February 2017

BC Centre for Disease Control
An agency of the Provincial Health Services Authority

LM LABS

LABORATORY TRENDS

A Report from the BCCDC Public Health Laboratory

Inside this Issue

LABORATORY NEWS *2*
HCV & HIV testing methodology change
Discontinuing *Mycoplasma* IgM serology
Parechovirus testing for infants

SPOTLIGHT *4*
Detection of influenza in cases of parotitis

SURVEILLANCE *5*
Seasonal influenza
Enterovirus D68
Carbapenemase producing organisms

OUTBREAKS *9*
Gastrointestinal outbreaks
Respiratory outbreaks

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Hepatitis C virus (HCV) & HIV and *Mycoplasma* IgM testing changes

Hepatitis C virus (HCV) & HIV testing methodology change

The BCCDC Public Health Laboratory (BCCDC PHL) performs all HCV RNA testing and HCV genotyping in BC. The laboratory also performs a limited number of HIV RNA tests to help confirm acute HIV infection, in prenatal women and their neonates, and for performing pooled nucleic acid testing of seronegative high-risk patients e.g., men who have sex with men, to detect pre-seroconversion infection.

In January 2017, the Abbott RealTime HCV and HIV-1 viral load assays replaced the Roche Cobas AmpliPrep/Cobas TaqMan HCV (v2) and HIV-1 (v2) tests for HIV & HCV RNA. The Abbott Realtime HCV Genotype II assay also replaced the VERSANT HCV Genotype 2.0 Assay for HCV genotyping.

The analytical performance of the Abbott assays was determined to be equivalent to the currently used tests in a retrospective evaluation. Reporting of HCV and HIV RNA results will not change. There will be a revised comment on HCV reports reflecting the slightly different limit of detection and dynamic range of the Abbott RealTime assay. HCV genotype reports will contain a revised comment reflecting the type of test used. Revised comments are as follows:

HCV RNA quantitative NAT report comment

Previously with Roche test:
The assay is quantitatively accurate between 15 and 100,000,000 IU/mL

Now with Abbott assay:
The assay is quantitatively accurate between 12 and 100,000,000 IU/mL

HCV genotype report comment

Previously with VERSANT test:
By line probe assay

Now with Abbott assay:
By nucleic acid testing

Abbott RealTime HCV and HIV-1 viral load assays replaced the Roche Cobas AmpliPrep/Cobas TaqMan HCV (v2) and HIV-1 (v2) ... Abbott Realtime HCV Genotype II assay also replaced the VERSANT HCV Genotype 2.0 Assay

Discontinuing *Mycoplasma* IgM serology

The BCCDC PHL has been using IgM serology in addition to nucleic acid testing (NAT) for detection of acute *M. pneumoniae* infection. *M. pneumoniae* IgM serology has significant limitations when used for the detection of acute infection. A recent analysis of *M. pneumoniae* IgM serology at the BCCDC PHL demonstrated that up to 70% of prenatal women had reactive *M. pneumoniae* IgM test results. This is consistent with highly variable positivity rates in the general population, ranging between 4%-55% depending on the population's age and the assay used[1,2]. Another challenge is that the laboratory typically does not receive acute and convalescent sera to assess for seroconversion which would help identify recent infections. Ultimately *M. pneumoniae* IgM reactive serologic results are unable to differentiate between acute disease, remote disease or a false-positive test result.

As a result, effective January 2017, testing for *M. pneumoniae* IgM will be discontinued at BCCDC PHL. Acute *M. pneumoniae* infection can, instead, be detected by NAT on respiratory specimens; lower respiratory specimens, such as sputum, are preferred.

If a sample is sent for *M. pneumoniae* IgM serology, the order will be resulted with the following comment:

"*Mycoplasma pneumoniae* IgM serology is no longer available. Reactive test results do not differentiate between acute infections, resolved infections, or false-positive results. If an acute infection is suspected please submit a sputum for *Mycoplasma pneumoniae* nucleic acid testing. If a post-infectious syndrome is considered please consult the BCCDC medical microbiologist at on-call at 604 661-7033."

