 13, 2014. Morb Mortal Wkly Rep. 2015;63(53):1243–4.

4. Skowronski D, Chambers C, Sabaiduc S, Murti M, Gustafson R, Pollock S, et al. Systematic community-and hospital-based surveillance for enterovirus-D68 in three Canadian provinces. Eurosurveillance [Internet]. 2015;20(43). Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21283

LAB NEWS

Respiratory pathogen panel testing

The BCCDC PHL screens clinical samples submitted for respiratory virus detection for Influenza A/B/RSV by an in-house developed reverse-transcription polymerase chain reaction (RT-PCR) assay. In the past, specimens were tested for a broader array of other viruses using the Luminex 200 xTAG Respiratory Viral Panel (RVP) fast assay if the Influenza A/B/RSV PCR was negative and the patient met one or more of the following: (i) <5 years old, (ii) part of an outbreak, or (iii) hospitalized (mostly by request). Only samples with requests for atypical bacterial agents were tested by an in-house developed PCR assay for *C. pneumoniae*, *L. pneumophila*, and *M. pneumoniae* (CLM).

Implementation of the MAGPIX assay, a syndromic panel, enhances the detection of respiratory pathogens.

In February 2016, the MAGPIX NxTAG Respiratory Pathogen Panel (RPP) assay replaced the older Luminex assay. This assay detects a full range of respiratory viruses (excluding MERS and SARS) as well as the atypical bacterial agents (see Table 1 for a full list of targets).

Analytical performance of the MAGPIX assay was determined to be equivalent to the older Luminex assay and the in-house CLM PCR in a retrospective evaluation.

From February to May of 2016, 100 samples were tested in a prospective head-to-head evaluation of MAGPIX and the CLM PCR assay. That is, all samples submitted for Luminex testing or CLM PCR were tested by both MAGPIX and CLM assays. The sensitivities and specificities of the CLM PCR and the MAGPIX assay were equivalent. Furthermore, samples sent only for viral testing yielded CLM positives, and samples sent only for CLM testing yielded viral agents. This consolidation into a comprehensive panel improved case detection.

As of August 15, 2016, samples submitted for either CLM or viral detection will both be tested by the MAGPIX NxTAG RPP assay instead of the in-house CLM PCR or the older Luminex assay using a new testing algorithm (Figure 1).

Table 1. Luminex MAGPIX NxTAG RPP assay targets

Viral Targets	Influenza A
	Influenza A H1
	Influenza A H3
	Influenza A 2009 HIN1
	Influenza B
	Respiratory Syncytial Virus A
	Respiratory Syncytial Virus B
	Parainfluenza 1
	Parainfluenza 2
	Parainfluenza 3
	Parainfluenza 4
	Human Bocavirus
	Human Metapneumovirus
	Rhinovirus/Enterovirus
	Adenovirus
	Coronavirus HKU1
	Coronavirus NL63
	Coronavirus OC43
	Coronavirus 229E
Bacterial Targets	*Chlamydophila pneumoniae*
	Legionella pneumophila (all serotypes)
	Mycoplasma pneumoniae

LAB NEWS

Respiratory Pathogen Panel Testing

CDC/Brian Judd

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Respiratory specimens submitted for viral testing will be first tested for Influenza A/B/RSV. If initial results are negative, samples meeting the criteria outlined above [(i) <5 years old, (ii) part of an outbreak, or (iii) hospitalized (mostly by request)] will be tested by the MAGPIX assay, which detects respiratory viruses and atypical bacterial agents.

Respiratory specimens submitted for CLM testing will be analysed by the MAGPIX assay and therefore undergo simultaneous respiratory viral detection.

Only one respiratory sample is required for CLM and/or respiratory viral testing.

Implementation of the MAGPIX assay, a syndromic panel, enhances the detection of respiratory pathogens.

