

BRITISH COLUMBIA'S  
PUBLIC HEALTH MICROBIOLOGY &  
REFERENCE LABORATORY

Laboratory Program

Highlights 2011-2012



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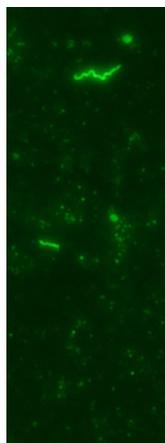
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## Introduction

On behalf of the staff of the Public Health Microbiology & Reference Laboratory (BCPHMRL) of British Columbia (BC), it is my pleasure to present our activity summary for the two years covering 2011 and 2012. More than 10 previous annual reports have shown how our laboratory and its work have served British Columbians and, within a national network, Canadians. Like other parts of the health care system we continue to evolve to meet change and challenges.

Because this is their work, it gives me great pleasure to highlight the work of the experts who deliver our specialized services. In our report, the leaders from each program describe innovations and improvements in their areas, as well as challenges and solutions.

In 2011 we were once again successful in obtaining international accreditation status through the College of American Pathologists (CAP), a tribute to the hard work and dedication to continued improvement by our outstanding team.

Our relatively small number of specialized and experienced staff members network with our

partners in BC's acute care and community diagnostic microbiology laboratories and as well with counterparts in Canada's system of public health laboratories. Our thanks go to our public health and medical microbiology partners for their ongoing support.

Our team is nimble and flexible; in fact, two of our 10 Core Functions require us to provide a rapid response to health care emergencies. In responding to the pressures of change, we look forward to ongoing evolution and improvement. Our 2013 strategic plan and our focus on innovation provide a fresh vision for public health in BC.



Judith Isaac-Renton, MD, DPH, FRCPC  
 Director,  
 BC Public Health Microbiology & Reference  
 Laboratory  
 Provincial Health Services Authority Laboratories



# 2011-2012 Highlights



# 188 EMPLOYEES



## FOCUS ON QUALITY

Accredited,  
College of American Pathologists,  
**April 2011**



Accredited,  
Enhanced Water Quality Assurance,  
**June 2011**



## MENTORSHIP

Number of graduate,  
post-graduate and co-op  
students mentored

# 40



## FUNDING

Total dollar value of awarded grants

# \$9.9M



## LIS PROJECTS

Sunquest 6.4.2 Project completed,  
**September 2012**



## ACADEMICS

Total number of publications,

# 64

Total number of abstracts,

# 81



## RECOGNITION

John G. FitzGerald Outstanding Microbiologist Award, Canadian Association for Clinical Microbiology and Infectious Diseases

*J. Isaac-Renton*

Queen Elizabeth II Diamond Jubilee Medal, Canadian Liver Foundation

*M. Krajden*

Distinguished Microbiologist Award, Canadian College of Microbiologists

*M. Petric*





# Organizational Structure

## Overview of Programs and Core Functions

The BCPHMRL at the BC Centre for Disease Control (BCCDC) site provides consultative and interpretative services, testing, and laboratory results analyses for clinical and environmental infectious diseases. We work in partnership with other microbiology laboratories and public health workers provincially and nationally.

The BCPHMRL, as the provincial communicable disease response unit, is required to meet internationally defined laboratory core function standards. Our Core Functions are:

- Emergency response including advanced containment, bio-terrorism and natural disaster responses
- Outbreak response (detection, interventions and management)
- Food and water testing for public health including accreditation support and legislated functions
- Leadership in integrated data management and quality management systems
- Policy advice to decision makers, provincially and nationally
- Reference level testing to support microbiology laboratories province-wide
- Applied public health research and education

Our highly specialized experts use advanced reference diagnostic tools, high level containment processes and procedures, and advanced molecular, genomic and metagenomic tools for rapid detection and fingerprinting of pathogens, working within the Lower Mainland Pathology and Laboratory Medicine Laboratory Group under the Provincial Health Services Authority (PHSA) plus laboratories outside the Lower Mainland. BCPHMRL is affiliated with the University of British Columbia (UBC) and is also a member of federal and provincial laboratory networks (including the Canadian Public Health Laboratory Network [CPHLN] and the Canadian Laboratory Response Network [CLRN]).

Our team produces over 2,000,000 test results a year through its centralized laboratory programs in serology (High-Volume Viral Serology and Zoonotic Diseases and Emerging Pathogens), along with smaller programs in Environmental Microbiology (food/water), Parasitology, Tuberculosis (TB)/Mycobacteriology, Public Health Advanced Bacteriology/ Mycology and Virology. These programs are supported by cross-cutting laboratory support functions including the Biosafety, Biosecurity, Biohazard Containment (BBBC) Program, Central Processing & Receiving, the Laboratory Information Management Team, the Molecular Microbiology & Genomics Program, Outbreaks and Surveillance, the Quality Assurance and Improvement Team, Technical Support, and the nationally funded Laboratory Liaison Technical Officer Program.

# Laboratory Programs & Core Functions





# Core Function

## Biosafety, Biosecurity, Biohazard Containment



The BBBC Program is central to the BCPHMRL mandate with services crucial to the functioning of the BCPHMRL and BCCDC. The two-person team includes the Public Health Lead and Biosafety Officer, Neil Chin, and Assistant Biosafety Officer, John Tansey. This duo takes on a considerable portfolio covering laboratory biological and chemical safety, biological containment services, biological security, and facilities management.



**NEIL CHIN**

Public Health Lead,  
Biosafety Officer

### Biosafety and Biocontainment

The BBBC Program is responsible for compliance with the Public Health Agency of Canada (PHAC)'s *Laboratory Biosafety Guidelines*, ensuring that biosafety precautions are followed for potential organisms coming in and out of BCPHMRL Containment Level 2 and Containment Level 3 (CL3) laboratories. This includes annual recertification with PHAC and the Canadian



**JOHN TANSEY**

Assistant Biosafety  
Officer

Food Inspection Agency (CFIA), annual review of laboratory safety inspections, review of the Laboratory Safety Manual and working with PHSA Employee Wellness to evaluate staff records and make recommendations for immunization and health surveillance. As one of the CL3 laboratory sites within the province (working with Risk Group 3 pathogens), BBBC oversees operations in this specialized containment facility, including training and orientation for staff and contractors, waste management/decontamination, personal protective equipment, security, maintenance, materials transport and transfer, annual recertification testing and maintenance of policies and procedures.

The BBBC team also provides general safety orientation for new staff and visitors and chairs the Laboratory Biosafety Advisory Council Meetings that are attended by safety representatives from all BCPHMRL Programs.

## Biosafety, Biosecurity, Biohazard Containment

### Emergency Response

The BBBC Program plays a critical role in our public health bioterrorism response, performing regular risk assessments, emergency and pandemic supplies management and maintenance of linkages with regional, provincial and national partners for emergency management activities such as exercises in chemical, biological, radiological and explosive events.



PHAC is the national coordinator for transport emergencies involving Infectious Substances Affecting Humans and Risk Group 4 pathogens. PHAC also maintains the Emergency Response Assistance Plan (ERAP). In BC the ERAP Team is managed by BBBC including coordinating several volunteer ERAP members with annual training on the potential handling of Risk Group 4 pathogens.

Response on a more local level includes management of the First Aid Attendant Program at the BCCDC and coordinating fire safety with the BCCDC through fire drill organization and evacuation route mapping. The BBBC is also involved in disaster planning and assists in seismic upgrades throughout the building.

### Facilities Management

BBBC works very closely with the building management team and the Joint Occupational Health and Safety Committee on matters related to the BCCDC structural operations and infrastructure including involvement in Service Level Agreements for laboratory equipment, heating, ventilation, and air conditioning and filtering services. The team liaises with contractors and building management in preventative maintenance; and repair and replacement of equipment such as autoclaves, biological safety cabinets and fume hoods. BBBC also maintain inventory and certifications of key equipment. They are on hand for equipment removal, space management and the coordination of generator testing and restoration of equipment after power outages. They also administer laboratory policies and governance for access and security.



## Biosecurity and the Human Pathogens & Toxins Act

In 2009, the Parliament of Canada passed the *Human Pathogens and Toxins Act* (HPTA) in an effort to ensure rigorous, nationally consistent controls over the possession, containment and movement of non-imported human pathogens and toxins.

Under the *Act*, the BCPHMRL has registered as a facility that works with Risk Group 2 and Risk Group 3 organisms. Pending are regulations that will dictate the implementation of HPTA. PHAC is consulting broadly and will be developing a regulatory framework that includes the following:

- Licenses: procedures required to engage in controlled activities
- Security screening: requirements needed for access
- Inventories: requirements needed for control of select pathogens and toxins
- Laboratory exposure reporting and prevention program: reporting on laboratory acquired infections
- Biological Safety Officers: qualifications and training required and roles in exercising regulations

As a member of national and provincial organizations, the BCPHMRL is working on a number of initiatives related to HPTA including reviewing access permissions and standardizing bioinventory databases. In 2011/2012, senior staff members participated in several stakeholder consultations with the Pathogen Directorate Consultation Secretariat of PHAC to refine a regulatory framework. Ongoing consultation will occur in coming years as the BCPHMRL moves towards HPTA implementation in 2015.

## Networks

Neil Chin is the Provincial Co-Chair of the Biosafety Officer's Network (BSON), providing leadership, guidelines development and support. As leaders in the areas of biosafety, biohazard containment and biosecurity, the BBBC Program not only is involved in BSON and HPTA but other national networks such as the CLRN where they assist with staff security clearance requirements, agreements for the import and transfer of pathogens and toxins for testing purposes and External Quality Assessment, and Chain of Custody protocols. Internationally, BBBC is a strong partner in the Cross Border Alliance and has led developments to standardize permits for the transfer of materials across the Pacific Northwest borders. The BBBC is also participating in the international Memorandum of Understanding with Washington State Public Health Laboratory to provide mutual aid through the sharing of public health laboratory services.



# Core Function

## Central Processing & Receiving



**DR. JUDY ISAAC-RENTON**

Public Health Laboratory  
Director

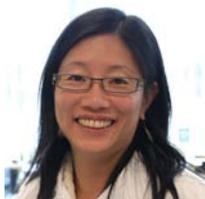
The Pre-Analytical area of the Central Processing and Receiving (CPR) Program located on the Lane Level of the BCCDC serves as BCPHML's "front end" for all specimens tested on the premises. In the Pre-Analytical site, specimens are received, labelled, sorted by the laboratory to which they are designated and triaged. Over 5,000 human and environmental samples from all over the province are received daily.



**AMELIA TRINIDAD**

Laboratory Manager

The CPR Program has undergone a number of enhancements in efficiency using Lean Principles. This included a recent implementation of a more efficient way of processing specimens using a system arranged by their time of arrival in the Laboratory.



**ANNIE MAK**

Section Head

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# Core Function

## Information Management



The two-person Laboratory Information Management (LIM) Team includes Laboratory Information Management Coordinators Rob MacDougall and Peter Ng. This important team works with all BCPHMRL Programs to ensure proper operation of the Laboratory Information Management Systems (LIS) (Sunquest and Legacy). The LIM Team is responsible for integrating new tests into the LIS including building order and result codes, worksheets and programming calculations, installing necessary instrument interfaces, and upgrading and testing software applications. The LIM Team also maintains the interfaces with the Fraser Health Authority (FHA), BCCDC partners and the private laboratories (LifeLabs and BC Biomedical Laboratories).

The team provides the link to the PHSA Information Management/Information Technology group and maintains the BCPHMRL network folders and drives, including improving folder security.

This Team provides specialized bioinformatics application maintenance and support including Applied Math's BioNumerics, a key platform for PulseNet Canada and NCBI BLAST®. These applications are integrated into the appropriate workflows at the BCPHMRL with servers, workstations and databases maintained. Training is provided for new users and on new versions.

Other duties include providing production statistics, internal and external data extracts, and billing reports; and maintaining Reportable Communicable Diseases (RCD) reporting. The Team also supports the information management needs for annual West Nile virus surveillance and reporting of water quality testing data through HealthSpace and WaterTrax®.

The LIM Team works with BCPHMRL Subject Matter Experts and with the Lower Mainland Laboratories (LML) Director, Laboratory Information Systems & Informatics, Raphael Lim.

## LIM Projects

The LIM Team participates in projects when laboratory data and its management are involved; some of these projects are described below.

### Automated RCD Reporting

In 2011, an automated RCD reporting program replaced what was once a manual system of reporting. This ensures same-day reports to Health Authority Medical Health Officers and improves ease of reporting for BCPHMRL staff. High-volume RCD test reports are processed via automated feed, enhancing time to results. (Some microbiology RCD test reports still require manual review.)

### Projects with BC Children's Hospital and BC Women's Hospital & Health Centre (CW) Hospital Laboratory

The CW laboratory is on the same Sunquest platform as BCPHMRL so test ordering and results are available through a common LIS. In 2012, BCPHMRL was asked to perform scenario and end-to-end testing and results validation for the CW implementation of eChart, an offshoot of the new Cerner electronic health record application.

### Environmental LIS

Sunquest is currently only a repository for clinical data. A separate, custom data warehouse is therefore required for environmental data (food, water and non-human tests). The goal of the Environmental LIS Project is to determine how Sunquest can be used to include these data types and thereby mitigate the eventual loss of expertise involved in maintaining this database and the additional resources required to sustain a separate LIS. Work began in 2012 to review modifiable data fields.

### Sunquest LIS Integration and Upgrade

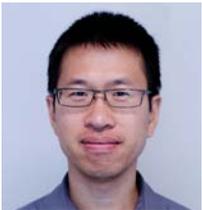
The BCPHMRL prepared for, tested, and implemented migration to a new Sunquest 6.4.2 LIS on September 15, 2012. This is the same platform that Vancouver Coastal Health Authority (VCHA) and Providence Health Care (PHC) currently use, meaning that orders and results among over 30 clinical and laboratory sites are now electronically delivered. This was a significant project requiring many hours of effort and dedication.

Laboratory subject matter experts worked diligently along with their coordinator (Y. Chang), LIM Coordinators (R. MacDougall and P. Ng), PHSA Director IMIT (R. Lim) and the Project Manager (D. Rhodes), over the course of a year to meet deadlines and launch a successful implementation. Laboratory staff members were asked to help, in addition to their regular bench work and associated duties. In total, nearly 300 order codes and over 22000 result codes were reviewed, built and tested, along with the systems framework. Scenarios were developed to assess the robustness of the LIS to real world situations with testing extended to partner sites from VCHA and PHC. Updates to standard operating procedures and training for all staff followed, including updates to the LIS Manual.

This common LIS platform means that the LML are not only linked to all the hospital information systems from VCHA and PHC but now also linked to upstream orders from FHA and the private laboratories (Lifelabs and BC Biomedical Laboratories). Benefits include shorter test turnaround times and better patient care.