References:

1. Thurman et al. Comparison of laboratory diagnostic procedures for detection of Mycoplasma pneumoniae in community outbreaks. 2009. Clin Infect Dis 48:1244-9.
2. Nir-Paz R, Michael-Gayego A, Ron M, Block C. 2006. Evaluation of eight commercial tests for Mycoplasma pneumoniae antibodies in the absence of acute infection. Clin Microbiol Infect 12:685–8.

testing for *M. pneumoniae* IgM will be discontinued at BCCDC PHL

Parechovirus testing for infants

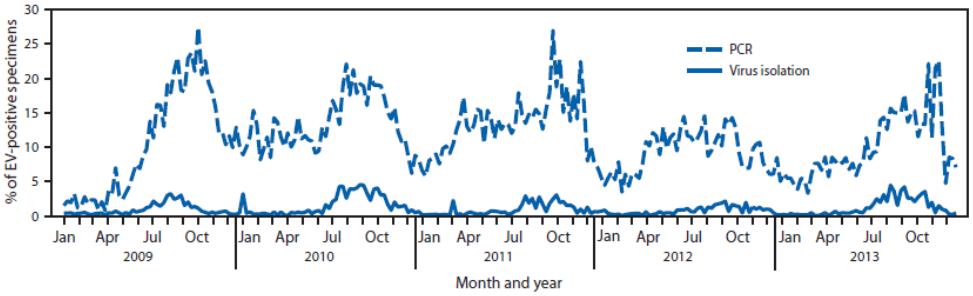
Parechovirus testing from CSF for all infants <6 months of age

Human parechoviruses are ubiquitous viruses that are closely related to enteroviruses and are a relatively common seasonal cause of viral sepsis-like illness and meningoencephalitis in young infants. Seasonality tends to overlap with enteroviruses (late summer to late fall) (Figure 1) and clinical presentation of meningoencephalitis is similar to enterovirus except gastrointestinal symptoms (vomiting and diarrhea) are more common and cerebral spinal fluid (CSF) analysis typically demonstrates absence of pleocytosis[2]. Central nervous system infection is most frequent in the first three months of life and is rare after six months of age. The clinical significance of detecting parechovirus in respiratory and stool samples is not clear given that during the season it is frequently found in well infants[3,4].

For viral testing requests on CSF, the BCCDC PHL tests all samples for enterovirus, herpes simplex virus (HSV) 1 & 2, and varicella zoster virus (VZV) by nucleic acid testing (NAT) while the BC Children's Hospital Microbiology Laboratory tests samples from infants for enterovirus, HSV 1 & 2, and parechovirus. To enhance the detection of parechoviruses in infants, effective January 16, 2017 all CSF specimens sent to the BCCDC PHL for viral testing from infants <6 months of age will be tested for enterovirus, HSV 1 & 2, and parechovirus at BC Children's Hospital. Testing for VZV in this population will be by request. If there are any questions regarding parechovirus testing, please contact the Medical Microbiologist on call at BC Children's Hospital.

all CSF specimens sent to the BCCDC PHL for viral testing from infants <6 months of age will be tested for enterovirus, HSV 1 & 2, and parechovirus at BC Children's Hospital

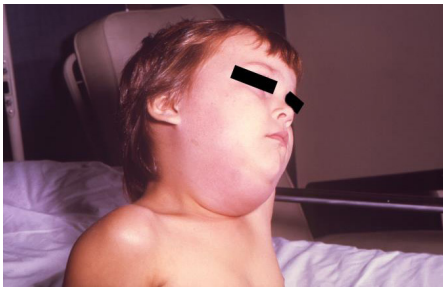
Figure 1. Proportion of specimens tested that were EV-positive and reported to the National Respiratory and Enteric Virus Surveillance System, by week and testing method used - United States, 2009–2013.[1]