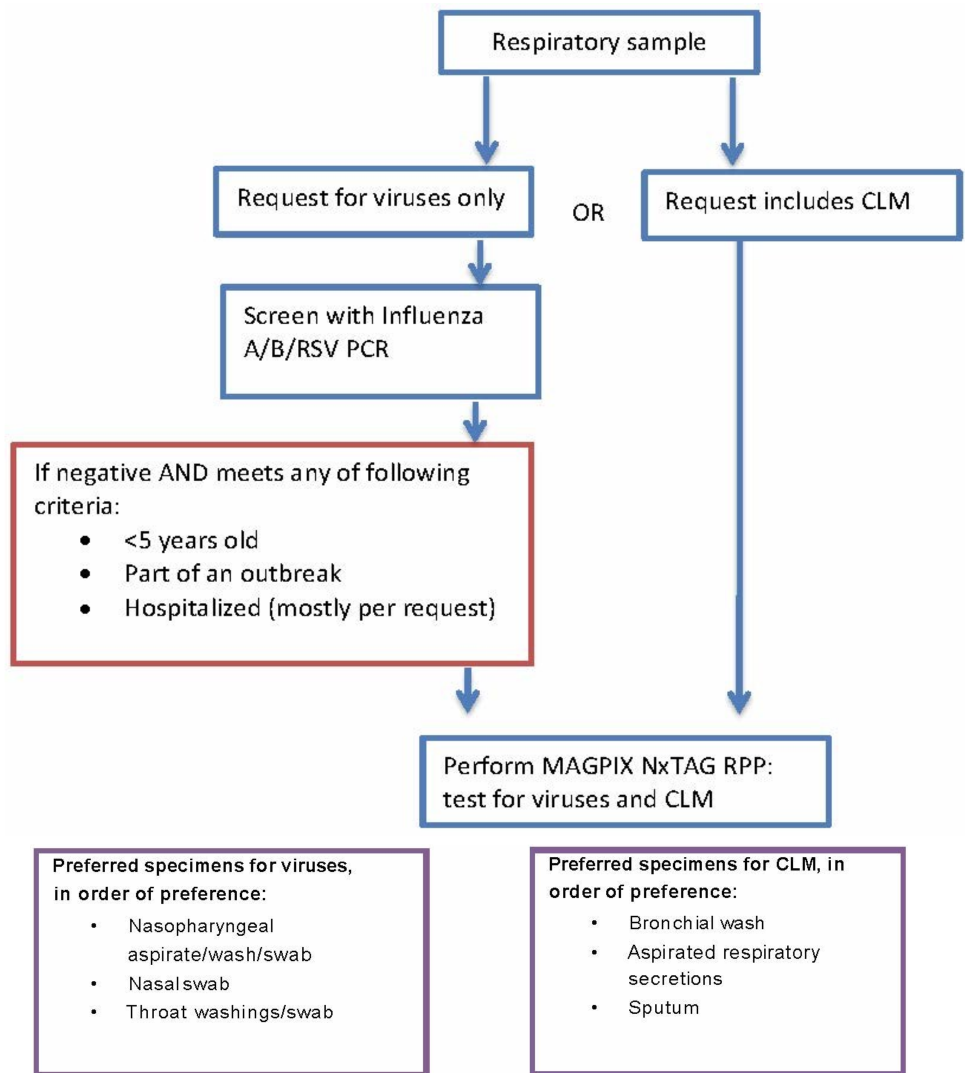
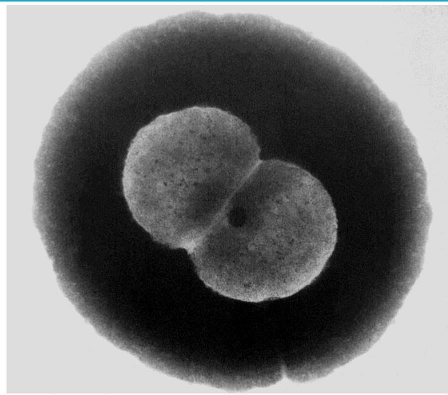


Figure 1. New testing algorithm for respiratory samples

SURVEILLANCE


CDC/Dr. Weisner

Neisseria gonorrhoeae

with Elsie Wong, Jason Wong and Troy Grennan

Gonococcal (GC) infection is a sexually transmitted infection (STI) caused by the gram-negative diplococci, *Neisseria gonorrhoeae* (*N. gonorrhoeae*). In British Columbia (BC), there has been a steady increase in reported GC infections since 1998 with a most notable 70% increase of GC infections in 2015 (3,160 cases) compared with 2014 (1,803 cases). In 2015, the increase was observed among both males and females (Figure 1), in all age groups, and across all health authorities. Although STIs are generally thought to be underreported for subpopulations, particular risk factors for GC infection include sexual contact with a person with confirmed or suspected GC infection; previous GC infection, sex work, street involved youth or homeless populatons.[1,2] Recommended treatment for GC infection involves dual therapy: a third generation cephalosporin (cefixime 800 mg PO in a single dose or ceftriaxone 250 mg IM in a single dose) along with a second agent (azithromycin 1 g PO in a single dose or doxycycline 100 mg PO bid for 7 days).[3]

The BCCDC PHL's Public Health Advanced Bacteriology and Mycology program routinely performs antimicrobial susceptibilities of *N. gonorrhoeae* positive isolates for a panel of antimicrobial agents that include ceftriaxone, cefixime, and azithromycin. The BCCDC PHL participates in proficiency through the National Gonococcal Antimicrobial Comparison Program. The minimum inhibitory concentration (MIC), the lowest concentration of antibiotic required to inhibit *N. gonorrhoeae* growth, is used to assess antimicrobial susceptibility.