# Molecular Microbiology & Genomics

## Core Function



**DR. PATRICK TANG**

Program Head



**DR. LINDA HOANG**

Associate Head



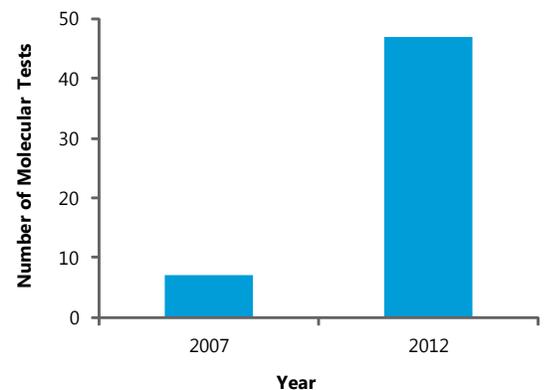
**ALAN MCNABB**

Section Head

This core program (previously known as Molecular Services) has been rebranded as the Molecular Microbiology and Genomics (MMG) Program to reflect the addition of a bioinformatician, a molecular coordinator and Next Generation Sequencing (NGS) capabilities. This small, but highly essential team supports all other BCPHMRL programs by developing and validating nucleic acid assays to identify and characterize novel and emerging pathogens as well as assisting in troubleshooting and improving methods for rapid detection of pathogens of public health importance.

Due to their short turnaround times and better sensitivities, molecular methods are increasingly relied upon in diagnostic laboratories. The current BCPHMRL molecular capacity (Figure 1) would not be possible without the day-to-day leadership and troubleshooting provided by these experts. Staff members work closely with all other programs in the BCPHMRL on polymerase chain reaction (PCR) testing, DNA sequencing problems, and molecular quality assurance activities such as internal

control monitoring of molecular performance. MMG staff train and provide competency assessments in molecular assays. They also partner with service program leaders to design, validate and implement new molecular tests. This team has been critical to the BCPHMRL rapid response to emerging and novel pathogens and to rapid detection of bioterrorism agents. Clearly a unique and fundamental team!



**Figure 1.** Molecular tests implemented at the BCPHMRL in 2007 compared to 2012.

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### Improving Detection of Shiga Toxin Producing *Escherichia coli*

The detection of Shiga Toxin producing *E. coli* (STEC), the cause of “Hamburger Disease” (bloody diarrhea and sometimes severe kidney damage) has traditionally been performed by the Public Health Advanced Bacteriology and Mycology (PHABM) Program using Vero cell culture, looking for the cytopathic effect (CPE) typical of the toxin. This method was complex involving a lengthy process and requiring highly specialized training. To detect STEC directly in samples, supernatant of stool samples submitted for testing were inoculated on Vero cells and then examined for 72 hours. Samples causing CPE typical of STEC were cultured and examined for the presence of STEC.

Working with the PHABM Program, the MMG Program evaluated 12 published real-time PCR assays for sensitivity and specificity. They determined that one of the assays was superior in sensitivity and range of serotypes of STEC. This assay was optimized to meet in-house requirements and further validated for the detection of STEC from clinical samples, decreasing the turnaround time compared to Vero cell culture. Standardization of testing and reading increased the detection rate from direct samples. The assay was transitioned from MMG to PHABM and is currently being used to screen all isolates and samples sent for the detection of STEC.

### Standardization of Real-Time PCR Assays and Sequencing Reactions

Strategic multiplexing of PCR targets results in cost saving and decreased turnaround time for the detection of multiple pathogens. MMG's commitment is to assay standardization using identical thermal cycling and master mix parameters with redesign of real-time PCR assays currently in use. Most of the redevelopment of assays has been accomplished with the Virology Program. Standardizing the laboratory to perform PCR for any virus at the same time on the same platform saves time and money. Further work is underway to extend this initiative to all Programs.

Typically DNA sequencing reactions require primer-specific annealing temperatures to produce amplified product. This means that, when using sequencing to identify isolates, different amplification parameters are needed to produce the required amplified DNA for sequencing. MMG has been working with PHABM to standardize all sequencing reactions. This is accomplished by optimizing primer size, changing reagent content, as well as tailing primers (5' end) with universal primers. Standard conditions prevent delays in identification due to backlogs in sequencing.

### Identifying Bacterial Isolates not Possible with Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Analysis (MALDI-TOF)

Although MALDI-TOF was developed in the 1980s it has only recently been introduced to diagnostic microbiology laboratories as a tool for routine bacterial and fungal identification. This identification of isolates based on their ribosomal proteins is a powerful tool but is not without limitations. Some subspecies, species or groups cannot be differentiated based on these proteins. The introduction of MALDI-TOF into many routine laboratories in BC and the types of isolates submitted to PHABM for reference identification will change to comprise mostly isolates that cannot be identified by MALDI-TOF. Aware of this development, MMG has reviewed the literature for additional gene targets (in addition to 16S rRNA) used to identify the species, subspecies or groups that are routinely not able to be identified using MALDI-TOF. Publications document a list of organisms that are not readily identified and a literature review of sequencing-based identification methods was undertaken for these organisms. To date, the databases for the identification of *Streptococcus*

## Molecular Microbiology & Genomics

species and *Staphylococcus* species, two genera that are not adequately identified by MALDI-TOF have been developed using secondary sequencing targets. Work continues on other groups or genera not well differentiated by MALDI-TOF and genes that can be used for their identification using genomics.

### Direct Detection of Bacteria from Clinical Samples

The direct detection of bacteria from clinical samples using a Nucleic Acid Amplification Test (NAT) can be problematic. When the pathogenic bacteria are present in high numbers, broad spectrum NAT assays such as those targeting the 16S rRNA gene are usually able to detect and identify these pathogens. This rapid genomic detection precludes the need for bacterial culture. However, when the pathogen is not present or is present in low numbers, such broad spectrum NAT assays may amplify non-bacterial DNA or even the DNA of bacteria that are contaminants.

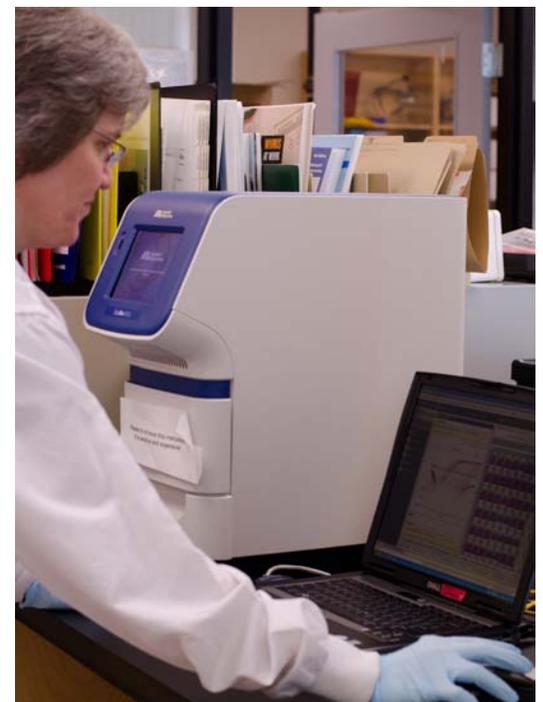
The MMG Program has investigated the existence of reagents purported to be bacterial DNA contaminant-free. Improvement of primer sets for direct amplification of the 16S rRNA targeted by the assay and introduction of newer reagents (primer concentrations and design for preferential amplification of bacterial DNA has resulted in a more robust assay). This revised NAT assay is now available for use if approved by a Medical Microbiologist.

### Improving Detection of *Bordetella pertussis*

The gold standard for the detection of *B. pertussis* is detection by NAT. Previously PHABM detected *B. pertussis* via conventional NAT, requiring a lengthy and complex procedure. MMG worked with PHABM to evaluate an improved real-time PCR for the detection of *B. pertussis*, targeting the IS481 sequence. The new assay is more sensitive and faster to complete. Software interprets positive versus negative samples, removing interpretation variation among technologists.

### Improving the Identification of *Mycobacterium* and *Nocardia*

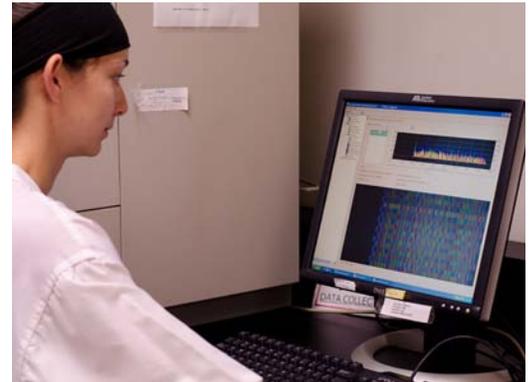
In 2005, the Tuberculosis (TB)/Mycobacteriology Program, in partnership with MMG, introduced 65 kiloDalton Heatshock Gene (hsp65) Sequencing as a replacement for conventional biochemical identification of *Mycobacterium* species. A large database with reference strains and unique sequences was created, saving time and costs. As the use of new molecular microbiology techniques has increased, a large number of new *Mycobacterium* and *Nocardia* species have been described from human, animal and environmental sources. During 2011/2012 our team reviewed the literature to determine which new *Mycobacterium* and *Nocardia* species had been described. These species were cultured and sequenced and an enhanced sequence repository was created. The addition of *Nocardia* species to the library has decreased testing turnaround times as the TB/Mycobacteriology Program can report *Nocardia* species directly rather than accessing another laboratory for identification.



### Detecting the Novel A(H1N1)pdm09 Reassortant Influenza Virus

In late 2010, a triple reassortment swine H3N2 virus was detected in the United States (US) in patients that had direct contact or lived in close proximity to swine. The virus was detectable as influenza A by our standard screening procedures. It contained the M, PB2, PB1, PA, NS, and NP genes from the A(H1N1)pdm09 strain, but also had the H3N2 genes H3 and N2.

The MMG Program conducted a monitoring program for the virus, applying assays that had previously been developed in-house, targeting the matrix gene and the haemagglutinin gene of the virus. No strains were found to be circulating in BC and surveillance was discontinued. Testing for this virus is available if approved by a Medical Microbiologist.



### Replacing Commercial Assays by In-House Validated Assays

Previously, cerebral spinal fluid (CSF) assays used by the Virology Program for the detection of herpes simplex virus (HSV) types 1 and 2 and West Nile virus were purchased from commercial sources. In partnership with the Virology Program, MMG standardized these assays onto high throughput real-time PCR instruments. Validation studies comparing the developed-in-house assays to commercial products found that the in-house assays were as specific and more sensitive. They could also be done at a fraction of the cost and updated as required. As better and cheaper master mix reagents are introduced to the market, our assays can be reviewed and continuously improved.

### Further Multiplexing of Herpes and Varicella zoster virus Detection Assays and Development of Adenovirus and Epstein Barr virus Detection Assays

In April 2010 the Virology Program transitioned herpes simplex (HSV) 1/2 detection (in genital and skin samples) from cell culture to a 'two tube duplexed' real-time PCR assay targeting HSV 1/2 and varicella zoster virus (VZV). The assay could also detect the presence of human DNA via a housekeeping gene. This initiative decreased turnaround time (generally reporting the same day as samples were received), increased the detection rates of HSV 1/2 and VZV, and allowed the detection of VZV from genital sources. This improvement also allowed the laboratory to assess whether a sample was collected properly by confirming the presence of human DNA. The Virology Program acquired a real-time thermal cycler capable of detecting four targets in a single reaction tube (4-plex) and MMG re-validated the 'two tube duplexed' assay to a 4-plex assay, further reducing labour and cutting costs by 50%.

In concert with the Virology Program, a real-time adenovirus assay was developed and validated by the MMG. The assay can detect members of all six adenovirus subgenera in less than an hour. Currently the assay is available only after consultation with a Medical Microbiologist and is awaiting transition to the Virology Program.

In partnership with the Virology Program at the BCPHMRL and the Virology Laboratory at St. Paul's Hospital, the MMG Program developed and validated a real-time PCR assay for the detection of Epstein Barr virus. The assay runs using our standard PCR parameters on an Applied Biosystem, Inc.® (ABI) 7500 real-time thermal cycler. This is part of the continuing process aiming for complete molecular detection capabilities for all viruses routinely causing disease in BC. Currently the assay is available only after consultation with a Medical Microbiologist, awaiting transition to the Virology Program.

## Next Generation Sequencing: Advanced Genomics for Public Health

In January 2011, an Illumina® MiSeq Next Generation Sequencer was integrated into the MMG Program under a UBC-funded grant. Its integration in our centralized Molecular Microbiology unit gave all BCPHML Programs the capability to generate gigabases of DNA sequencing data in less than 2 days. This instrument allows for whole genome sequencing of multiple microbes in a single sequencing run.

To answer specific public health questions, the MMG Program, in collaboration with other BCPHML Programs, has sequenced isolates of *Clostridium difficile* to determine strain clonality, *Haemophilus influenzae* to detect possible emerging virulence factors, unusual *Neisseria* and *Pasturella* species to provide whole genome sequence data as a basis for possible emerging pathogens, *Campylobacter jejuni* to corroborate a novel subtyping method, *Borrelia burgdorferi* to determine if specific spirochete strains were carried by different hosts, *Clostridium botulinum* to examine an isolate from an unusual food source, and *Legionella pneumophila* as a proof of concept for deep amplicon sequencing to detect mixed pathogen populations. It has also been used to compare *Salmonella enterica* sv. Enteritidis and examine single-nucleotide polymorphism patterns.

In the case of whole genome sequencing of *Salmonella* Enteritidis, NGS provides the laboratory with a high-resolution typing tool capable of further resolution for strain relatedness (fingerprinting) to allow the laboratory to detect and track outbreaks where current technologies such as Pulsed-Field Gel Electrophoresis (PFGE) are unable to differentiate. This new technology platform will provide additional response for more accurate molecular (now genomic level) epidemiology, leveraging two Genome Canada grants awarded to Dr. William Hsiao to develop a comprehensive analysis platform using NGS whole genome sequencing data. Moving forward, further applications of this platform will be developed for use in public health microbiology.



## Core Function

# Outbreaks & Surveillance



In 2011, the BCPHMRL partnered with public health in the investigation of 384 outbreaks. Gastrointestinal (GI) outbreaks accounted for 67% (not including seven food-related outbreaks). The highest number of GI outbreaks was observed in January. There were 117 influenza-like illness (ILI) outbreaks investigated with the largest numbers in the months of January to March, reflecting the extended winter transmission experienced in 2011.

A mumps outbreak started in December 2010 with mumps cases occurring in several Health Authorities throughout 2011. A localized measles outbreak was detected and managed in February.

In 2012, the BCPHMRL assisted in the investigation of 446 outbreaks, GI outbreaks accounted for 69% with the highest number again observed in January. February, March and December were also typically busy months for GI investigations. There were 134 ILI outbreaks investigated with the highest numbers in January and December. The mumps outbreak from 2011 continued into 2012 as described below. Two travel-related cases of measles were observed in April and July.

Below are some significant events investigated by BCPHMRL with BCCDC and Health Authority partners.

