May 2023

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

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Welcome to new staff

Dr. Titus Wong has joined the BC Centre for Disease Control (BCCDC) Public Health Laboratory (PHL) as medical microbiologist. In addition to these duties, Titus has a large Provincial Health Services Authority (PHSA) portfolio, serving as the BCCDC medical director, infection prevention & community health, PHSA executive medical director, infection prevention and control & medical staff wellness and continuing as the medical co-director for the Provincial Infection Control Network of BC.

Although she has not been formally introduced in publications, Dr. Catherine Hogan has also been supporting the Parasitology Program as program head/medical microbiologist since 2020. In addition to her capacity with the Parasitology Program, Catherine has been an active researcher in infectious diseases diagnostics during the SARS-CoV-2 pandemic as well as applying metablomics approaches to infectious diseases.

Successful accreditation by the College of American Patholgists

Following an inspection by the team from MolecularMD Corp, the College of American Pathologists (CAP) provided official reports of the full accreditation status of the BCCDC PHL in September of last year. Passing the inspection is a credit to all BCCDC PHL staff contributing to maintaining compliance with checklist items and following a continuous improvement mindset. Considering how the COVID-19 pandemic has impacted operations at all levels, passing accreditation is a testament to all the hard work in maintaining a laboratory that meets the rigourous quality standards as set by CAP.

The CAP model is special as other practicing laboratory professionals form the inspection team. The benefits of this peer-based framework include a mutual benefit of learning how best practices are undertaken at different laboratories.

COLLEGE of AMERICAN PATHOLOGISTS

CERTIFICATE OF ACCREDITATION

BCCDC Public Health Lab
Lower Mainland Pathology & Lab Medicine
Vancouver, British Columbia, Canada
Mel Krajden, MD

CAP Number: 2523501
AU-ID: 1037574

The organization named above meets all applicable standards for accreditation and is hereby accredited by the College of American Pathologists' Laboratory Accreditation Program. Reinspection should occur prior to **April 5, 2025** to maintain accreditation.

Accreditation does not automatically survive a change in director, ownership, or location and assumes that all interim requirements are met.

Kathleen G. Beavis, MD, Accreditation Committee Chair

Emily Volk, MD, FCAP, President, College of American Pathologists

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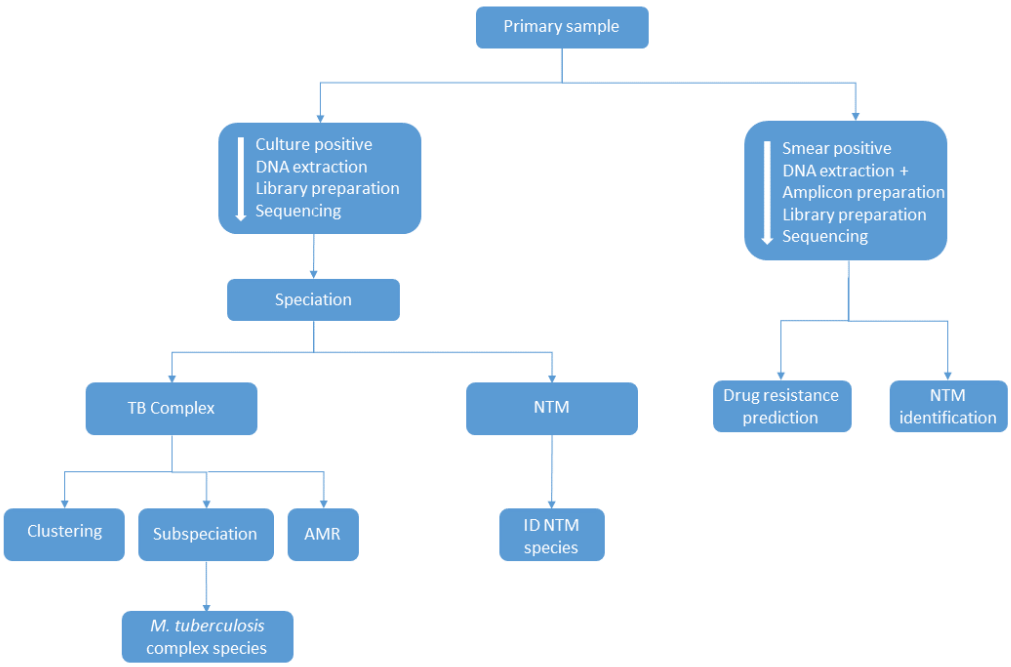
TB/Mycobacteriology transition to whole genome sequencing