Since 2006, 0.5% (21/4,180) of isolates showed an MIC ≥ 0.25 µg/mL to cefixime. Although no isolate was fully resistant to cefixime or ceftriaxone and no treatment failures were reported in BC during this period, an increasing trend in percentage of isolates with elevated MIC (i.e., reduced susceptibility) to cefixime or ceftriaxone was observed in 2006-2010. This trend had reversed in 2011-2015. Similarly, the increasing trend in percentage of isolates with elevated MIC to azithromycin in 2006-2011 also reversed in 2012-2015 (Figure 2).

"The decline observed in 2011-2015 for reduced susceptibility to cefixime or ceftriaxone among tested isolates is encouraging"

The decline in reduced susceptibility to cefixime or ceftriaxone observed between 2011-2015 among tested isolates is encouraging and, may in part be due to population-level replacement of resistant strains with more susceptible strains, as well as changes in the Canadian and provincial gonorrhea treatment guidelines to more effective regimens (i.e., increased cefixime dosage, dual therapy, or improved medication adherence due to single dosage).

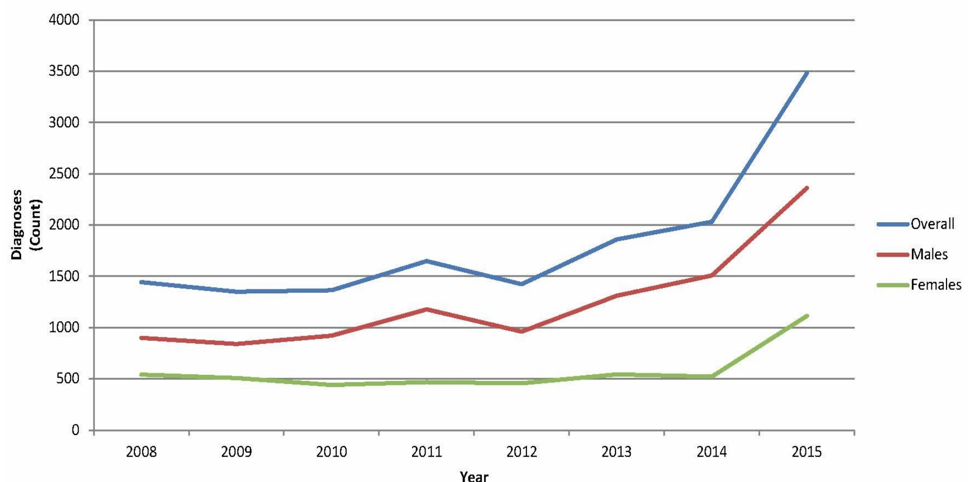


Figure 1. Gonorrhea diagnoses in BC, 2008-2015

Neisseria gonorrhoeae

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These trends will be closely monitored in order to inform future gonorrhea treatment recommendations. The continued threat of emerging resistance reinforces the need for STI prevention and control measures such as increased testing for gonorrhea, partner testing and treatment of gonorrhea, and tests of cure, as well as the need for antibiotic stewardship to ensure effective treatments for bacterial infections.

References

1. Public Health Agency of Canada. The chief public health officer's report on the State of public health in Canada, 2013: infectious disease – the never-ending threat. Ottawa: Public Health Agency of Canada; 2013 Sep. Retrieved from http://www.phac-aspc.gc.ca/cphorsphc-respcacsp/2013/assets/pdf/2013-eng.pdf

2. Public Health Agency of Canada. Canadian guidelines on sexually transmitted infections: gonococcal infections chapter – revised: July 2013. Ottawa: Public Health Agency of Canada; 2013 Jul. Retrieved from http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/assets/pdf/section-5-6-eng.pdf