### Mumps Outbreak

In January 2011, a mumps outbreak originated in the Whistler area but included cases from other parts of VCHA, Vancouver Island Health Authority (VIHA) as well as out-of-province. Peak numbers were identified in May-July with affected people being mainly residents of the Lower Mainland. The outbreak later spread to other parts of FHA and the Interior Health Authority (IHA). A total of 132 cases in BC were reported through laboratory (positive Immunoglobulin (Ig) M) or PCR) and epidemiological confirmation. Mumps virus type G was found to be the dominant genotype, although three cases with genotype F (a strain commonly circulating in China) were also identified. As the majority (48%) of cases occurred in the 21-30 year age range, targeted immunization campaigns were held in Whistler Village in April 2011 and in other parts of VCHA. In 2012, five cases were identified in residents of VIHA and VCHA.

## Outbreaks & Surveillance

### Measles Outbreak

In 2011, a measles outbreak originating in the Revelstoke area in February resulted in eight cases, all with measles virus genotype D4. In October, two additional cases were identified through serology. In 2012, two measles cases were detected, both genotype B3 (endemic to many African countries); the affected patients acquired their infections in Uganda and Afghanistan. One case of rubella was confirmed in June 2011.

### Pertussis (Whooping Cough) Outbreak

An outbreak of *Bordetella pertussis* was first reported in FHA late in 2011. Of great risk to young children, this respiratory bacterial pathogen later spread throughout the Lower Mainland. Test volumes for *B. pertussis* were substantial in 2012 compared to volumes in 2011. Although the actual number of cases was elevated in 2012, percent positivity rates for pertussis NATs were comparable or even lower than positivity rates in 2011 (Figure 2). Increased incidence of pertussis in the summer months in both 2011 and 2012 was noted.

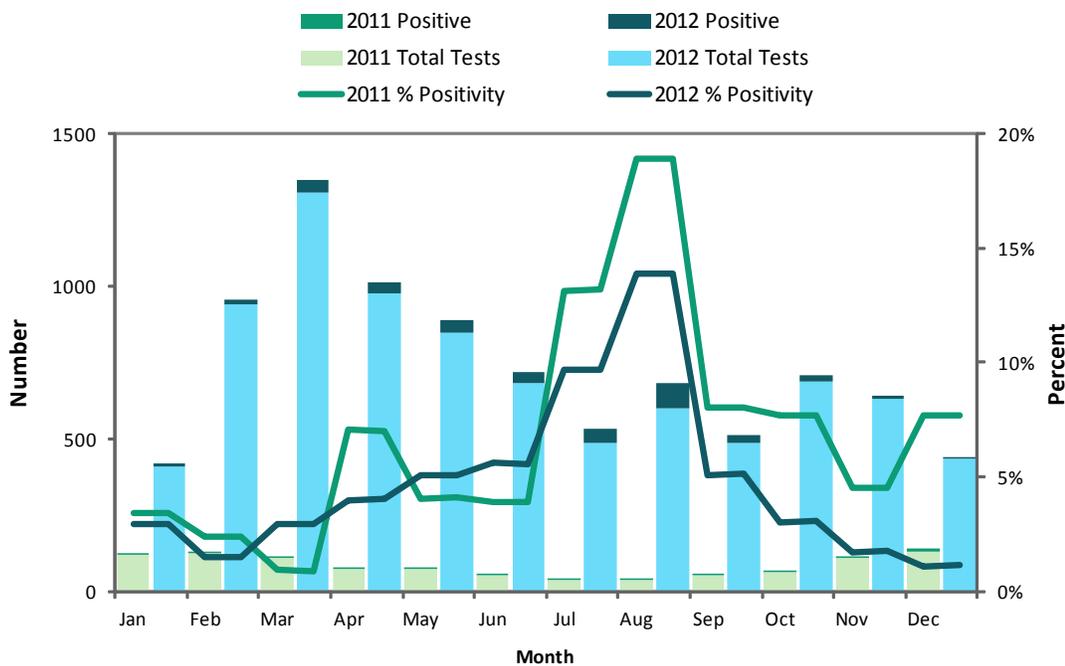


Figure 2. *Bordetella pertussis* test volumes and positivity, 2011-2012.

## Outbreaks & Surveillance

### Salmonella Clusters and Outbreaks

Several clusters of *Salmonella* Enteritidis infections (determined by identical fingerprinting by PFGE) were linked to different food establishments/events from June to October, 2011. An outbreak of *S. Enteritidis* at a catered event was detected early in November, 2011. The Environmental Microbiology and PHABM Programs at the BCPHMRL worked with VCHA public health to investigate the outbreak. Over 100 attendees and staff became ill at the event; tiramisu was identified as the infected food source. Thirteen cases of *S. Infantis*, an uncommon serotype in BC, occurred in November 2011. The majority had visited a Shawarma Restaurant in VCHA while two unrelated cases with different PFGE patterns reported travel outside Canada.

### Food-Related Outbreaks

*Clostridium botulinum* was detected in watermelon jelly and in patient samples after a person from Vancouver Island presented with neurological symptoms consistent with botulism. The recalled product was sold at various locations in BC in 2010 although no further cases were detected.

The first documented outbreak of Diarrhetic Shellfish Poisoning (DSP) in BC occurred in August 2011; more than 60 cases were linked to mussel consumption in VCHA/VIHA and CFIA detected DSP biotoxin in the harvest area. A voluntary recall of lots harvested in July and August 2011 was made by the harvester and distributors. *Vibrio parahaemolyticus* of submitted food samples (mussels and sauce) was also detected by the BCPHMRL.



An outbreak of *Salmonella* Braenderup was investigated in July 2012 and linked to visits to a popular Vancouver restaurant. Contaminated mangoes were determined to be the source of infection which resulted in 15 cases with the same PFGE pattern (BraeXAI.0021). CFIA issued a recall of mangoes (which were distributed throughout Western Canada and the US). This foodborne outbreak was documented in Alberta and many US states.

A recall of various beef products was issued across Canada in September 2012 after cases of *E. coli* O157:H7 illness were reported in Alberta. Analysis by both PFGE and Multi-locus Variable Number Tandem Repeat Analysis (MLVA) (an additional fingerprinting method to distinguish it from the common PFGE pattern found) confirmed the outbreak in 18 cases from Alberta, Newfoundland and Labrador, Quebec and BC. The products were distributed to various retailers across Canada, the US and internationally.

### ***Mycoplasma pneumoniae* Outbreak**

BCPHMRL worked with federal and provincial public health partners to investigate a *Mycoplasma pneumoniae* outbreak on a naval ship that had been at sea for several weeks in August 2012. Based on positive IgM serology, NAT and clinical data, *M. pneumoniae* was identified in many patients. Of the crew of about 200 individuals, 28 cases of atypical pneumonia were initially identified by *Mycoplasma* IgM reactivity and/or a positive NAT result. Transmission to family members was observed once the vessel docked at Vancouver Island.

### **Laboratory Surveillance and Outbreak Coordinator**

Yin Chang is the BCPHMRL Laboratory Surveillance and Outbreak Coordinator (LSOC), responsible for overall outbreak coordination and leading surveillance and information management initiatives. Key duties include laboratory communications, and coordinating outbreak data, coordinating with teams responsible for data repositories such as Sunset and the Public Health Reporting Data Warehouse, managing public health requisitions and coordinating the BCPHMRL Guide to Programs and Services. The LSOC liaises regularly within the BCPHMRL Programs, BCCDC, Health Authority and national public health laboratory partners on matters concerning outbreaks, surveillance and project-based work. Other key communications include the monthly *Laboratory Trends* report that describes laboratory news, projects and surveillance to a wide audience of laboratory and non-laboratory partners at the local and national levels.

Alongside the BCPHMRL Information Management Coordinators, the LSOC is a member of the BCPHMRL Information Management Team and contributes to information management projects and needs, including requests for data analysis. The most significant project for 2012 was the laboratory coordination of the Sunquest 6.4.2 Implementation Project as previously described. The LSOC was the BCPHMRL Lead and worked closely with the Project Manager and Team to manage BCPHMRL workplans including supporting build and testing requirements. For this project, the LSOC coordinated BCPHMRL subject matter experts and provided regular project communications to the BCPHMRL Leadership Team. In future the LSOC will assist in the development of standards for laboratory-wide surveillance through the use of various data sources. She is also a member of the Information Skills Development Team.

As a member of the Continuous Quality Improvement Team, the LSOC contributes to quality initiatives including projects and accreditation readiness. In 2012, the LSOC supported the internal quality assessment process of the BCPHMRL, using the General Checklist from CAP. This self-assessment activity was integral to preparations for the 2013 CAP audit.

### Laboratory Liaison Technical Officer

Kim Macdonald is the BCPHMRL/National Microbiology Laboratory (NML) federally-funded Laboratory Liaison Technical Officer (LLTO), whose roles are to assist with collaborations and communications among federal and provincial public health laboratory counterparts and to assist with surveillance and reference services at the BCPHMRL. Our LLTO works closely with the BCPHMRL LSOC.

Surveillance work included participation in projects of the Canadian Network for Public Health Intelligence (CNPHI), such as the Measles and Rubella Surveillance and the *Listeria* Detection and Surveillance using Next Generation Genomics Programs. Kim is also involved in C-EnterNet testing, fingerprinting and data exchanges between the BCPHMRL and the second Canadian C-EnterNet Sentinel Surveillance Site in FHA (Chilliwack, Abbotsford, and Burnaby).

The LLTO's role in BCPHMRL reference services has included molecular subtyping assays such as PFGE, analysis of fingerprinting data and creation of fingerprinting meta data. As a member of the Core Team, she also works closely with members of the MMG Program including Dr. Natalie Prystajecy (Molecular Microbiology & Genomics Coordinator) and Dr. William Hsiao (Bioinformatician).

One of Kim's most notable 2010-2011 projects was the evaluation of the Comparative Genomic Fingerprinting (CGF) assay for subtyping *Campylobacter jejuni*. Using BC outbreak and sporadic isolates, followed by a prospective study on subsets of clinical isolates, she validated the new assay, supported by the C-EnterNet project. Baseline and trend studies in CGF pattern distribution will follow. The CGF assay (designed by Dr. Eduardo Taboada, Laboratory for Foodborne Zoonoses, PHAC) was initially evaluated against Multi-Locus Sequence Typing (MLST) using environmental, food, and clinical isolates. The assay was found to be as discriminatory as MLST, and in some cases, more so. The assay is also less costly, easier, and quicker to perform than PFGE and MLST. Dr. Natalie Prystajecy initially recognized this assay as being of potential use to the BCPHMRL and has been working with our LLTO and the C-EnterNet surveillance program. This work was presented at the Canadian Association for Clinical Microbiology and Infectious Diseases (CACMID)-Association of Medical Microbiology and Infectious Disease (AMMI) Meeting (2012) and the Canadian *Campylobacter* Workshop (2012). The recent acquisition of, and training on, the Qiagen QIAxcel for automated capillary electrophoresis expedited the production of results and subsequent analysis. The CGF method is in the process of implementation in the PHABM Program.

# Core Function

# Quality Management System

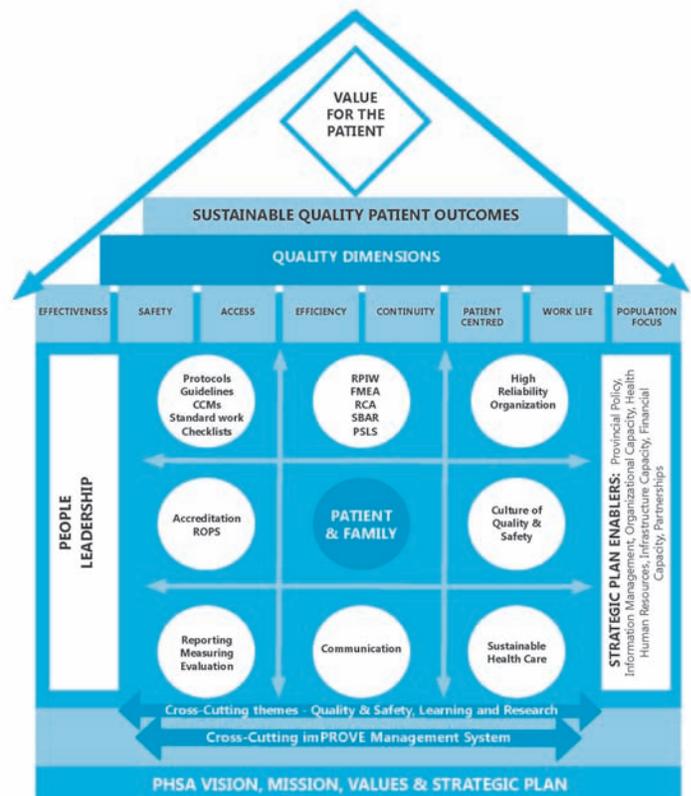


Core Functions are the defined international standards that any provincial or state public health reference laboratory must meet to deliver their unique services. The Quality Management System (QMS) leadership Core Function is fundamental to all the other Core Functions and Program Services in its foundation of continuous improvement. Our Quality System Essential-based QMS underpins quality services in all Programs and is the framework to meet standards of accreditation bodies. BCPHMRL aligns its QMS with that of the LML and the quality principles of the PHSA where all actions are focussed around the patient and family.

One of the quality initiatives that enabled more efficient management of the ever-growing volume of policies, procedures and other documents was the 2010 adoption of the SoftTech Health LabQMS™ application. Continuing to refine the use of LabQMS™ in 2011/12 has facilitated meeting quality benchmarks and accreditation requirements for document control, provided access for annual reviews for documents and enabled improvements in rapid information access.

BCPHMRL's dedication to these quality standards and continuous improvements, as described below, has been reflected in successful accreditation inspections

at the provincial level by the BC Diagnostic Accreditation Program (June 2010), Enhanced Water Quality Assurance (June 2011) and internationally through CAP accreditation in 2009 and again in 2011.



The Provincial Health Services Authority Quality House

## Quality Management System

### BCPHMRL Quality Team

The BCPHMRL Quality Team includes three core teams dedicated to quality management and improvement and reports to the Public Health Laboratory Leadership Team. These include the Staff Development Team (SDT), Continuous Quality Improvement (CQI) Team and Internal Quality Assessment (IQA) Team.

Chaired by Alan McNabb, the mandate of the SDT is to promote ongoing staff education and training. An example of education supported by SDT was the Applied Maths BioNumerics course offered in December 2012 with an overview of the public health fingerprinting software application as well as a more intensive workshop for users. Current work includes preparing for an information management skills development and genomics lecture series with related workshops.

The mandate of the CQI Team is to seek opportunities for improvement and to translate them into action. The CQI Team is chaired by Dr. Mabel Rodrigues and co-chaired by Yvonne Simpson. All Programs are represented on the CQI Team and members work on several quality improvement projects over the year. Examples are review of returned reports, improvement in telephone communication, and standardization of specimen handling across laboratories.