References:

1. Abedi GR, Watson JT, Pham H, Allan W, Oberste S, Gerber SI. 2015. Enterovirus and Human Parechovirus Surveillance - United States, 2009–2013. MMWR 64(34);940-943.
2. Sharp J, Harrison CJ, Puckett K, Selvaraju SB, Penaranda S, Nix WA, Oberste MS, Selvarangan R. 2013. Characteristics of young infants in whom human parechovirus, enterovirus or neither were detected in cerebrospinal fluid during sepsis evaluations. Pediatr Infect Dis J 32:213-216.
3. Kolehmainen P, Oikarinen S, Koskiniemi M, Simell O, Ilonen J, Knip M, Hyoty H, Tauriainen S. 2012. Human parechoviruses are frequently detected in stool of healthy Finnish children. J Clin Virol 54:156-161.
4. van den Bergh MR, Biesbroek G, Rossen JW, de Steenhuijsen Piters WA, Bosch AA, van Gils EJ, Wang X, Boonacker CW, Veenhoven RH, Bruin JP, Bogaert D, Sanders EA. 2012. Associations between pathogens in the upper respiratory tract of young children: interplay between viruses and bacteria. PLoS One 7:e47711.

Detection of influenza A(H3N2) in cases of parotitis



Source: CDC Public Health Image Library

Yin Chang, BCCDC PHL
Dr. Danuta Skowronski and Catharine Chambers, BCCDC Influenza & Emerging Respiratory Pathogens

Acute parotitis involves swelling of one or both of the salivary glands and can be viral or bacterial in nature. Although commonly a symptom of mumps virus infection, there have been parotitis cases following infection with influenza virus. During the 2014–2015 influenza season in the United States, over 200 cases of influenza-associated parotitis were reported from 25 US states where previously only a dozen cases were ever reported.[1] Parotitis appeared to be linked to infection with influenza A (H3N2) virus.[1] Findings of laboratory-confirmed influenza A infection among children and adults with suspected mumps infection in Great Britain[2] and Scotland[3] were also reported for this period.

In response to these reports during the 2014/15 season, the BCCDC evaluated specimens submitted for suspect mumps assessment but that were negative by mumps virus real-time reverse transcription polymerase chain reaction (RT-PCR) through further influenza A virus, influenza B virus and respiratory syncytial virus testing virus and respiratory syncytial virus using the BCCDC PHL in-house RT-PCR multiplex assay.[2] Of the 122 specimens tested, 13% were found to be positive for influenza A virus with 81% of these characterized as belonging to the A(H3N2) 3C.2a clade of viruses that predominated during the 2014/2015 season in Canada.[2]

In this current respiratory season where influenza A(H3N2) once again is the dominant circulating virus, notably again dominated by clade 3C.2a variants, clinicians should consider influenza when patients present with parotitis.

Note that the different viruses have different specimen requirements: a buccal swab or blood test is ideal for mumps and nasopharyngeal or nasal swabs are preferred for influenza. Please refer to our Guide to Programs and Services for more information.

References:

1. Influenza & Parotitis: Question & Answers for Health Care Providers. Available from: https://www.cdc.gov/flu/about/season/questions-answers-parotitis.htm. [Accessed 27 Jan 2017].
2. Thompson CI, Ellis J, Galiano M, Ramsay M, Brown KE, Zambon M. 2015. Detection of influenza A(H3N2) virus in children with suspected mumps during winter 2014/15 in England. Euro Surveill 20(31).
3. Shepherd SJ, MacLean AR, Aitken C, Gunson RN. 2015. Letter to the editor: There is a need to consider all respiratory viruses in suspected mumps cases. Euro Surveill 20(33): pii=21210.
4. Chambers C, Skowronski DM, Sabaiduc S, Murti M, Gustafson R, Pollock S, Hoyano D, Allison S, Krajden M. 2015. Detection of influenza A(H3N2) clade 3C.2a viruses in patients with suspected mumps in British Columbia, Canada, during the 2014/15 influenza season. Euro Surveill 20(36):pii=30015.