3. Lester R, Montgomery C, Arnold B, Makaroff S, Spencer A, Ogilvie G. British Columbia treatment guidelines: sexually transmitted infections in adolescents and adults 2014. Vancouver: British Columbia Centre for Disease Control; 2014 Aug. Retrieved from http://www.bccdc.ca/resource-gallery/Documents/Communicable-Disease-Manual/Chapter%205%20-%20STI/CPS_BC_STI_Treatment_Guidelines_20112014.pdf

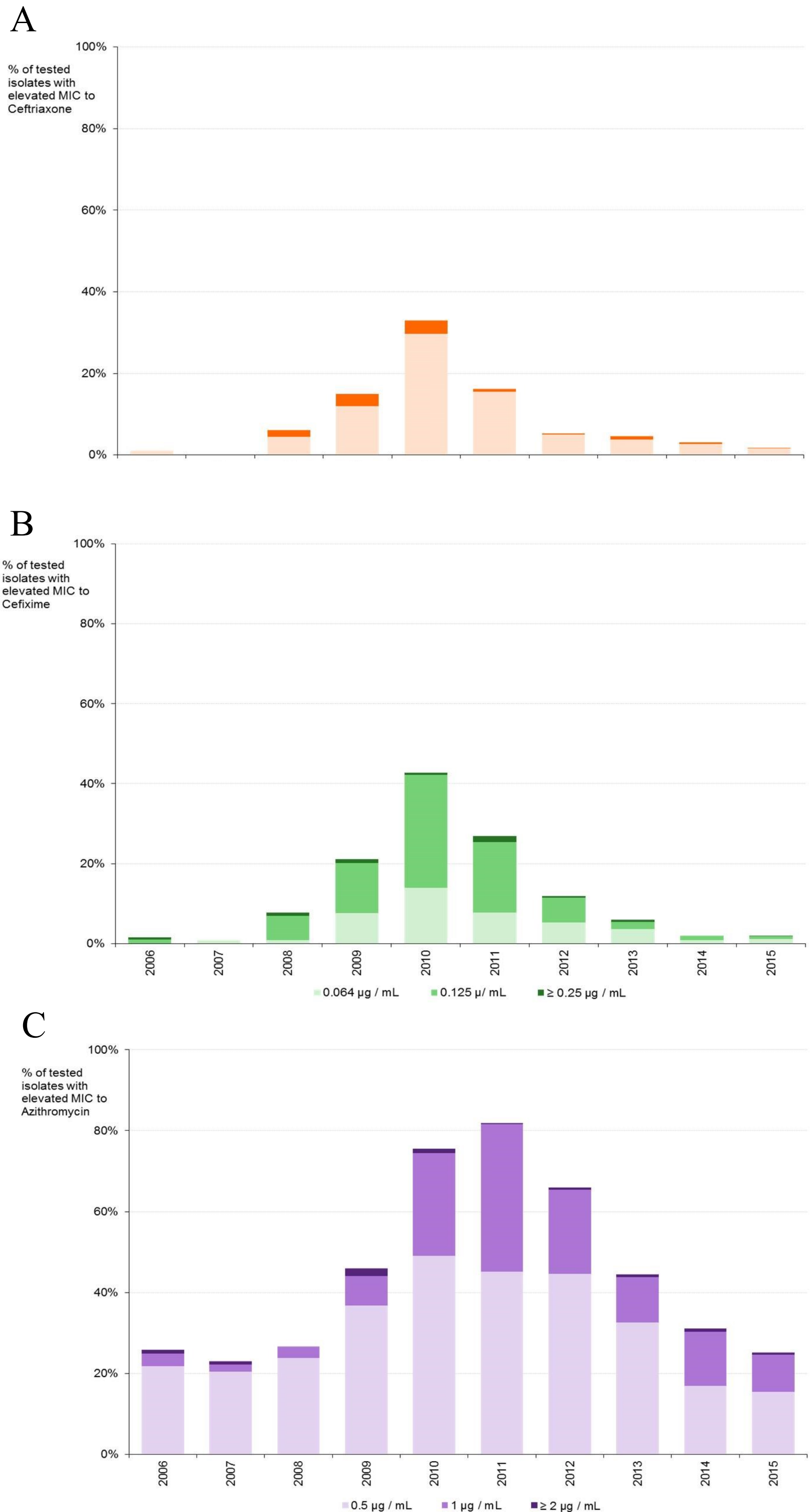
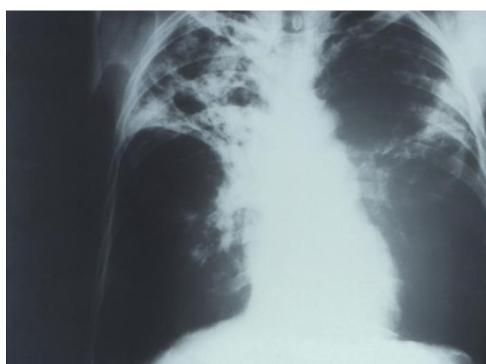