The IQA Team, chaired by Quantine Wong with the assistance of Brian Auk, has a mandate to internally evaluate program services. The IQA Team performs internal assessments and site inspections to prepare for accreditations. In 2012, the CQI Team Members became CAP Champions, performing IQAs based on the CAP General and Molecular checklists.

These educational, improvement and assessment activities promote a culture of quality throughout the BCPHMRL and reflect the commitment of all staff members to patient safety and CQI. As noted in our previous reports, 'Quality is the touchstone of all we do.'

### Provincial Point of Care HIV Testing Program

Launched on April 1, 2011, this PHSA-funded (BCCDC-managed) program provides Point of Care (POC) tests and supplies to health care settings that meet program requirements. The laboratory support to BCCDC was to develop a provincial Quality Reference Manual and framework (developed by Kathy Chambers, Coleen McAloney and others) to implement HIV POC in communities. Laboratory staff members work with sites throughout the province to optimize their readiness and ability to use the tests through partnerships, assessment and training of health practitioners.

Currently, there are 54 provincial clinic sites in all Health Authorities in BC including community public health and non-public health clinics, correctional facilities and participating First Nations communities. The Program provides ongoing training, guidelines, support, test kits and supplies documentation templates, and troubleshooting, as well as a centralized repository of provincial POC HIV test statistics.



Dr. Isaac-Renton showing appreciation by serving up some ice cream to staff at the 2011 CAP Celebration.

# Core Function

## Technical Support



The Technical Support Program provides in-house users at the BCPHMRL with quality-assured culture media and reagents. As well, it leads the waste stream management services, along with our BBBC Team.

Working with the various Programs at the BCPHMRL, over 280 different media have been optimized by Technical Support for the detection of various microbes in food, water and clinical samples. Due to the nature of the work at the BCPHMRL, specialized media for target organisms is often needed. In 2011, more than 470,000 media orders were filled, rising to over 518,000 in 2012. The principal consumers are for testing in PHABM and Environmental Microbiology Programs (Figure 3). Technical Support also routinely assesses the quality (productivity and selectivity) of media produced and maintains standards of practice to meet accreditation guidelines.

Other important services provided by Technical Support are the cleaning and sterilizing of laboratory glassware and managing laboratory waste produced by the BCPHMRL, including the decontamination of infectious waste. These procedures represent a critical containment barrier and meet requirements set by the *Laboratory Biosafety Guidelines*.

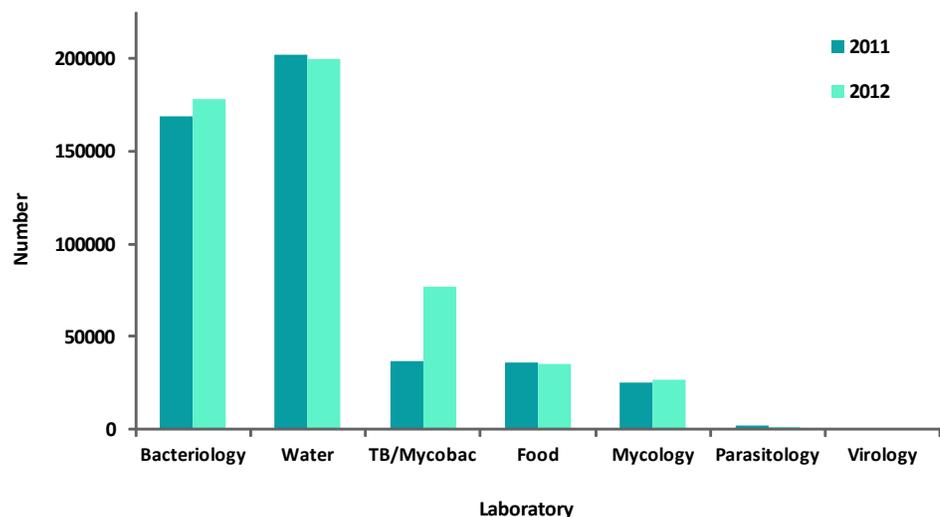


Figure 3. Media distribution (including production) at the BCPHMRL, 2011-2012.

# Core Function

## Training & Education



Along with the research projects and activities described in this report, education is another key Core Function of the BCPHMRL. Teaching activities range from training technical staff from Health Authorities to training staff from other BC laboratories in collecting, processing and transporting of samples. The BCPHMRL also supports education at the undergraduate to post-graduate levels. The summer cooperative student education program is an opportunity for microbiology and Bachelor of Medical Laboratory Science undergraduate students to work in a public health microbiology laboratory, performing water testing, supporting West Nile virus surveillance, and assisting in other work. These placements provide valuable experiences for the trainees and sometimes lead to more permanent positions within the BCPHMRL. Senior staff and Program Leaders regularly supervise masters, doctoral and post-doctoral students. The rotation at the BCPHMRL is also a significant term for UBC Faculty of Medicine Medical Microbiology Residents and Infectious Disease Fellows as the education and mentorship program provided by BCPHMRL is unique.

Communicating and disseminating research work is accomplished within the BCCDC as well as outside within the microbiology community and in professional

forums as noted under the Academic Contributions section of this report. The CACMID–AMMI conference is often a showcase of the work performed within the BCPHMRL with staff presenting at both the 2011 (Vancouver) and 2012 (Quebec City) meetings to disseminate their findings and share new knowledge with colleagues.

In 2012, in follow up to our strategic priorities and led by the Public Health Laboratory Leadership Team, the SDT initiated creation of an educational information management program. The Information Skills Development Team (ISDT), with Subject Matter Experts, aims to expand the knowledge base involving data management and storage within the BCPHMRL. Centred on standardizing the use of spreadsheet software, correct file taxonomy and nomenclature, and a standard data dictionary, the ISDT will engage all Programs at the BCPHMRL. A second initiative called the Advanced Skills Development Team (ASDT) under the leadership of the BCPHMRL Bioinformatician, focuses on bioinformatics knowledge to enable us to meet future needs in this rapidly expanding field. Both ISDT and ASDT are long-term programs with workshops, information sessions, and hands-on program-based projects for internal staff.



# Environmental Microbiology



**DR. JUDY ISAAC-RENTON**

Program Head,  
Medical Microbiologist



**JOE FUNG**

Section Head

The Environmental Microbiology (EM) Program provides consultation and testing services and data analysis for clients and for policy advice, primarily testing for investigations, surveillance, legislated drinking water monitoring, for safe food and water. Our staff members are also responsible for fingerprinting of bacterial, parasitic and viral isolates related to food or waterborne diseases. This includes testing clinical samples for botulism, and the cause of GI outbreaks including norovirus and sapovirus.

In past years, there have been increasing improvements in testing methods using molecular microbiology and genomics; EM has partnered with federal and provincial investigations in many studies. Experts in environmental microbiology, staff members support the BC Provincial Health Officer (PHO) in maintaining the quality of private and public laboratories through the legislated approval program.

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### Gastrointestinal Disease Outbreaks

#### Norovirus

Norovirus continues to be the leading reported etiologic agent of GI outbreaks in BC (69%). The next closest, rotavirus, accounts for only about 3% of reported GI outbreaks (Figure 4). As a whole, the number of GI outbreaks from 2011 to 2012 was lower than the average in 2006-2010 (Figure 5) – possibly due to changes in genotypes observed. Most GI outbreaks in 2011 and 2012 occurred in residential care (50%) and hospital (27%) settings (Figure 6).

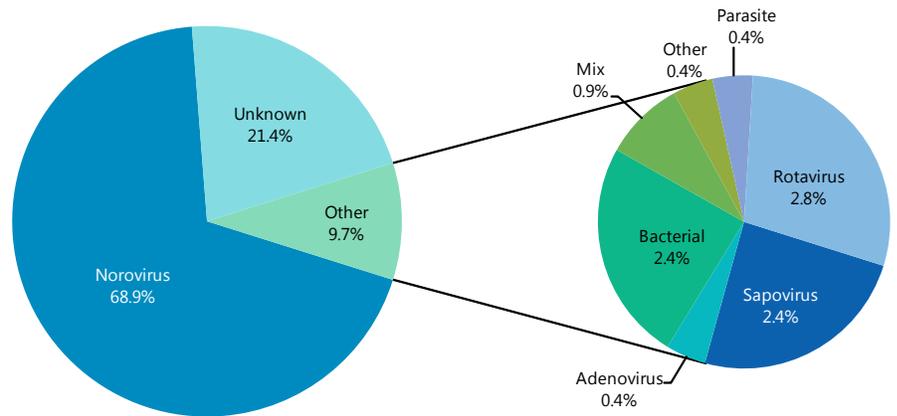


Figure 4. Reported GI outbreak etiologies from 2011 to 2012.

Towards the end of 2012, there was a marked increase in number of reported GI outbreaks across BC as compared to previous seasons (Figure 5). Due to the ongoing norovirus outbreak assessment program (confirmed outbreak isolates in BC are genotyped to track the molecular epidemiology of transmission), BCPHMRL was able to determine that the increase was due to the replacement of previous dominant norovirus genotype GII.4K New Orleans 2009 with GII.4 Sydney 2012. This strain replacement was not unique to BC; higher than normal norovirus incidence was reported globally associated with GII.4 Sydney 2012. Genotyping data show that GII.4 Sydney 2012 was first observed in a single outbreak in BC in February 2012. Since June 2012, GII.4K New Orleans 2009 has nearly disappeared, being replaced by the new strain (Figure 7). No differences in virulence have been reported between genotypes.

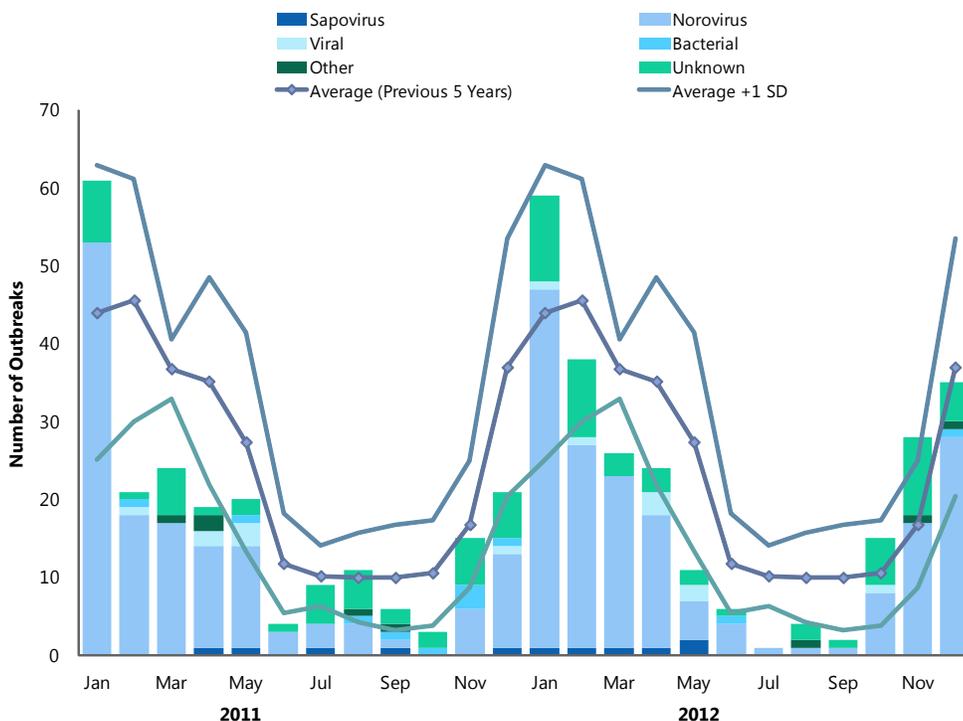
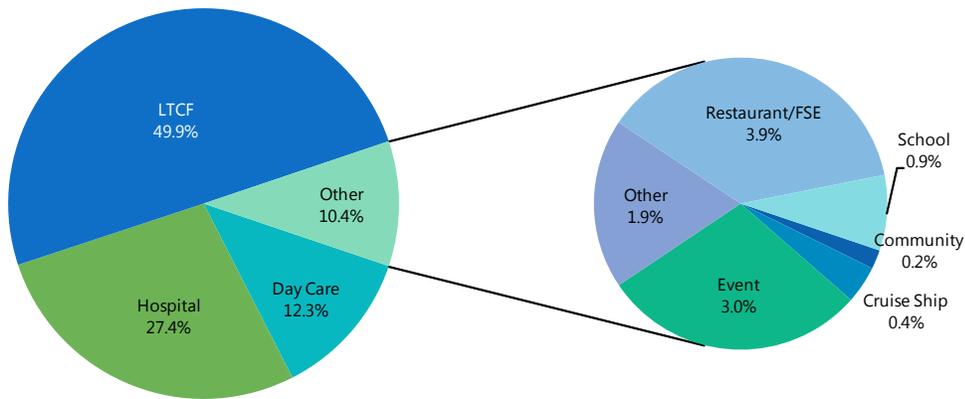
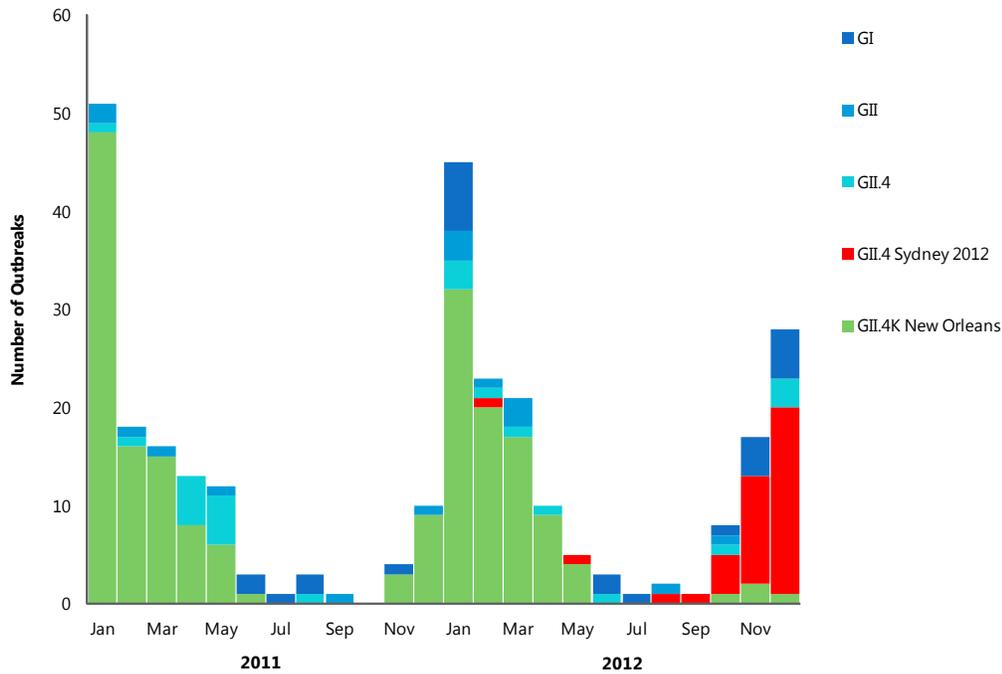


Figure 5. Reported GI outbreak etiologies from 2011 to 2012 by month.