In this current respiratory season... clinicians should consider influenza when patients present with parotitis.

Recommendations from the US Centres for Disease Control (CDC)[1]

The CDC suggests that influenza be included in the differential diagnoses for acute viral parotitis even in the absence of respiratory symptoms. During an outbreak of mumps in the community, testing for mumps infection is a priority but testing for alternative pathogens should also be considered, including testing influenza if influenza is circulating in the community at the same time.

Seasonal influenza

BC is experiencing substantial influenza activity this season. Test volumes have been steadily increasing since the end of November with over fourfold increase in some weeks in January compared to weekly submissions in October-November (Figure 2). In weeks 1-4 (January 1-28), a total of 3484 samples were tested for respiratory pathogen testing. During this period, 1375 (39%) samples were positive for influenza (1336 (97%) influenza A and 39 (3%) influenza B). This was a significant increase in submissions and detections compared to December 4-31 (weeks 49-52) where 1541 samples were tested and 284 (18%) samples were positive for influenza A and 4 (0.2%) samples were positive for influenza B. All of the influenza A subtypes were A(H3N2) during this period (weeks 49-52). Influenza A positivity rates have increased from a weekly average of 8-16% in October-mid December to weekly detection rates of 19-45% in January. The dominant subtype has been A(H3N2) with only 4 cases of A(H1N1)pdm09 this season. Weekly rates of influenza B have been 2% or less thus far.

Sample submissions this season have surpassed test volumes from the same period in 2015/16 (Figure 3). From the end of November to the end of December, there was a 44% to 175% increase in samples received and tested compared to the same weeks last season. In the early week of January, test volumes continued to surge to nearly 200% more than comparative weeks in 2015/16. Rates of influenza A detection were also significantly higher in December and January in contrast to similar weeks last season when a mixture of influenza B, influenza AH(H3N2) and A(H1N1)pdm09 co-circulated.

Figure 2. Respiratory testing volumes and influenza detection rates by week resulted, Virology Program, BCCDC PHL. Test volumes include initial screening and subtyping. Subtyping requests from other sites are not included.

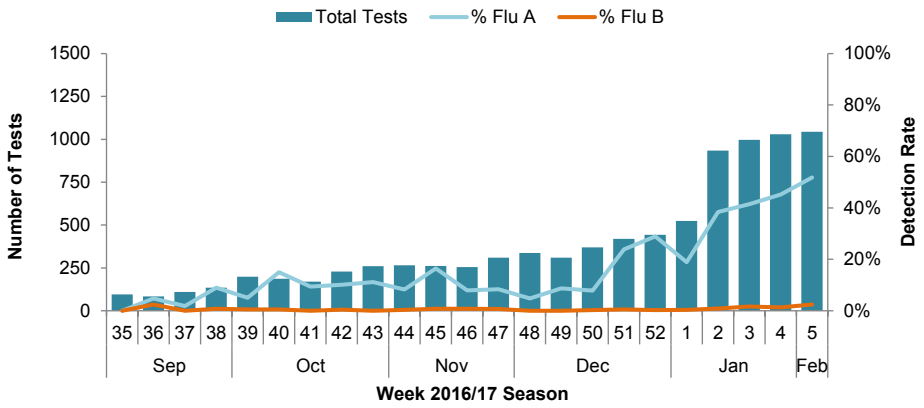
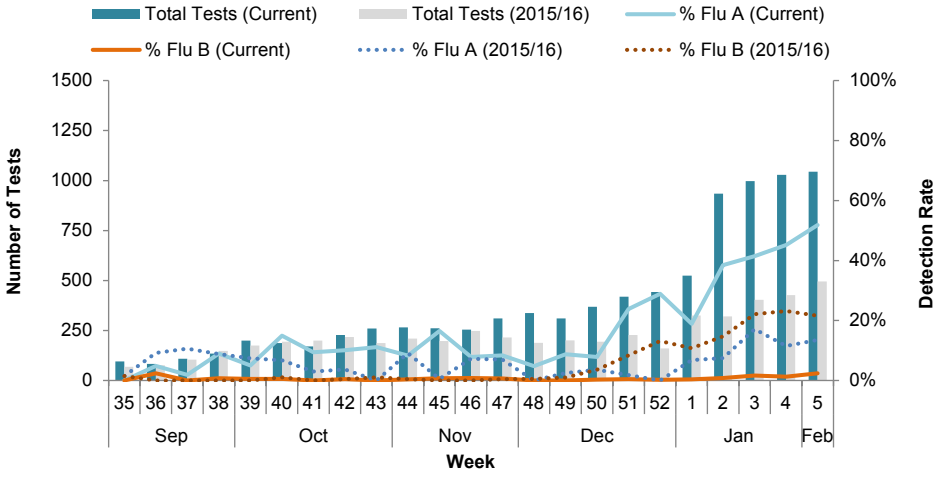