Figure 2. Figure 2. Percentage of tested *N. gonorrhoeae* isolates with elevated minimum inhibitory concentrations (MICs) to Ceftriaxone (A), Cefixime (B), and Azithromycin (C) from 2006- 2015, Public Health Advanced Bacteriology and Mycology Program

SURVEILLANCE



CDC

Tuberculosis

Drug-resistant strains of tuberculosis (TB) pose an emerging threat to control of the disease in Canada. Although estimates of anti-TB drug resistance in Canada and BC are thought to be below global estimates there remains a risk of imported immigrant cases or from residents becoming infected with a drug-resistant strain from travel to areas with a higher prevalence of these circulating strains.[1,2] As such, ongoing TB drug susceptibility surveillance is important locally.

The TB/Mycobacteriology Program of the BCCDC PHL performs *Mycobacterium tuberculosis* complex (MTBC) drug susceptibility testing using the BD MGIT 960 fluorometric proportion method. Isolates are tested against critical concentration levels of first-line anti-tuberculosis drugs including isoniazid (INH, 0.1 µg/mL), rifampin (RMP, 1.0 µg/mL) and ethambutol (RMB, 5.0 µg/mL). Pyrazinamide (PZA) is only performed when isolates show resistance to INH and/or RMP or when requested. Streptomycin, a second line anti-TB drug, is also part of this susceptibility panel.

The resistance patterns of MTBC patient isolates from 2007 to 2015 for BC are shown in figure 1. From 2007 to 2011, mono-resistance to one of the first-line drugs has been on the rise from 7.4% in 2007 to 11.3% in 2011. Although there was a decrease in mono-resistance in 2012 and 2013, mono resistance was 10% in 2014 and 12.6% in 2015. Poly-resistance has varied from 0% to 0.9% of isolates during this period and was observed at 0.4% in 2015. Multi-drug resistance has decreased from a high of 2.2% in 2014 to 0.8% in 2015.

"...mono-resistance has been on the rise [while] multi-drug resistance has decreased"

The TB/Mycobacteriology Program, along with other participating Provincial Laboratories, report results of tuberculosis drug susceptibility testing to the Canadian Tuberculosis Laboratory Surveillance System (CTBLSS) for national monitoring of tuberculosis drug resistance patterns. The various national resistance patterns have shown relative stability from 2007 – 2014 with mono-resistance fluctuating between 6.7% and 9% and multi-drug resistance varying between 0.6% and 1.4% during this period (figure 2). BC has had years (2008 – 2014) where levels of mono resistance have been slightly higher than what CTBLSS has reported nationally.