# Environmental Microbiology



**Figure 6.** Reported GI outbreak etiologies from 2011 to 2012 by month.



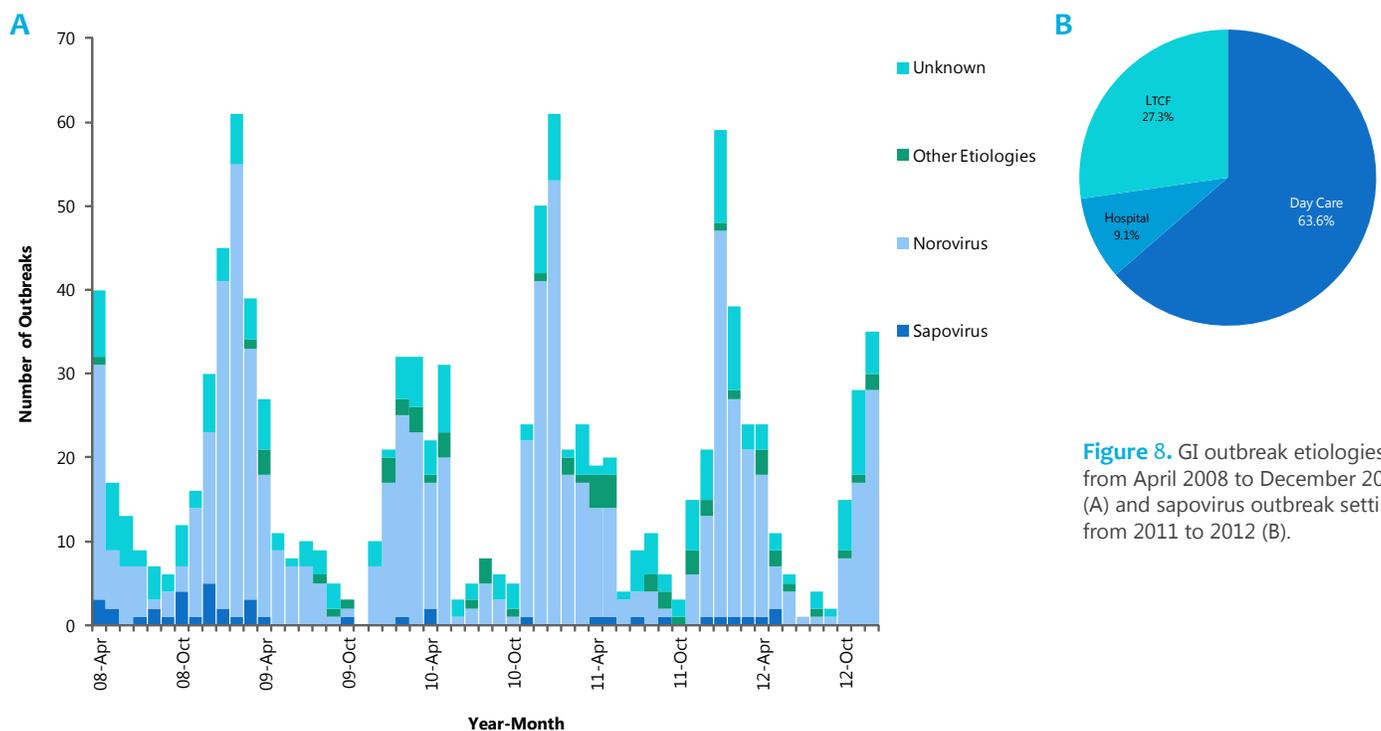
**Figure 7.** Norovirus genotypes in BC from 2011 to 2012.

## Environmental Microbiology

### Sapovirus Testing

As part of improvements for better detection methodologies for foodborne/GI outbreaks, sapovirus real-time reverse transcription PCR (RT-PCR) was introduced in February, 2012. It is now part of the GI outbreak testing algorithm. Sapovirus is a member of the *Caliciviridae* family and therefore structurally and genetically similar to norovirus. Although it has been reported that symptoms caused by sapovirus are similar to those of norovirus, there are clear differences in outbreak patterns. For example, sapovirus only accounts for 2-5% of all reported GI outbreaks in BC. The majority of the sapovirus outbreaks occurred during the 2008-2009 winter seasons, followed by sporadic activity in the two subsequent seasons (Figure 8A).

At this time, sapovirus causes outbreaks primarily in day care settings (64%) (Figure 8B) while norovirus occurs mainly in long-term care facilities (50%) (Figure 6). There is limited information about sapovirus transmission or outbreak patterns but further monitoring of this virus will shed light on whether it could become a major causative agent of GI outbreaks.



**Figure 8.** GI outbreak etiologies from April 2008 to December 2012 (A) and sapovirus outbreak settings from 2011 to 2012 (B).

## Food Poisoning Outbreaks

### Multi-Provincial *Escherichia coli* O157:H7

A multi-province *E. coli* O157:H7 outbreak, involving 4 provinces (Alberta, Quebec, Newfoundland and BC) was investigated between September and October, 2012. A total of 18 cases were detected with BC having 3 cases (indistinguishable PFGE and MLVA patterns). The BCPHMRL EM Program tested a beef sample collected from the home of a confirmed case and four food samples from the home of another case. *E. coli* O157:H7 was isolated from one with PFGE and MLVA fingerprinting pattern indistinguishable from the outbreak strain. EM worked closely with PHABM participating in Outbreak Investigation Coordinating Committee meetings led by PHAC to investigate the source of the infection and recall the food from further distribution.

### Diarrhetic Shellfish Poisoning

2011 marked the first reported outbreak of DSP in BC. Linked to mussel consumption, this outbreak involved 62 cases and 15 food establishments within the Lower Mainland and Vancouver Island. Illnesses were caused by okadaic acid group toxins produced by dinoflagellate algae (shellfish consume the algae and accumulate toxin). The investigation was multi-jurisdictional involving partners from several Health Authorities and CFIA. Cases experienced symptoms of nausea, diarrhea, vomiting, abdominal pain and cramps about 5-15 hours after food consumption. The BCPHMRL tested clinical and food samples for the presence of enteric pathogens while CFIA tested leftover mussel samples for lipophilic shellfish toxins including those of the okadaic acid group. Following this investigation, changes were made to the Canadian Shellfish Sanitation Program including increasing the sampling frequency and the number of monitoring sites along the BC coastline.



### Scombroid Fish Poisoning

In 2011, seven people visited the hospital due to food poisoning after ingesting contaminated tuna served by a fast food chain. The cases presented with symptoms of dizziness, nausea, flushing and vomiting shortly after consuming tuna sandwiches. Tuna was tested by the CFIA and found to have very high levels of histamine (produced when bacterial enzymes metabolize naturally occurring histidine in fish and most common when fish is held at ambient temperatures for several hours).

### Salmonella Enteritidis Outbreaks

*Salmonella* Enteritidis caused two egg-related foodborne outbreaks in 2011. The first involved a catered event that took place in November attended by more than 300 company employees. A variety of food was served which included a tiramisu dessert. Following the event, a third of the attendees became ill with abdominal cramping, fever and watery diarrhea with a median incubation period of 34 hours. *S. Enteritidis*, the causative organism, was first detected in clinical samples submitted by ill attendees. A food item from the event (tiramisu dessert) had been frozen and was tested. Further investigation determined that raw eggs were an ingredient in the dessert. All positive clinical samples and food isolates were serotyped as *S. Enteritidis*.



*S. Enteritidis* was the cause of a second outbreak with six people becoming ill after consumption of bakery products. During the investigation it was discovered that the restaurant was using temperature-abused eggs from an unapproved source. Eggs from the establishment were laboratory tested and *Salmonella* was detected on the shells.

### Staphylococcus aureus Food Poisoning

In November 2011, a holiday meal was served to 300 workers. About 15 people became ill with vomiting within 4 hours of the meal. Laboratory testing of leftover food items determined that the turkey samples were heavily contaminated with *Staphylococcus aureus*, an organism that can proliferate in foods cooked ahead of time and not properly stored.

## Botulism Updates

### Investigation

The EM Program carried out laboratory investigation of suspected foodborne botulism in 2011, subsequently confirmed to be a *Clostridium botulinum* Type B outbreak. This interesting and unusual outbreak (even a single case is considered an outbreak) was presented at CACMID-AMMI 2012 in Vancouver.

A previously healthy adult female was admitted to the hospital with bulbar paralysis and upper limb weakness. Botulism was suspected to be the cause of the symptoms. Serum and stool samples were submitted for testing but *C. botulinum* toxin was not detected by standard or enhanced procedures.

With Health Authority follow up, implicated foods were collected from the patient's home for laboratory examination. One of the foods, an opened jar of watermelon jelly, tested positive for *C. botulinum* Type B toxin. This commercially-prepared product was purchased from a charity booth and had been kept at room temperature for some time prior to consumption.

Since this food (jelly) has not been previously reported as a source of botulism, pH and water activity were also investigated by testing two unopened jars from different batches. One jar showed a pH value of 5.55 and water activity of 0.966 while the second jar showed a pH of 5.41 and water activity of 0.977. Both sets of results were indicative that watermelon jelly can support growth/toxin production by *C. botulinum*.

### Canadian Laboratory Response Network (CLRN) Member

In 2011, the EM Program became a partner of the CLRN. Collaborating with colleagues from PHAC and NML, senior staff took part in extensive training to learn procedures for detecting botulinum toxins using an Enzyme-Linked Immunosorbent Assay method and NAT to detect toxin genes in samples implicated in a bioterrorism event. Ongoing proficiency panels are performed to maintain competency in the methods.

## Enhanced Water Quality Assurance

The The EWQA Program (EWQA) is enabled by the dedication of its staff and volunteers from private and public testing laboratories and works for the provision of safe drinking water for residents of BC. EWQA continues to carry out its legislated mandate of supporting the approval, by the PHO, of water microbiology laboratories for drinking water testing. The dedicated volunteer auditor teams carried out the peer-review public health Quality Assurance work, led by the Provincial Coordinator, and supported by the Steering Committee and the Quality Assurance Advisory Group. Under this program, there are 16 PHO-approved water testing laboratories. These laboratories are located throughout BC and Alberta, with testing laboratories located in each of BC's five Health Authorities.

The PHO Approved Laboratory List is updated as required, when laboratories are newly accredited, choose to retire their certificate or add new testing methods. The list indicates the current approved environmental laboratories, along with the test targets (total coliforms, fecal coliforms and *Escherichia coli*) and the test method that the laboratory is approved for. The list is available online on both the [EWQA](#) and [Ministry of Health](#) websites.



## Environmental Microbiology

### Food Quality Check Program

The Food Quality Check Program provides laboratory testing services to Environmental Health Officers to assess the sanitary quality of ready-to-eat foods from food service establishments. Testing includes bacterial indicator organisms and aerobic plate counts. The program is primarily focussed on education but under certain circumstances it is used to carry out surveys on specific food/pathogenic types for gaining information and for public health interventions.

A total of 206 samples from a variety of foods were submitted for testing for aerobic plate count and presence of total coliforms, fecal coliforms, *E. coli*, *Staphylococcus aureus* and *Bacillus cereus* (Figure 9). Of the samples tested, 25% (2011) and 29% (2012) exceeded the guideline for aerobic plate count and 6% (2011) and 7% (2012) were unsatisfactory for fecal coliforms. Guideline levels for *E. coli* were exceeded by about 1% in 2011 and 2% in 2012 (Figure 10). For *B. cereus*, 21% of samples were positive and 3% exceeded the guidelines (Figure 10). For *S. aureus*, 10% of samples were positive but none exceeded the guidelines.

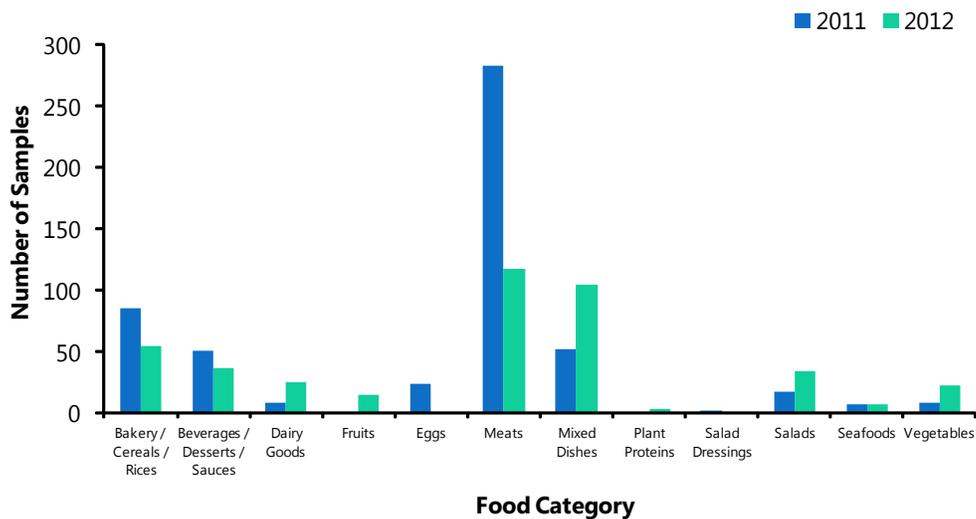


Figure 9. Number of food samples tested by food category, 2011-2012.

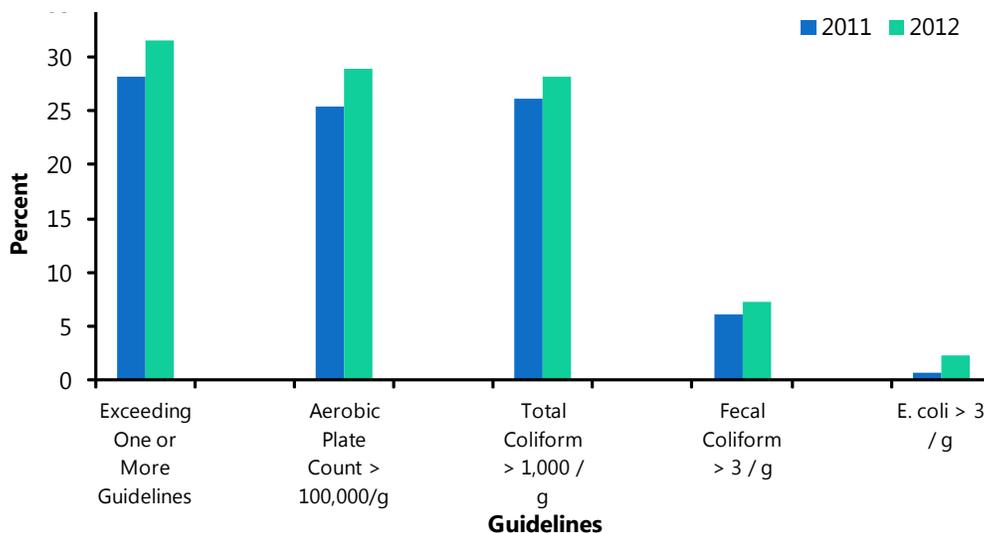


Figure 10. Percent of food samples exceeding food safety guidelines, 2011-2012.