Figure 3. Respiratory testing volumes and influenza detection rates for the 2015/16 season and current season by week resulted, Virology Program, BCCDC PHL. Test volumes include initial screening and subtyping. Subtyping requests from other sites are not included.



Seasonal influenza

To date, adults 60 years and over also accounted for nearly 60% of the cases in the current season compared to 35% in the previous season (Figure 4). The large number of influenza outbreaks observed in longterm care (LTC) facilities (see page 9) have contributed to this trend and are indicative of the adverse effects of influenza A(H3N2) on this population.

Figure 4. Age group at time of collection for patients with influenza detected in the 2015/16 and current season, from weeks 35-4 (September-January), Virology Program, BCCDC PHL.

Influenza testing algorithm:

BCCDC PHL uses an in-house RT-PCR multiplex assay that detects influenza A virus, influenza B virus and respiratory syncytial virus. When influenza A is detected, a subtyping RT-PCR–based assay specific for H3 and H1 hemagglutinin genes is performed. Further molecular typing is performed to detect H5 and H7 subtypes if the specimen is negative by the H3 and H1 assay and has an adequate viral load to enable typing.

Enterovirus D68

Following the widespread outbreak of enterovirus D68 (EV-D68) in the US and Canada in the fall and early winter of 2014, EV-D68 largely disappeared in 2015 with only one case identified in February. With the reemergence of EV-D68 in August of 2016, the BCCDC PHL Virology Program once again started enhanced surveillance for the subtype. In general, all enterovirus/rhinovirus positive specimens identified by the respiratory pathogen panel, as well as all respiratory specimens collected from patients less than 20 years old were screened by polymerase chain reaction for EV-D68. Clinically relevant cases suspected of having EV-D68 were also tested.

In total there were 84 cases of EV-D68 in 2016 compared to 222 cases in 2014 (Figure 5). The majority of cases continued to be in children 0-5 years old; however, there was a marked difference between this season where children 0-5 years old comprised 67% of EV-D68 cases compared to 2014 when 38% were from this age group (Figure 6). There was also more EV-D68 detected in adults 20-59 years old in the 2014 season (25%) compared to this past season (12%) but this likely had to do with this season's testing strategy.

The US Centers for Disease Control also reported zero cases in 2015 and similarly noted sporadic and limited EV-D68 activity in 2016[1].

Please note: Routine EV-D68 testing at the BCCDC PHL was discontinued in January 2017.

Figure 5. Entervirus D68 cases detected in 2016/17 compared to 2014/15 by month resulted, Virology Program, BCCDC PHL.