Advancements in whole genome sequencing (WGS) methods has vastly changed the landscape of microbial diagnostics in recent years. The COVID-19 pandemic has also accelerated development of a genomics program at the BCCDC PHL as the value of sequencing has become more apparent. One of the targets for genomics is improving TB diagnosis, resistance profiling and clustering capabilities. To respond to time-consuming and costly assays, the TB/Mycobacteriology laboratory along with the BCCDC PHL bioinformatics team has been working towards a consolidated workflow using WGS. Work on transitioning to mycobacteria WGS started over 5 years ago, with the bioinformatics pipelines development intensifying in the last 2 years. Now with an optimized wet lab workflow, the mycobacteria pipelines will be able to:

- sub-speciate the *Mycobacterium tuberculosis* complex (MTBC);
- predict anti-microbial resistance (AMR) profiles;
- offer higher resolution TB cluster identification and monitoring using core genome multilocus sequence typing (cgMLST)/SNP (single nucleotide polymorphism) analysis; and,
- provide early genotypic detections of *M. tuberculosis* drug resistance markers.

Further work is currently underway to include testing of non-tuberculous mycobacteria (NTM), as well as provide testing on smear-positive primary samples for analyses such as organism identification and drug-resistance predictions. Some of the phenotypic methods this new workflow will replace include biochemical (Niacin/Nitrate) testing for speciation, conventional PCRs (*Mycobacterium bovis* BCG identification), and Sanger sequencing for drug resistance targets on cultured isolates. cgMLST/SNP-based determination of relatedness will also replace mycobacterial interspersed repetitive units (MIRU) typing that often took weeks to complete. After *M. tuberculosis* isolates have grown from primary patient samples, these new analyses will be available within a 3-7 day turnaround time from growth on solid media, with testing performed weekly. The TB/Mycobacteriology laboratory is in the process of validating testing on growth from liquid cultures, which will further reduce the time to report compared to traditional approaches. The complete workflow is outlined in Figure 1. Validation of the pipelines are in their final stages.

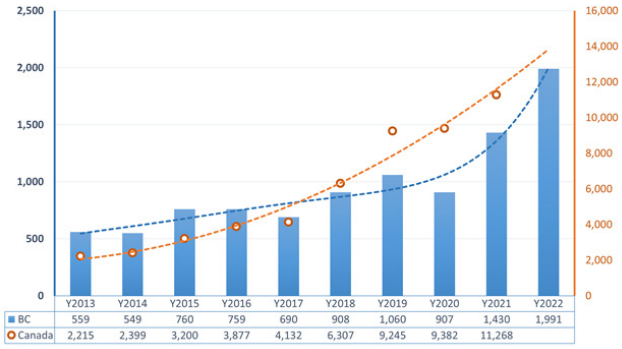
Figure 1. Mycobacteria WGS workflow.



Syphilis subtyping and macrolide resistance[+]

Increases in rates of syphilis have been observed both nationally and provincially (Figure 2). To better understand the strains that are circulating in the current epidemic, molecular characterization and resistance profiling were performed on a subset of polymerase chain reaction-positive syphilis samples from 2013-2022.

Figure 2. The infectious syphilis case numbers for British Columbia (blue) and Canada (orange) in the past decade. Data acquired from BCCDC STI reports and Canada Communicable Disease Report. Data for 2021 (Canada) and 2022 (BC) have not been finalized.



The enhanced CDC (ECDC) typing scheme incorporates the following elements: the number of 60-bp repeats in the acidic repeat protein (arp) gene, the restriction digest pattern of the *T. pallidum* repeat (tpr) gene, and tp0548 gene sequence typing. The study revealed 38 genotypes in the 10-year dataset, with the most common strain of T. pallidum being 14d/g (52%), followed by 14d/d (17%), 14d/f (5%), and 8d/g (3%). More than half of the genotypes (22/38) are represented by only one case (0.3%) (Figure 3). Further examination and stratification of the typing data by year indicate that some genotypes were present before 2016 (14b/g and 20d/c), some have emerged after 2019 (14a/g, 14b/d, 15d/f, and 14d/d) while others have persisted over the duration of this study (14d/f and 14d/g) (Figure 4).

Macrolide resistance based on the detection of a point mutation in the 23S rDNA gene using a restriction fragment length polymorphism assay demonstrated that 97% of syphilis cases in the study were macrolide-resistant, predominantly due to A2058G mutation (97% of all resistant), with A2059G mutation (3% of all resistant) being less common. This finding is consistent with global trends and has implications on treatment guidelines.