### Legislated Water and Food Microbiological Quality Monitoring

One of the main responsibilities of the EM Program is to support public health surveillance of drinking water, recreational water and suspected sewage via testing with bacterial indicator organisms (total coliforms, fecal coliforms and *E. coli*).

Figures 11 and 12 show the number of samples tested by different water types and water systems across BC.

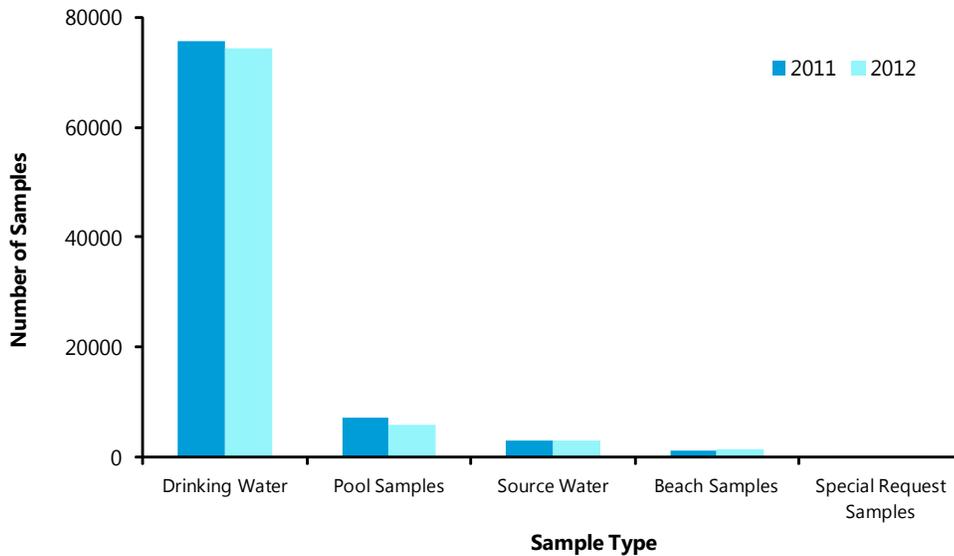


Figure 11. Number of water samples received per sample type, 2011-2012.

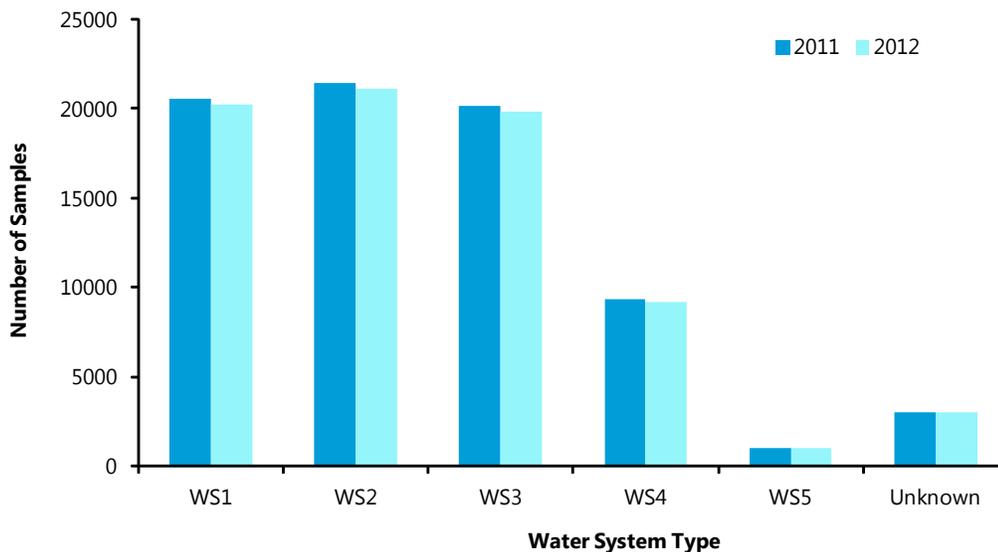


Figure 12. Number of water samples received per system type, 2011-2012. Categories of public water supply systems: WS1: >300 connections; WS2: 15-300 connections; WS3: 2-14 connections; WS1: 1 connection; WS5: other types e.g. daycares and restaurants.

## Innovations and Improvements

Over the last 2 years, the EM Program has been involved in a variety of projects with our public health partners. Most of this work arose either from client requests for assistance, development of our Core Functions or to validate and implement advances in environmental microbiology methods. The following examples highlight some of this work.

### BBQ Meat Safety

Working with VCHA and other Health Authority Environmental Health Officers and Drinking Water Officers, our food safety experts assessed, using developed laboratory protocols, preparation methods and sanitary qualities of Chinese-style barbecued meat products from retail food establishments in the Lower Mainland. The intent of the study was to compare food preparation methods and sanitary quality and to use laboratory results (aerobic plate count, total coliforms, fecal coliforms, *E. coli*, *S. aureus* and *B. cereus*) to determine whether these foods present a potential health hazard to consumers. A total of 206 food samples were tested.

Results showed:

- 27% exceeded the guideline for aerobic plate count
- 11% and 0.5% tested unsatisfactory for fecal coliforms and *E. coli*, respectively.
- 3% exceeded the guideline for levels of *B. cereus*
- 10% were positive for *S. aureus* although none exceeded the unsatisfactory limit.

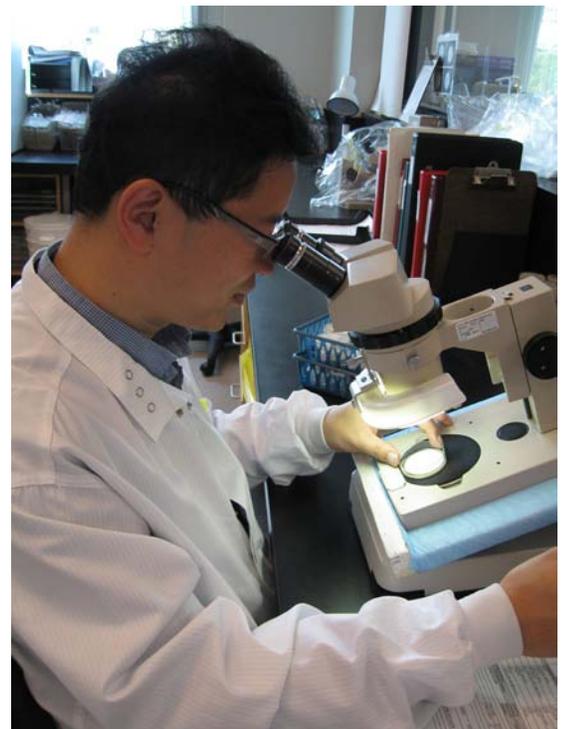
Data were helpful in on-the-ground policy and food inspection follow-up work.

### Norovirus Sequencing

As a member of the national ViroNet network, our team carried out select DNA sequencing. Results showed when and where a new norovirus strain first emerged. Subsequent to that detection, this novel strain went underground only to emerge in an explosive fashion, replacing the current circulating genotype and causing widespread episodes of abrupt onset diarrhea and vomiting. This rapidly emerging genotype was particularly difficult for patients and staff in acute care hospitals and long-term care facilities in all Health Authorities. Communications about this emerging strain were sent out to partners across BC and Canada.

### *Campylobacter* CGF

The EM Program partnered in the development of a new molecular microbiology tool to better address the question of strain-relatedness for *Campylobacter*. Working with our LLTO, the MMG Program, the C-EnterNet Team and the PHABM Program, food isolates from outbreaks were included with human samples for phenotyping and genotyping using CGF (as previously described). Other work was undertaken with FHA public health and private/public laboratories, BCCDC epidemiologists and C-EnterNet.



## Environmental Microbiology

### Waterborne Pathogen Detection and Typing

Ongoing collaborations with several watershed managers assessed parasite occurrence (*Giardia* and *Cryptosporidium*) to permit better watershed management and public health protection. Genomic sequencing of these protozoans allows public health risk assessment by differentiating between human-infective and human non-infective strains.

### Collaboration with FHA on C-EnterNet Sentinel Surveillance

Starting in 2011, EM, as part of the BC sentinel site group, partnered with C-EnterNet and FHA public health to perform pathogen risk assessment on various recreational water sites in FHA and to support fingerprinting of bacterial samples from patients (to be compared with food service isolates). All pathogens detected in environmental samples are fingerprinted by molecular methods (PFGE). Comparison of environmental isolates to human patient isolates assists in public health assessments from “farm-to-fork”.

### Whole Genome Sequencing Advances

With the recent acquisition of an Illumina® MiSeq by the MMG Program, BCPHML has joined laboratories able to use NGS, a system to massively parallel DNA sequencing, impacting microbiology world-wide. Work is in progress to sequence *C. botulinum* type B organisms causing outbreaks since it is rare in Canada. With the complete genomic sequence of outbreak-related isolates, transmission patterns may be better defined and questions answered. For example, EM is asking why botulinum type B is such a rare event. Where are these microbes coming from?

### Genome Canada and Canadian Water Network Partnerships

Current laboratory tools to assess microbial water quality are unsatisfactory as testing approaches rely on methods developed at the turn of the 20th century. These culture-dependent approaches are slow, non-specific and poorly represent the range of microbial contaminants that may be present in a contaminated watershed. Drs. Judith Isaac-Renton, Patrick Tang, Natalie Prystajek and William Hsiao, along with researchers from UBC, Simon Fraser University (SFU) and across Canada received \$3.2 million in funding from Genome Canada, Genome BC, the SFU Community Trust and PHAC to launch a project called “Applied metagenomics of the watershed microbiome”. The project aims to improve water quality in Canada and abroad using genomics and metagenomics to develop novel tools to assess water quality. Two novel tools will be developed: a Water Health Profile tool to assess general water quality and a Microbial Pollution Profile tool to help identify the source of pollution.



Find out more information at [www.watersheddiscovery.ca](http://www.watersheddiscovery.ca).

For routine monitoring of water quality, there has been limited uptake of emerging technologies which require extensive validation before industry uptake occurs. However, no formalized validation criteria exist for molecular water quality testing. Drs. Isaac-Renton, Tang and Prystajek also received funding from the Canadian Water Network for a project called “Innovation to application: Creating a pipeline for validation and uptake of emerging water testing technologies” which aims to improve test uptake by developing validation criteria. It also aims to ease the interaction between test creators and test end-users. This work is being carried out by a cross-Canada team, including researchers in Manitoba, Ontario and Quebec.

## National Network Highlights



In addition to being a key member of the CRLN response team for botulism testing and back-up to PulseNet Canada with certified cross-trained staff (surge capacity), the EM Team is a member of the CPHLN Water Food Safety Subcommittee. This group works closely with other public health laboratories in Canada and the US to fingerprint norovirus.

Following the widespread and serious *Listeria* contamination of deli-meats (consumed by particularly vulnerable populations across Canada), the Weatherill Report (2009) noted that food testing laboratories were fragmented. As a result of this report to Parliament and supported by the Chief Medical Health Officers across Canada, CFIA was commissioned to develop a plan to improve on this

fragmentation. In 2012, the Assistant Deputy Minister of Population Public Health, Ministry of Health, appointed the EM Program Head to represent BC on a Laboratory Network of Networks Steering Committee with a mandate to focus on developing a strategy to improve capacity in advanced microbiology methods and to defragment food testing in Canada.

## Lean Initiatives

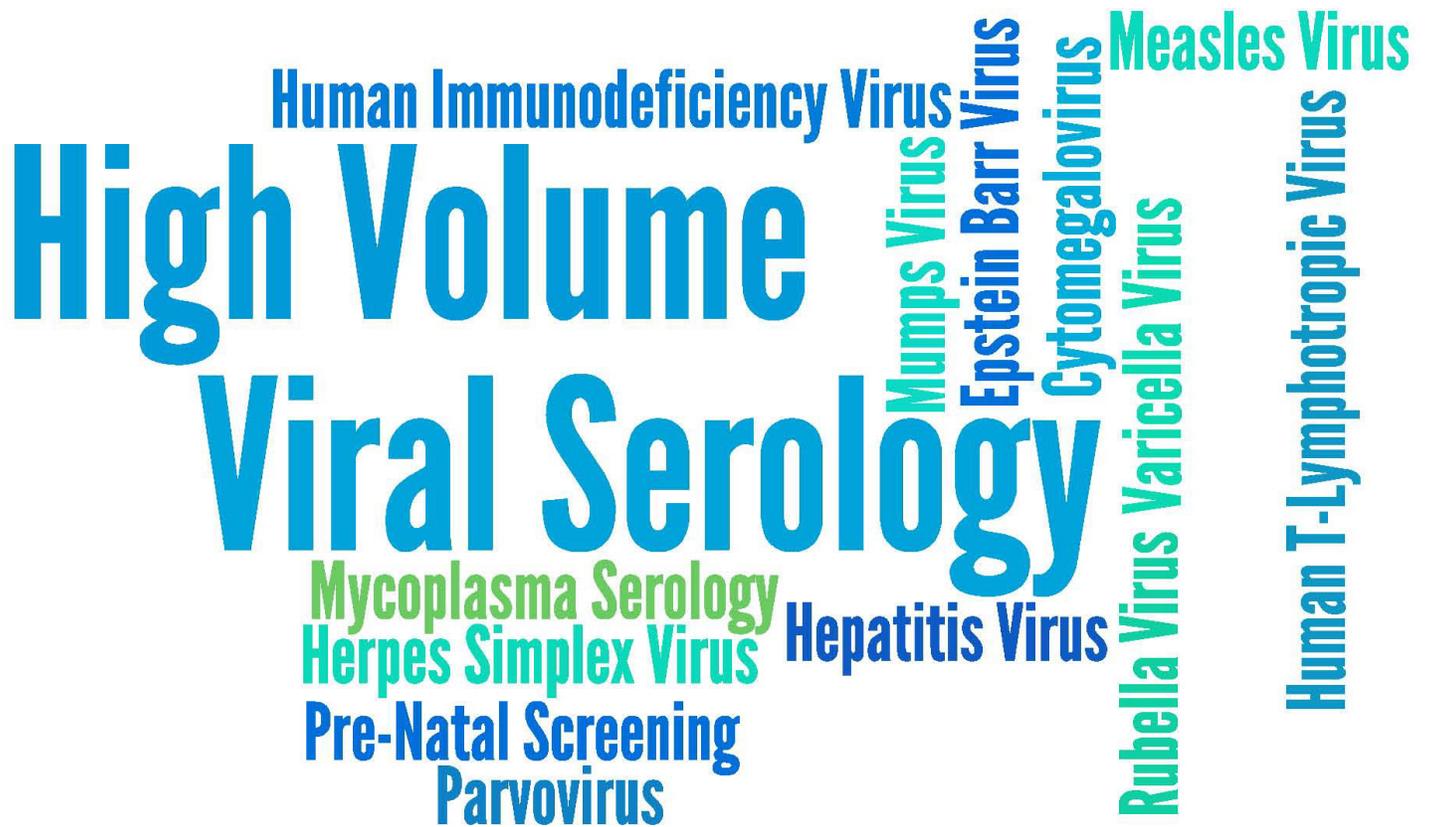
Well-known principles and tools for reducing waste and increasing effectiveness (derived from the Toyota Production System) have been applied widely in business. More recently these principles, often referred to as Lean principles, have been used by QMS experts in health care. PHSA, as a provincial lean principle (imPROVE) leader, works with many groups including laboratories, to carry out training, Value Stream Mapping and kaizen events carried out by staff (on the “gemba” or workplace). These projects are called Rapid Process Improvement Workshops or RPIWs in PHSA terminology. EM, the first to carry out a kaizen event in PHSA Laboratories, went on to help others and to see one of its staff members volunteer to become lean trained and inform two other Programs in Value Stream Mapping.