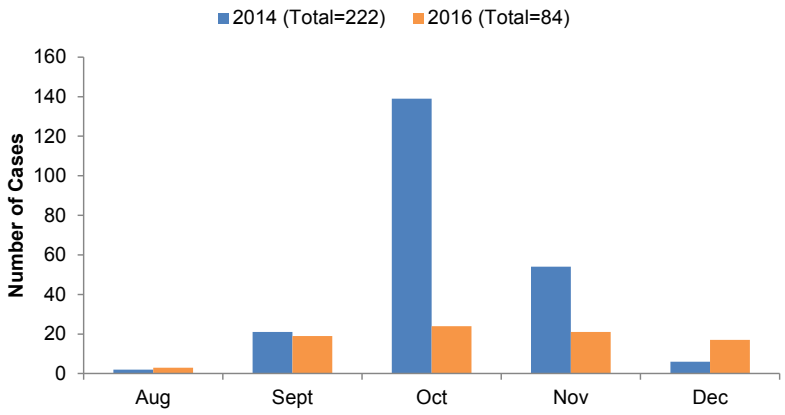
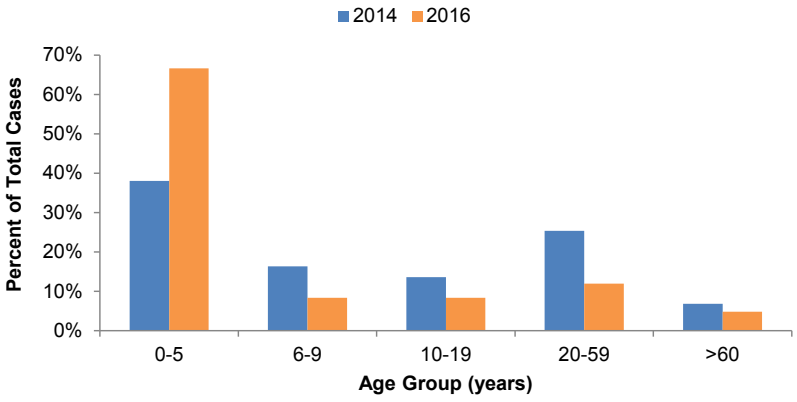


Figure 6. Age groups of entervirus D68 cases detected in 2016/17 compared to 2014/15 by month resulted, Virology Program, BCCDC PHL.



References:

1. Non-Polio Enterovirus. Available from: https://www.cdc.gov/non-polio-enterovirus/about/ev-d68.html#2016.

Carbapenemase producing organisms

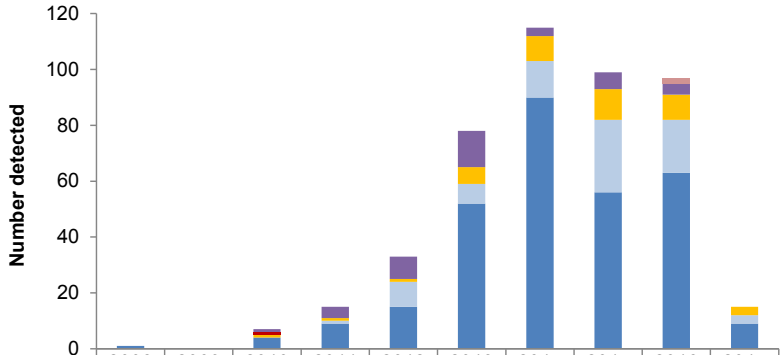
Working collaboratively with other microbiology laboratories and health care facilities' infection prevention and control in the province, the BCCDC PHL Public Health Advanced Bacteriology/Mycology Program provides molecular and genotypic testing of suspect isolates for carbapenemase genes. New cases of Carbapenemase Producing Organisms (CPO) are reported to the Provincial Infection Control Network of BC (PICNet) who monitor trends in CPOs as part of the provincial surveillance program.