This study has uncovered some important molecular trends in some syphilis cases in BC over the last decade. The 14d/g strain is predominant in the province and it is a strain that has been seen over the span of the study period, unlike some other strain such as the next most common strain, 14 d/d, which has arisen over the last few years. Continued surveillance activities will be important in monitoring any changes to these trends, particularly as syphilis cases increase and treatment options are diminished with increased macrolide resistance.

Figure 3. Distribution of subtypes as determined by the ECDC genotyping for syphilis samples from 2013-2022 (n=311).

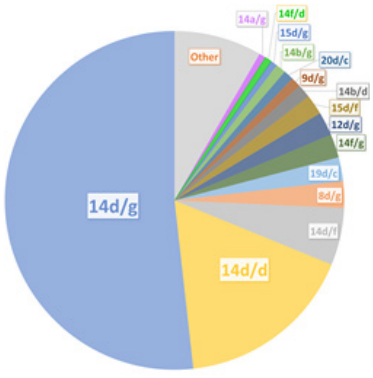
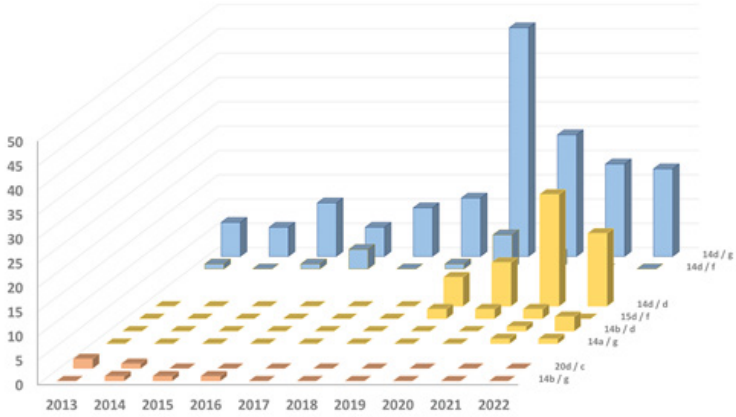


Figure 4. Select *T. pallidum* subtypes grouped over 2013-2022 (orange: 14b/g and 20d/c); yellow: 14a/g, 14b/d, 15d/f, and 14d/d; in blue: 14d/f and 14d/g).



[+]Presented at the 2023 AMMI Canada-CACMID Annual Conference: Lee M-K, Li A, Kaweski S, Tee J, Hon B, Wu H, Gagnier L, Carruthers E, Chahil N, and Morshed M. (2023, Mar 28-31). *Molecular Subtyping and Macrolide Resistance Surveillance of Treponema pallidum in British Columbia*.

Mpox testing and surveillance at the BCCDC PHL*

Mpox is a disease caused by the monkeypox virus and is typically a zoonotic virus with endemicity in central and western Africa. Contact with infected animals was primarily the cause of infection but human to human transmission is also possible with respiratory spread, contact with infected bodily fluids or vertical transmission from mother to fetus as avenues of transmission. Prior to 2022 outbreaks were limited to either transmission within or travel to endemic areas[1,2] or due to contact with animals from the region[3].

In May of 2022, a case of mpox was detected in London who reported travel to Nigeria. This index case gave rise to a cluster of cases in the UK with no travel history to central and western Africa. Subsequent cases were soon found in other regions in Europe with further transmission to other parts of the world. By July 23 the WHO declared mpox as a Public Health Emergency of International concern. As of March 14, 2023 there have been 86,516 cases reported from 110 countries[4].