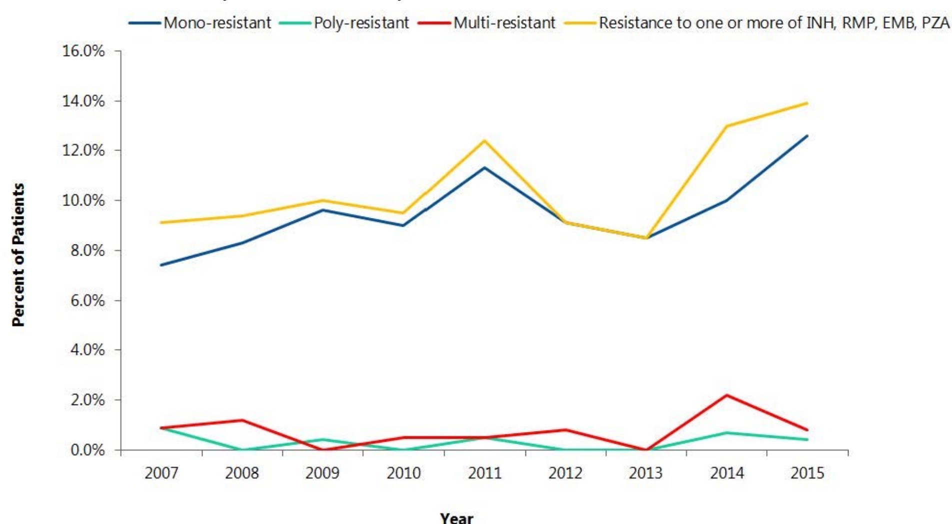


Figure 1: Percent of TB patients who have MTBC isolates that are mono-resistant, poly-resistant and multi-resistant to first-line TB drugs in British Columbia, 2007 – 2015. Resistance profiles are defined as: mono-resistance, resistance to one of the first-line drugs (INH, RMP, EMB or PZA); poly-resistance, resistance to two or more fist-line drugs not including the combination of INH and RMP; and multi-drug resistance (MDR-TB), resistance to at least the two best first-line anti-tuberculosis drugs, INH and RMP, but which does not meet the definition of extensively-drug resistance TB (XDR-TB).

SURVEILLANCE

Tuberculosis

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The World Health Organization reports that in 2014 an estimated 3.3% (95% Confidence Interval (CI): 2.2-4.4%) of new TB cases and 20% (95% CI: 14-27%) of previously treated cases were MDR-TB strains.[2] It is reassuring that BC resistance rates remain below global resistance rates. This confirms the importance of TB drug susceptibility testing to support appropriate prevention and treatment of TB.

References

1. WHO | Global tuberculosis report 2015 [Internet]. WHO. World Health Organization; 2015 [cited 2016 Sep 1]. Available from: http://www.who.int/tb/publications/global_report/en/

2. Tuberculosis: Drug Resistance in Canada 2014 [Internet]. Ottawa, Ca: Public Health Agency of Canada; 2015. Available from: http://healthycanadians.gc.ca/publications/diseases-conditions-maladies-affections/tuberculosis-drug-resistance-2014-resistance-antituberculeux/index-eng.php

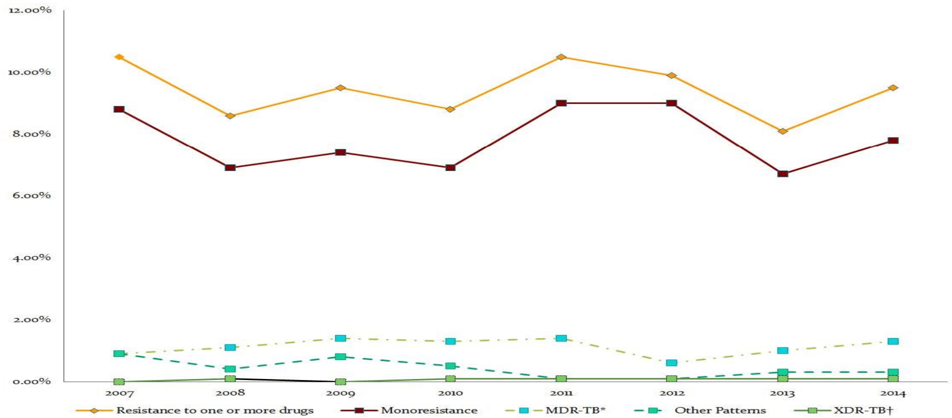


Figure 2: National TB drug resistance patterns as a percentage of isolates tested 2007 – 2014. Source: tuberculosis-drug-resistance-2014-antituberculeux-eng.pdf, Public Health Agency of Canada, Nov 2015.

Zika virus

with Mark McCabe

During 03 January – 22 October, 2016, there were 1,969 individuals in British Columbia (BC) and Yukon Territory (YT) who have been tested for Zika virus (ZIKV). There are 37 confirmed ZIKV cases tested in BC (20 female cases, 17 male cases, three non-BC/YT residents) and overall positivity remains consistant at 2%, all associated with travel to the Caribbean, Central or South America; and 13 persons under investigation (nine females, four males).

Testing volume trends have been variabe, but with a notable increase in test volume during epidemiology weeks 31 – 38 (31 July – 24 September, 2016), likely associated with travel to the Brazil Summer Olympic Games, an area with active autochthonous ZIKV transmission (figure 1).

Testing volume continues to be greatest in females of childbearing age, suggesting populations at risk of vertical transmission of ZIKV represents the largest proportion of those being tested (data not shown).