The latest counts for cases of carbapenem-resistant Enterobacteriaceae in BC can be found in Figure 7 (updated from our September 2015 issue). To date, there have been 432 patients with carbapenem-resistant organisms: 273 harboured the New Delhi Metallo-β-lactamase-1-gene (NDM-1), 56 cases with OXA-48 carbapenemase and 37 cases with the *Klebsiella pneumoniae* carbapenem (KPC) β-lactamase gene; some patients had multiple resistance factors including 22 patients with NDM-1 and OXA-48 carbapenemase, three cases with NDM-1 and KPC genes, and one other case with the KPC β-lactamase gene as well as a the Verona integron-encoded metallo-β-lactamase (VIM) gene. Thirty-nine cases with the *Serratia marcescens* enzyme (SME) resistance gene have also been identified.

The Public Health Advanced Bacteriology/Mycology Program is also routinely screening for colistin resistance through the detection of the mobilized colistin resistance (*mcr*-1) gene when screening for carbapenemase resistance. First reported in 2015 from China, *mcr*-1 resistance threatens already strained treatment options for some multidrug-resistant infections as colistin is a last-resort drug. Surveillance for *mcr*-1 resistance is critical as the gene is plasmid-mediated and thus can easily spread to multiple organisms. In BC, there have been two cases of *mcr*-1 resistance to date including one with co-resistance with a NDM-1 gene.

In BC, there have been two cases of *mcr*-1 resistance to date including one with co-resistance with a NDM-1 gene.

Figure 7. Carbapenem-resistant Enterobacteriaceae detected since 2010, Public Health Advanced Bacteriology & Mycology Program, BCPHMRL. Counts include 22 cases with NDM-1 and OXA-48, three cases with NDM-1 and KPC, one patient with KPC and VIM and one patient with NDM-1 and *mcr*-1.

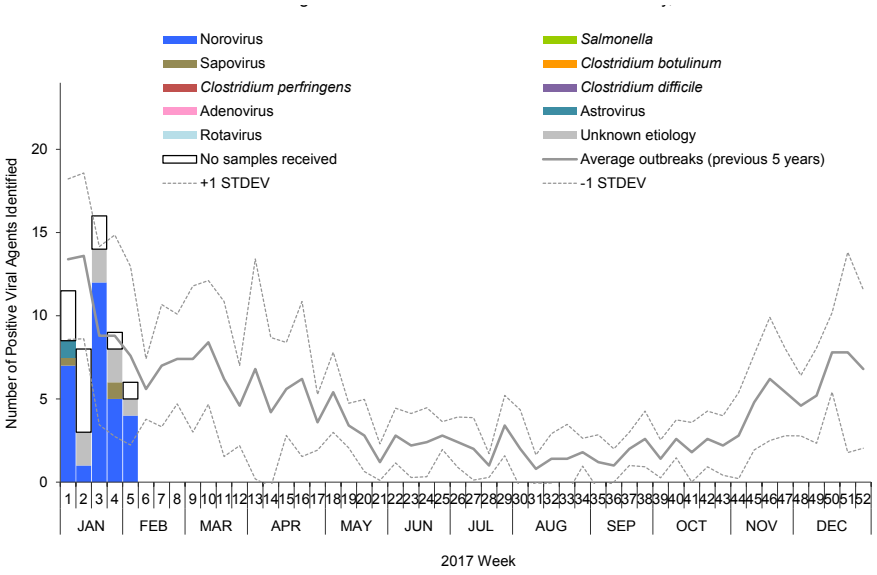


	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Total*	1	0	7	15	33	78	115	99	97	15
MCR-1 (2)									2	
SME (39)			1	4	8	13	3	6	4	
IMP (0)										
VIM (1)			1							
KPC (41)			1	1	1	6	9	11	9	3
OXA-48 (78)				1	9	7	13	26	19	3
NDM-1 (299)	1		4	9	15	52	90	56	63	9