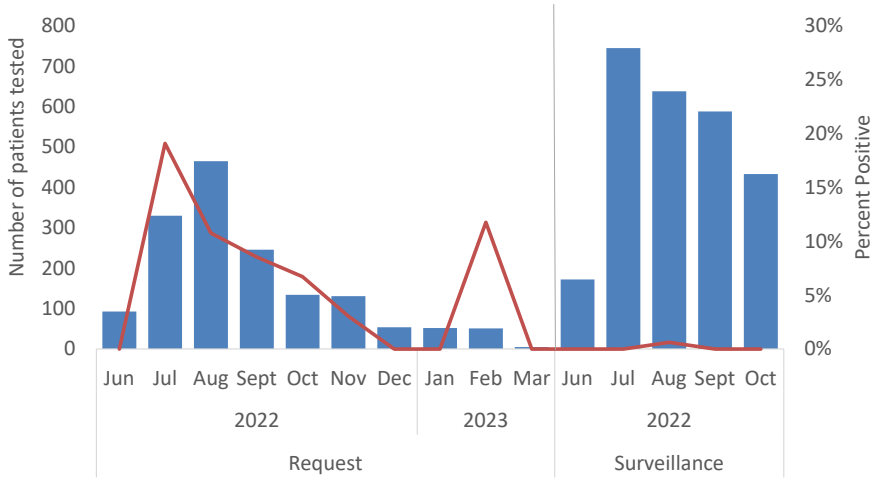
The outbreak in Canada saw cases detected first in Quebec followed by Ontario, Alberta and BC with a total of 9 provinces and territories reporting. As of March 17, 2023 the total number of confirmed cases was reported as 1,478 with the majority (83%) of cases coming from Ontario and Quebec[5].

In response to the emergence of mpox virus in Canada, the BCCDC PHL validated a laboratory-developed real-time polymerase chain reaction (PCR) assay in June 2022 based on the publication by Li et al[6]. The laboratory also supported the verification of this assay for use at two other laboratories in the province (St. Paul's Hospital and Royal Jubilee Hospital). To further confirm that possible variants would not affect the sensitivity of the assay, all mpox virus PCR negative samples were reflexed for testing by the commercial RealStar® Orthopoxvirus PCR assay from altona Diagnostics for samples collected between September and December 2022.

From June to October, 2022, the BCCDC PHL was also performing mpox surveillance testing on a subsample of mucosal/lesion swab specimens submitted for HSV/VZV testing. In addition, with the help of STI clinics that serve populations at highest risk of mpox, add-on surveillance testing was also included for their submitted mucosal/lesion swab samples.

In total, 4148 individuals were tested by mpox PCR at the BCCDC PHL between June and March 2, 2023: 1572 by request and 2576 by add-on testing. The percent positivity was 10% (n=164) by requested testing and 0.2% (n=4) by add-on testing. Positivity of requested testing cases peaked in July (19%) before falling in subsequent months (Figure 5). No cases were detected December-January and the outbreak was declared over in BC. Cases once again were detected in February (n=6; 12% positivity).

Figure 5. Monthly testing and positivity of requested samples and add-on surveillance samples by result date.



The demographics and risk factors of all cases identified with both requested and add-on testing matched the known outbreak epidemiology, primarily affecting men who have sex with men. The median age of cases tested by request and by add-on testing were comparable at 33 years and 34 years, respectively. The 20-29 and 30-39 year age groups had the highest number of patients forwarded for testing by both requested and add-on testing.

Reflex testing of mpox virus PCR negative samples to the pan-orthopoxvirus assay was performed on 431 cases collected between September and December, 2022. All of these samples were also found to be negative by RealStar® Orthopoxvirus PCR, confirming that the mpox PCR in use was not affected by potential deletions from mpox variants circulating at that time.

The surveillance strategy that was implemented had low yield of positive cases, suggesting that diagnostic testing by request during this outbreak captured cases acutely ill with lesions very well.

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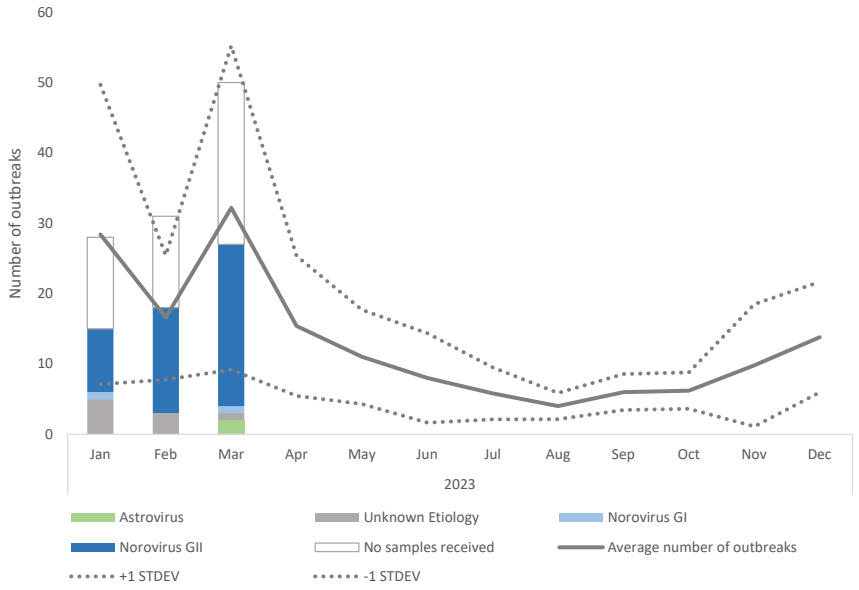
* Presented at the 2023 AMMI Canada-CACMID Annual Conference: Gunadasa K, Lee T, Lam A, Cheung B, Chan M, Chow R, Chang Y, Tsang F, Tyson J, Prystajecky N and Jassem A (2023, Mar 28-31). *Automatic surveillance and reflex PCR testing in response to mpox emergence in Canada*.