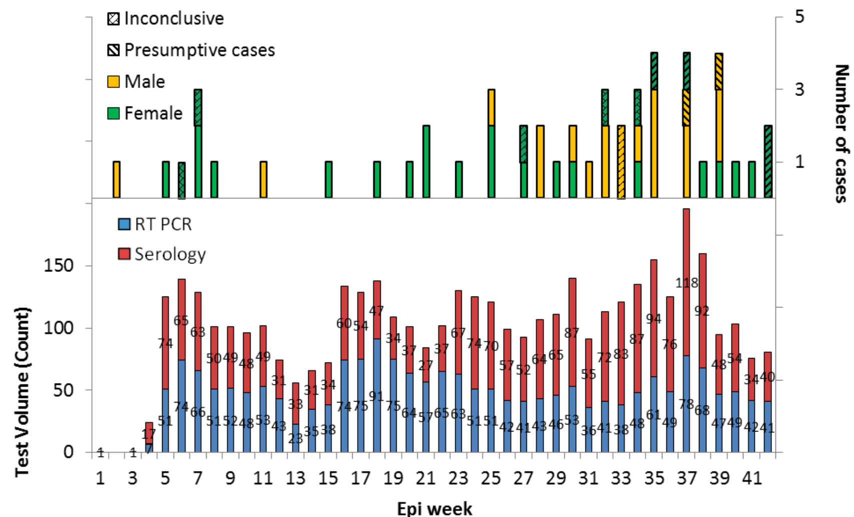


Figure 1. Weekly Volume of Tests for Zika Virus RT PCR and Serology*(Epi Week 1-42** 2016, n=4,262)

*Note: test volume represents number of tests performed, not number of individuals tested, as individuals may be tested by both methods, or may have subsequent testing performed at a different date

**Epi week based on received date of first sample(s) submitted for test volume and based on initial resulted date for cases

SURVEILLANCE

Influenza

BC has experienced earlier than usual influenza activity this season with influenza A(H3N2) being the dominant subtype. Based on result date, there were 83 (12% positivity) influenza detections during epidemiology weeks 40-42 (2 -22 October, 2016) at the BC Centre for Disease Control Public Health Laboratory (BCCDC PHL) compared to the same period the the 2015-16 (n=33, 5%) and 2014-2015 seasons (n=23, 5%) (figure 1). During this period 81 isolates were influenza A(H3N2) subtype and there were 2 influenza B detections. Influenza A activity continues to be higher than other provinces for this period.

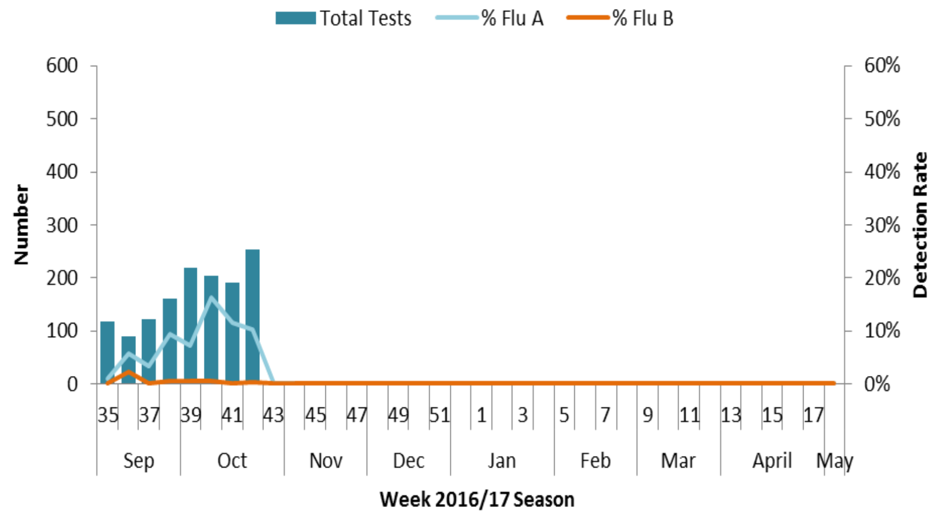


Figure 1. Respiratory testing volumes and influenza detection rates, Virology Program, BCCDC PHL

OUTBREAK

Influenza-like illness

Entero/rhinoviruses have been the dominant agent detected in facility influenza-like illness outbreaks (ILI OBs) reported to the BCCDC PHL so far this influenza season. During epidemiology weeks 40 – 42 (2 – 22 October, 2016) there have been 16 ILI OBs reported to the BCCDC PHL, lower than the 28 ILI OBs reported during the comparable period in 2015. Entero/rhinoviruses were detected in 69% of these ILI OBs during this period, comparable to previous surveillance (79% and 59% in 2015 and 2014, respectively) (figure 1).