Gastrointestinal outbreaks

In January, there were 50 gastrointestinal outbreaks investigated by the BCCDC PHL (Figure 8). Outbreaks were investigated from 23 (46%) LTC facilities, nine (18%) restaurant/food establishments, eight (16%) daycares, seven (14%) hospitals, and four (8%) other event types. Samples were received from 38 (76%) of these outbreaks with norovirus detected in 29 (76%) (14 from LTC facilities, seven from restaurants/food establishments, seven from hospitals and two other event types/locations). Of the norovirus positive outbreaks, seven were linked to the provincial outbreak related to the consumption of raw/improperly cooked oysters. This has since been expanded to a national outbreak with cases in Alberta and Ontario. Sapovirus was detected in one daycare while another had mixed infection of sapovirus and astrovirus.

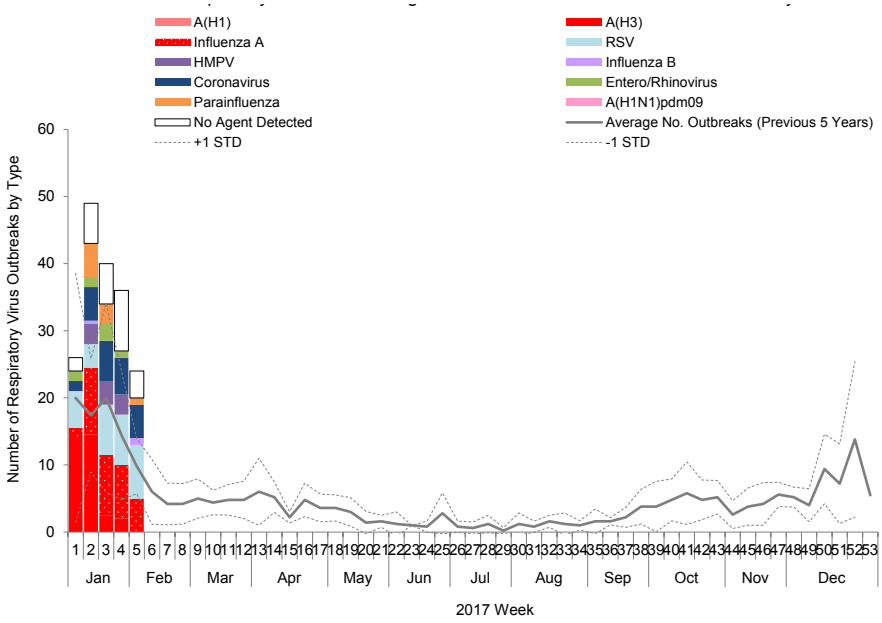
Figure 8. Gastrointestinal outbreaks investigated* in 2017, Environmental Microbiology, Public Health Advanced Bacteriology & Mycology, Parasitology and Virology Programs, BCCDC PHL. The data available are from outbreaks in which the BCCDC PHL has been notified. Some acute care microbiology laboratories are also testing for norovirus in the province and these data may not include outbreaks from all health authorities.



Respiratory outbreaks

In January, there were 168 outbreaks investigated to date from 167 LTC facilities and one hospital (Figure 9). With the exception of week 1, the number of outbreaks have surpassed historical weekly submissions from the past five years. Influenza A/influenza A(H3) was detected in 65 (39%) of these outbreaks while respiratory syncytial virus (RSV) was detected in 35 (21%). The next most common virus detected was corona virus in 24 (14%) outbreaks followed by human metapneumovirus (HMPV) in 12 (7%) outbreaks, parainfluenza in 11 (7%) outbreaks and entero/rhinovirus in eight (5%) outbreaks. Twenty-one of these outbreaks had two viruses detected amongst the different individuals sampled.

Figure 9. Influenza-like illness outbreaks investigated in 2017 to date, Virology Program, BCCDC PHL. Note that some outbreaks are not reflected here if they are awaiting subtyping.



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LABORATORY TRENDS

February 2017

LM LABS

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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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