Ling Li became a certified Lean Greenbelt Champion in 2012.

## Information Management Initiatives

Since the new commercial software and LIS purchased by PHSA Laboratories for its many clinical laboratories could not address the specialized water and food testing needs of the BCPHMRL, EM staff members continued to enter, validate and report food and water testing using the “legacy” system. Due to the risks associated with this aging system, the EM Team partnered with PHSA IMIT to launch an investigation into suitable software complements (“Best of Breed”) to the clinical Sunquest System. Finding few options to support this specialized food and water work, the EM/IMIT team began to explore whether the new Sunquest 6.4.2 System could be used for environmental sample accessioning, testing and reporting. Close ordering/reporting linkages with water purveyor clients, as well as Environmental Health Officers and Drinking Water Officers in all Health Authorities, are also required. The work continues to look promising with new order and result codes evaluated in a test environment and with code and links made to results distribution vendors (WaterTrax®, HealthSpace); end-to-end testing has also begun.



# High Volume Viral Serology



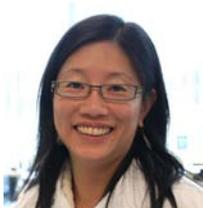
**DR. MEL KRAJDEN**

Program Head,  
Medical Microbiologist



**DR. MARTIN PETRIC**

Clinical Virologist



**ANNIE MAK**

Section Head



The High Volume Viral Serology Laboratory, the analytical arm of the Central Processing & Receiving Program, provides high-volume viral serology testing province-wide including testing for HIV, hepatitis, rubella, and other viruses as well as prenatal microbiological screening.

Detection of acute HIV infection in the men who have sex with men (MSM) population is a recent and unique program in the province and across Canada and is a relatively new part of High Volume Viral Serology.

The program operates at high efficiency processing more than 1,200 samples and 2,000 tests per day. It continues to work under lean principles to enhance quality and turnaround times while maintaining accuracy, safety and cost savings through high throughput strategies.

Due to the high volume and automated nature of the laboratory, technical staff are therefore able to focus their expertise on specialized laboratory requests and quality-related activities.

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## High Volume Viral Serology

### Hepatitis A Outbreak Support

For the last 7 years, the diagnosis of acute hepatitis A virus (HAV) has involved a dual enzyme immunoassay (EIA) screening approach. Screening for anti-HAV employs one manufacturer's EIA and reactives are confirmed with another manufacturer's EIA. This strategy helps reduce the number of false positive anti-HAV-IgM results. When a confirmed anti-HAV-IgM is identified, serum is routinely submitted to the NML for HAV genotyping. This strategy helps to identify single source HAV clusters. In 2012, BC reported 35 cases of HAV infection including six identified as genotype 1B related to a frozen fruit blend product.

### Hepatitis A outbreak on Central Vancouver Island

On central Vancouver Island an outbreak of hepatitis A occurred over 17 months from October 2010 to March 2012. Infected cases totalled 91 of which 21 were hospitalized. As only 15% to 20% of cases develop clinical illness severe enough to require medical attention it is likely that the outbreak affected about 500 people. In an effort to control the outbreak, nearly 13,000 people were immunized. NML HAV A genotyping was helpful in confirming outbreak-related cases and identifying sporadic cases unrelated to the outbreak.

### Pooled HIV NAT Detects Acute HIV in BC

The contribution of acute HIV infection (AHI) to transmission is widely recognized, particularly for MSM who account for the majority of new HIV diagnoses in BC. It is estimated that AHI accounts for 25% to 60% of onward HIV transmissions. During acute HIV infection, a person is not aware of being infected but very high viral loads mean the infection is easily transmitted; however, when these people are informed that they are infected, they change their risk activities and reduce the risk of transmission.

As the RT-PCR assay is costly and because the viral load in these patients is very high, the sera of 24 patients can be tested as a single pool. Pooled NAT can detect HIV infection 7-15 days after infection compared to 20-30 days for 3rd generation EIA tests. Pooled NAT following negative 3rd generation EIA testing was implemented in April, 2009 for six clinics in Vancouver accessed by MSM adults as part of a research project funded by the Canadian Institutes of Health Research. Of 217 new HIV diagnoses in the first 4 years of pooled NAT use, 54 (25%) cases of AHI were diagnosed (25 detected by pooled NAT only), mostly among MSM (208, 96%). This work was done in collaboration with Dr. Mark Gilbert, Surveillance & Online Sexual Health Services, Clinical Prevention Services, BCCDC.



A diagnosis of AHI may result in the prevention of one to three additional infections in the year following diagnosis compared to diagnosis of established HIV infections. Assuming a lifetime cost of medical care of \$303,100 CDN per individual newly diagnosed with HIV, one averted HIV infection would justify the cost of pooled NAT over a 3-year period. The 25 AHI cases diagnosed through pooled NAT averted an estimated \$9.2 to \$27.7 million CDN in medical costs.

### Immunity to Measles Virus Infection in Prenatal British Columbians

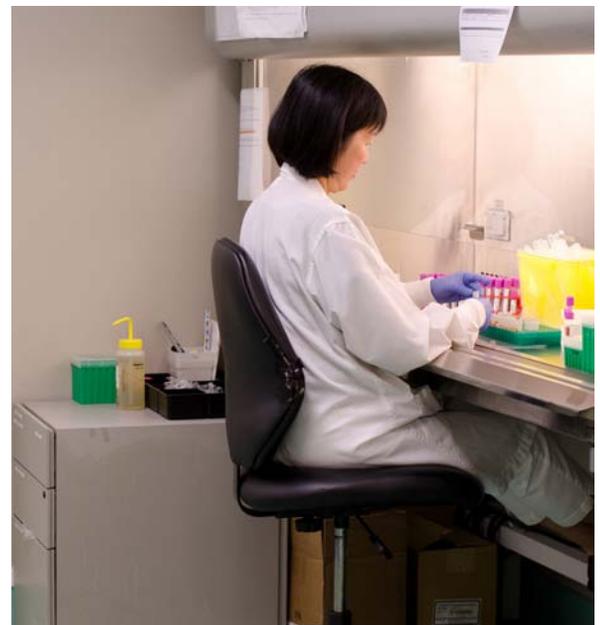
Population level immunity to measles may change over time due changes in immunization programs. Serology studies can be used to assess immunity in the adult population, especially when detailed immunization history is lacking. A serosurvey for antibody to measles was conducted by birth cohort (those born between 1960-69 and 1970-79) to explore the correlation measles immunity using a quantitative assay.

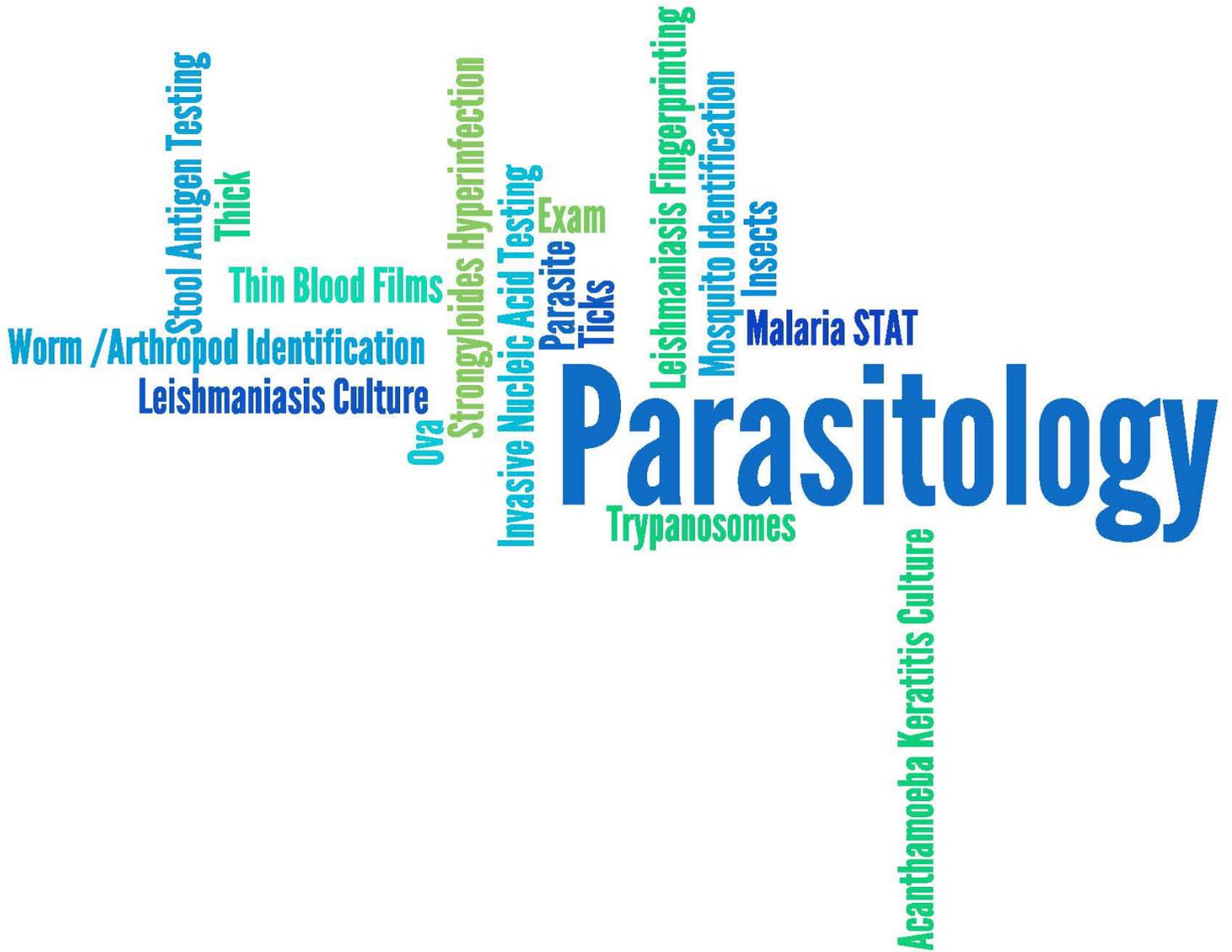
**Table 1.** Measles seroimmunity results for individuals born 1960-69 and 1970-79.

Year	Born 1960-69		Born 1970-79	
% Measles IgG Positive* <b>(Quantitative Assay)</b>	95% (631/661) (94-97%)		88% (588/665) (86-91%)	
	Born 1960-64	Born 1965-69	Born 1970-74	Born 1975-79
% Measles IgG Positive* <b>(Quantitative Assay)</b>	97% (228/234) (95-99%)	94% (403/427) (92%-97%)	91% (303/332) (88-94%)	85% (285/333) (81-89%)

\*Positive denotes IgG levels > 337mIU (A450 > 0.200) using the Quantitative Assay

These data confirmed that individuals born in the 1960's were more likely to be measles seropositive (95%) and have higher measles antibody levels than individuals born in the 1970s (88%) (Table 1) probably because older individuals were exposed to wild-type measles infection which induces a more durable immune response. In contrast, younger individuals are dependent on vaccine-induced immunity for seroprotection. This information suggests that additional vaccinations later in life may be required to maintain adequate levels of immunity to prevent measles outbreaks. We also confirmed that the results from a previously used qualitative measles assay correlated well with the newer quantitative assay. Quantitative measles, mumps and varicella zoster serological testing were implemented in September, 2012.





# Parasitology



**DR. JUDY ISAAC-RENTON**

Program Head,  
Medical Microbiologist



**QUANTINE WONG**

Section Head

The Parasitology Program provides province-wide public health parasitology, reference support, and diagnostic and medical consultative services. Unlike many other areas in microbiology, automation and new technologies have had relatively minor impact. As a provincial reference and resource, the high level of service provided is completely dependent on the experience and expertise of highly trained and experienced medical technologists.

The provincial leadership role played by this Program is carried out by a medical, technical and scientific team performing reference-level characterization of intestinal parasites, detection of blood and tissue parasites, and identification of medically important ectoparasites. The Parasitology Team also leads the province's Lyme and West Nile virus surveillance programs, identifying vectors for subsequent PCR identification in the Zoonotic Diseases & Emerging Pathogens Program.

**TELEPHONE**  
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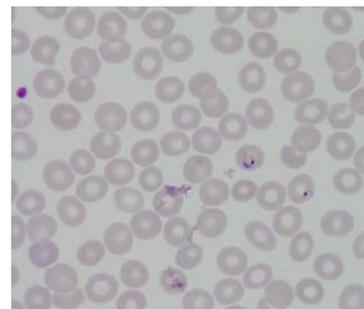
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## Parasitology

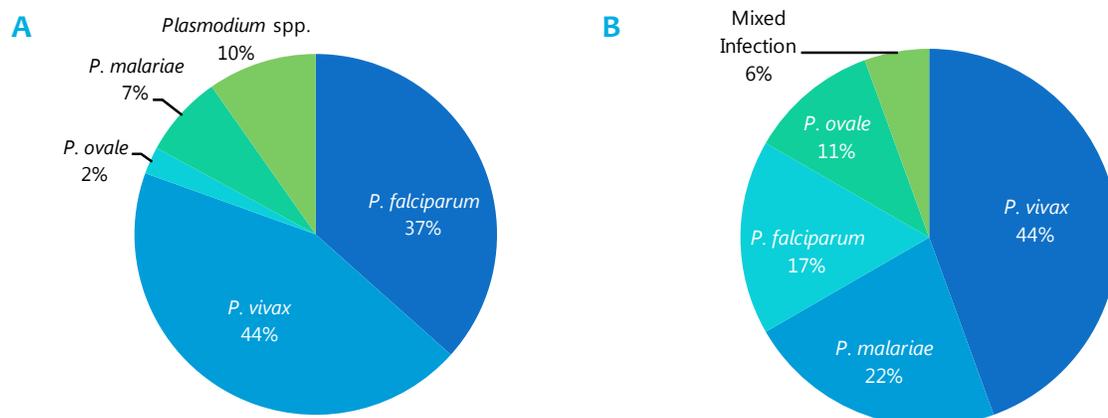
### Malaria Services

Five species of *Plasmodium*, a protozoan causing malaria, can infect and be transmitted by humans. The vast majority of deaths are due to *P. falciparum* but *P. vivax*, *P. ovale*, and, to a lesser degree, *P. malariae* also result in severe illness. The zoonotic species *P. knowlesi*, found in Southeast Asia, causes malaria in macaques and has recently been shown to cause severe infections in humans.