Gastrointestinal outbreaks

From January to March there were 109 gastrointestinal (GI) outbreaks investigated by the BCCDC PHL (Figure 6). The number of outbreaks investigated in February and March were on the upper end of the number of outbreaks investigated in previous years. Outbreaks were investigated from 52 (48%) longterm care facilities (LTCF), 46 (42%) daycares/schools, 7 (6%) hospitals, two other facility/event types (2%) and two restaurants (2%). Samples were received from 56% of these outbreaks with norovirus detected in 50 (82%) (from 37 LTC facilities, six hospitals/acute care facilities, five daycares/schools, and two restaurants). Astrovirus was also detected from two daycares/schools.

Figure 6. Gastrointestinal outbreaks investigated in 2023 (Jan-Mar), 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.

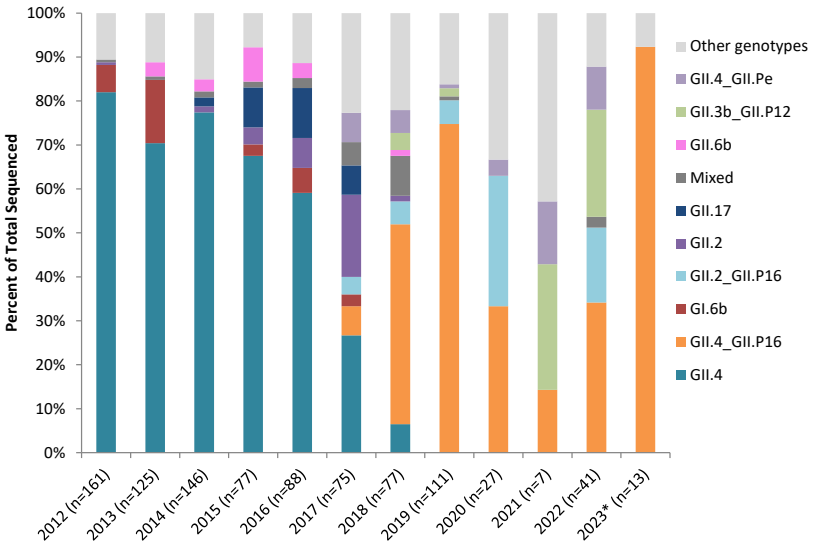


Norovirus sequencing

The Environmental Microbiology Program of BCCDC PHL provides norovirus genotyping by sequencing the norovirus polymerase gene (region B) and Capside gene (region C). From 2012 to 2017 genotype GII.4 predominated as the genotype most detected in the samples submitted for sequencing. In 2018, the dominate genotype switched to GII.4_GII.P16 with GII.2 _GII.P16 and GII.3b_GII.P12 also detected in 2020 and 2021 (Figure 7). The US is also observing similar patterns with GII.4_GII.P16 as the dominate genotype in the last few years (CaliciNet Data).

The SARS-COV-2 pandemic impacted the number of outbreaks investigated between 2020-2021. Volumes are now recovering with a slightly later season for norovirus detection.

Figure 7. Norovirus genotypes sequenced by Environmental Microbiology, BCCDC PHL, 2012-2023 (to date).



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The Public Health Laboratory at the BC Centre for Disease Control (BCCDC) provides consultative, interpretative testing and analyses for clinical and environmental infectious diseases in partnership with other microbiology laboratories and public health workers across the province and nationally. The BCCDC PHL is the provincial communicable disease detection, fingerprinting and molecular epidemiology centre providing advanced and specialized services along with international defined laboratory core functions. The Provincial Toxicology Centre conducts toxicology testing and analysis for clinical patients, including therapeutic drug monitoring, drug screening tests and forensic toxicology analyses for the BC Coroners Service.

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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