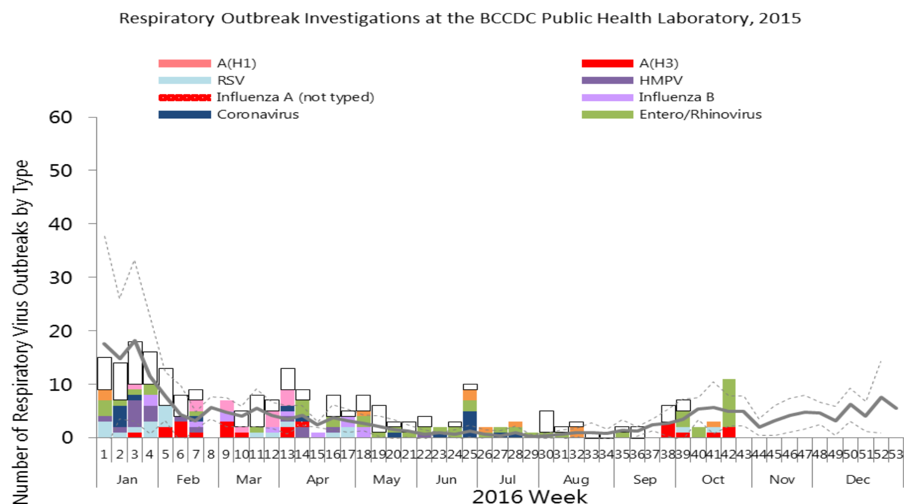
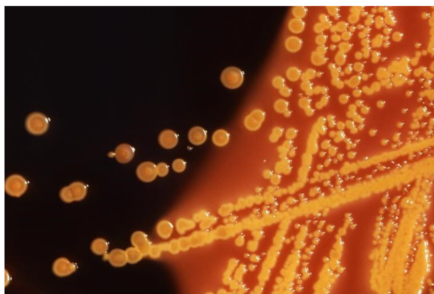


Figure 1. Influenza-like illness outbreaks investigated* in 2015, Virology Program, BCCDC PHL* The data available are from outbreaks in which the BCCDC PHL has been notified. Some acute care microbiology laboratories are also testing for influenza in the province.

SPOTLIGHT

People and papers of the BCCDC PHL

Screening of stool samples for STEC using a pooled nucleic acid amplification test



CDC

In a paper published in the Journal of Clinical Microbiology authors including Drs. Agatha Jassem, Matthew Croxen, Linda Hoang, and Natalie Prystajecky, as well as Ana Paccagnella from the BCCDC PHL; and Katerina Pintar of the Public Health Agency of Canada, with generous support from FoodNet Canada, studied the efficacy of a pooled nucleic acid amplification test (NAAT) to screen for O157 and non-O157 serotypes of Shiga Toxin-producing *Escherichia coli* (STEC). These serotypes of STEC are associated with enteric illness; however, traditional culture-based methods under-detect non-O157 STEC. In both a retrospective and larger prospective study the authors found that performance of a post-enrichment pooling strategy was comparable to testing individuals by NAAT. Furthermore, they found significant consumable cost and labour savings associated with the pooled NAAT approach. This efficient approach can lead to more accurate assessment of underrepresented non-O157 STEC detection and drive public health interventions.

Jassem AN, Chou F, Yang C, Croxen MA, Pintar KDM, Paccagnella A, Hoang L. and Prystajecky N. A Pooled Nucleic Acid Amplification Test for Screening of Stool Specimens for Shiga Toxin-Producing *Escherichia coli*. J Clin Microbiol [Internet]. American Society for Microbiology; 2016 Aug 24 [cited 2016 Sep 1]; doi: 10.1128/JCM.01373-16

Genome Canada Grants

Congratulations to Dr. William Hsiao for receiving two of the 16 national grants – totalling $500,000 – from Genome Canada and the Canadian Institutes of Health Research's 2015 Bioinformatics and Computational Biology Competition. Multiple researchers from the BC Centre for Disease Control will participate on these two projects in collaboration in with researchers from the Public Health Agency of Canada, Simon Fraser University (SFU) and McMaster University. Dr. Hsiao is principal investigator (PI) on the project to develop Genomic Epidemiology Application Ontology (GenEpiO) to improve data integration and sharing of infectious disease surveillance and antimicrobial resistance information across public health agencies; and he is co-PI in developing PathOGIST, a computational tool to improve subtyping of pathogens using public health microbiology data, with computer scientists from SFU.

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GenomeCanada

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.

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