Malaria is typically diagnosed by the microscopic examination of blood smears or by antigen-based rapid tests. The latter are generally quick and easy to use but users should be mindful that they may remain positive for a period of time post-treatment. Molecular techniques that use NAT PCR to detect the parasite's DNA have been developed but are not widely used in malaria-endemic areas due to their cost. In the Parasitology Program, malaria NAT is used as a quality assurance procedure. Hundreds of malaria cases are referred annually to the Parasitology Program for confirmation. Below are graphs summarizing which *Plasmodium* species infected patients diagnosed in 2011 and 2012 (Figure 13).



*Plasmodium falciparum* ring forms



**Figure 13.** Malaria cases and their *Plasmodium* species vectors identified in 2011 (A) and 2012 (B).

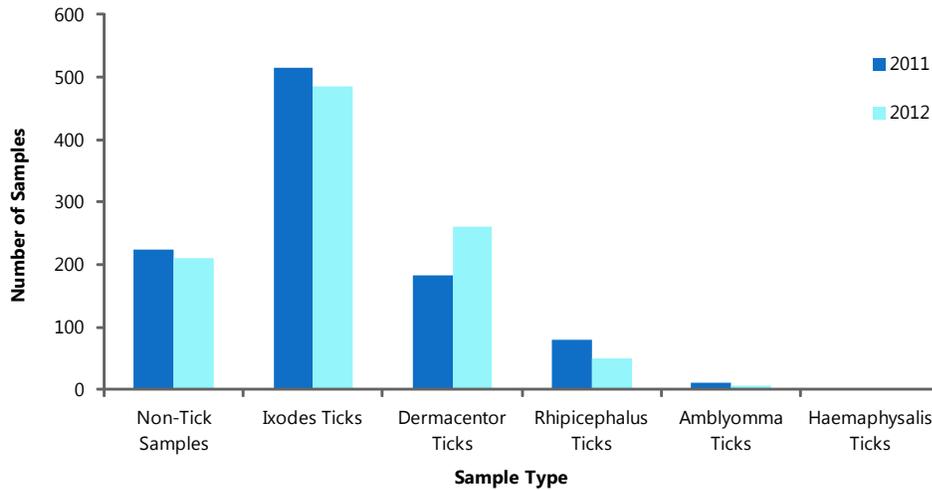
### Referred in for Identification

Many samples sent to the Parasitology Program for identification are ticks with the most common identified being the *Ixodes* and *Dermacentor* ticks (Figure 14). BC has a genus of ticks (*Ixodes*) that can transmit the pathogenic bacterium *Borrelia burgdorferi* responsible for Lyme disease. Non-tick samples sent in for identification included worms, proglottids and other arthropods. Since 2005, the Parasitology Program has also overseen mosquito surveillance for West Nile virus, the most widely distributed mosquito-borne disease in North America. Thousands of mosquito pools are sent in for identification by various provincial Health Authorities during surveillance (each pool may contain up to 50 mosquitoes). The mosquitoes are identified to the genus level, and in the case of *Culex* mosquitoes (the most likely vector for West Nile virus), to the species level. Only female *Culex* mosquitoes are tested for West Nile virus by NAT.



Female *Ixodes pacificus*

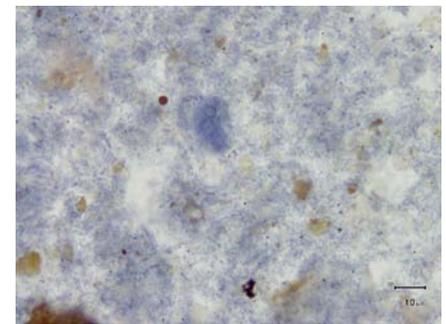
# Parasitology



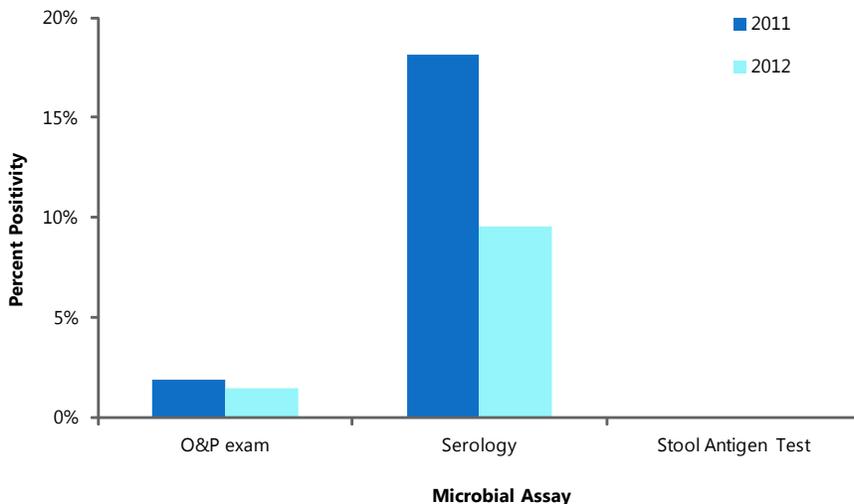
**Figure 14.** Tick and non-tick samples identified, 2011-2012.

## Challenges of Amoebiasis

Diagnosing amoebiasis can be a challenge. Ova and parasite (O&P) exams, serology tests and stool antigen tests are performed in the Parasitology and Zoonotic Diseases & Emerging Pathogens Programs. Microscopically via O&P examination, pathogenic *Entamoeba histolytica* cannot be differentiated from non-pathogenic *Entamoeba dispar*; results are reported as *Entamoeba histolytica/dispar*. Serological, stool antigen and NAT tests for *E. histolytica* can aid in the diagnosis of amoebiasis but also have limitations: serology becomes reactive after 2 weeks of infection but may stay reactive for many years while stool antigen and NAT tests are not widely used. In 2011 and 2012, less than 2% of samples were positive for *E. histolytica/dispar* by O&P exam (Figure 15) and all stool antigen tests were negative for *E. histolytica*. In 2011, 18% of cases submitted for serology were positive and about 10% in 2012 (Figure 15) but cases are difficult to interpret in situations where serology is reactive and there are no clinical signs and symptoms.



*E. histolytica/dispar* trophozoite



**Figure 15.** Amoebiasis detected by different microbial assays, 2011-2012.

### Severe *Strongyloides stercoralis* Infections

Potentially life-threatening, *Strongyloides stercoralis* infection is diagnosed via microscopic observation of larvae in fecal specimens. As the provincial reference service, the Parasitology Program performs both the Agar Plate Method and the Baermann Technique for the detection of *S. stercoralis* larvae (see below). These procedures are more sensitive than the usual direct smear or fecal concentration methods, especially in situations where parasite concentrations are low.

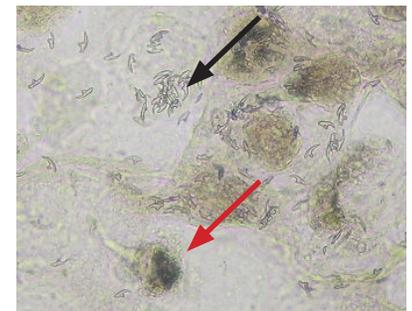


Using the Baermann Technique for *Strongyloides* detection.

- In the Agar Plate Method, a fresh fecal sample (non-refrigerated) is placed onto agar plates, and the plates are sealed to prevent accidental infections and held for 2 days at room temperature. As viable larvae move over the agar, they carry bacteria with them, thus creating visible tracts over the agar. Daily search for furrows on agar plates for up to 6 consecutive days results in increased sensitivity for diagnosis of both *S. stercoralis* and hookworm infections. Sediments from the plates are also examined under the microscope to confirm the presence of larvae.
- The Baermann Technique relies on viable larvae migrating from a fresh non-refrigerated fecal sample placed on a wire mesh with gauze in contact with tap water. Larvae migrate through the gauze into the water and settle to the bottom of the funnel, where they can be collected and examined. The advantage of this method is that it examines a greater amount of fresh stool, possibly providing a better chance of larval recovery in a light infection. This procedure may recover both viable and non-viable larvae.

### New Species of Tapeworm Detected

Researchers from the Universities of Guelph and Saskatchewan, working with BC veterinarians, wildlife biologists, and trappers, identified a European strain of a pathogenic tapeworm (*Echinococcus multilocularis*) in one dog and 10 of 27 coyotes trapped near Quesnel, BC. The findings were published in the 2012 winter issue of *BC Trapper* magazine, "Finding of a new tapeworm in coyotes in central British Columbia".



*Echinococcus multilocularis* cyst with mass of hooklets (black arrow) and an emerged protoscolice (red arrow).

### Genotyping of Pathogenic *Acanthamoeba*

*Acanthamoeba keratitis* is a serious corneal disease caused by members of a genus of free-living amoebae, *Acanthamoeba*. The disease is predominantly associated with contact lens use. Using sequence analysis of *Acanthamoeba* strains isolated over 23 years by the Parasitology Program, this study aimed to determine if the significant increase in *Acanthamoeba* cases from 2003 to 2007 was due to a clonal outbreak. In the analysis the number of isolates (from different cases) sent to BCPHMRL appeared to increase in 2003, reaching a peak between 2004 and 2006, then declining. Molecular phylogenetic analysis showed that all the *Acanthamoeba* isolates studied from 1987 to 2010 belonged to the T4 genotype. This is consistent with the predominant pathogenic genotype found worldwide. Using the 18S rDNA ASA.S1 (DF3 region) genotyping method, it was found that in BC most strains within the same year had different sequences (Figure 16). Some isolates between 2004 and 2006 shared the same genomic sequence, but the majority had different sequences (genotypes); thus these events were not due to a clonal outbreak.

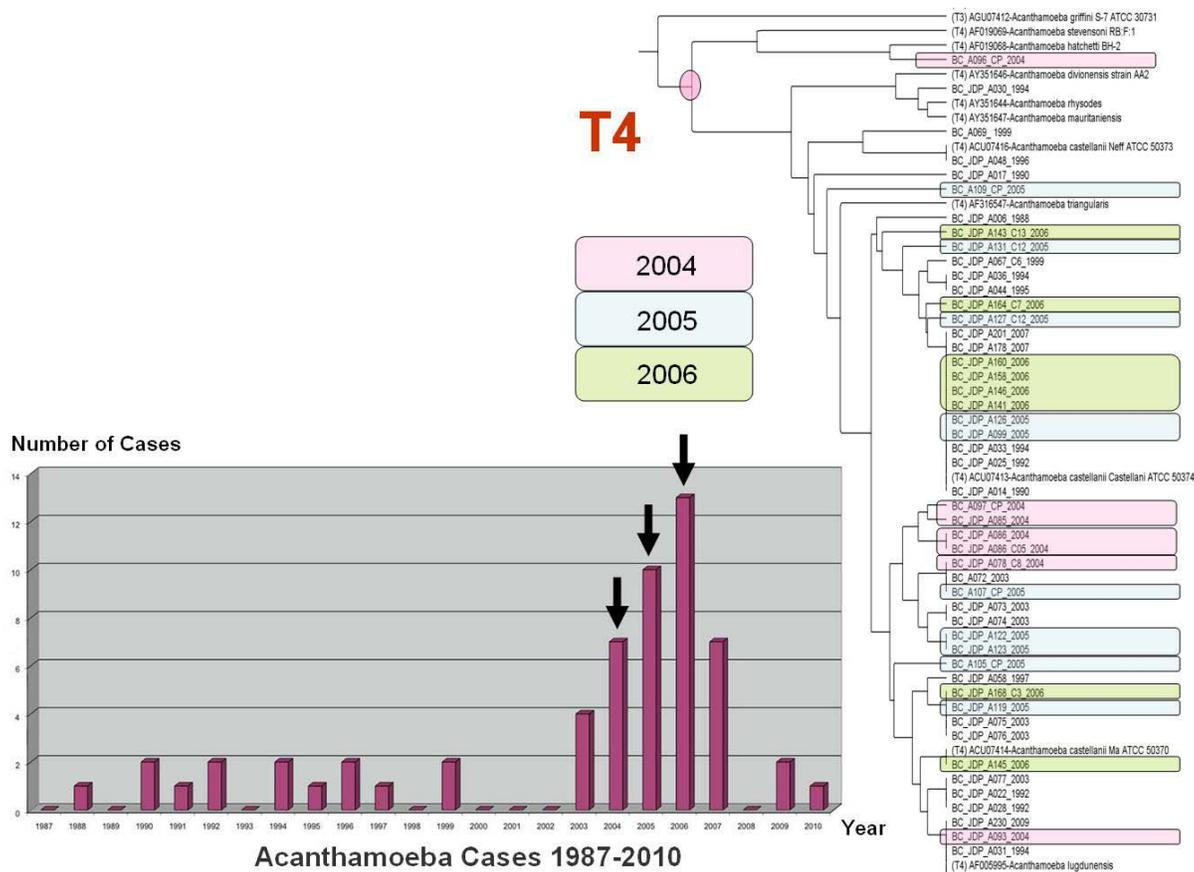
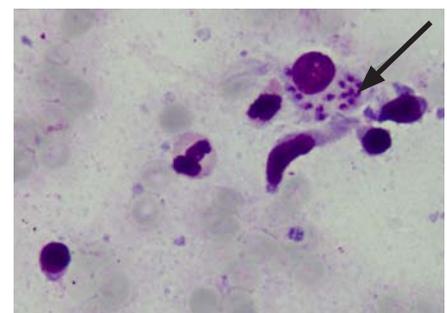


Figure 16. Phylogenetic tree of the 18S rDNA DF3 region of *Acanthamoeba keratitis* strains from BC cases, 1987-2010.

### Leishmania - A Twenty Year Review

The Parasitology Program presented 20 years of *Leishmania* data at the 2013 CACMID conference in Quebec City; the overall positivity rate was 26% (Figure 17). A poster, '*Leishmania* - A Twenty Year Retrospective Review', showcased a traveller to a *Leishmania*-endemic country who presented at a Lower Mainland acute care hospital with many typical *Leishmania* cutaneous lesions. Providing a comprehensive diagnostic service for the detection of this invasive parasite and its infection, leishmaniasis is part of the provincial reference services provided by BCPHMRL for potentially serious infections. The analysis suggested a need to collect multiple samples to enable a diagnosis.



Giemsa stained smear of *Leishmania* amastigotes (indicated by the arrow)

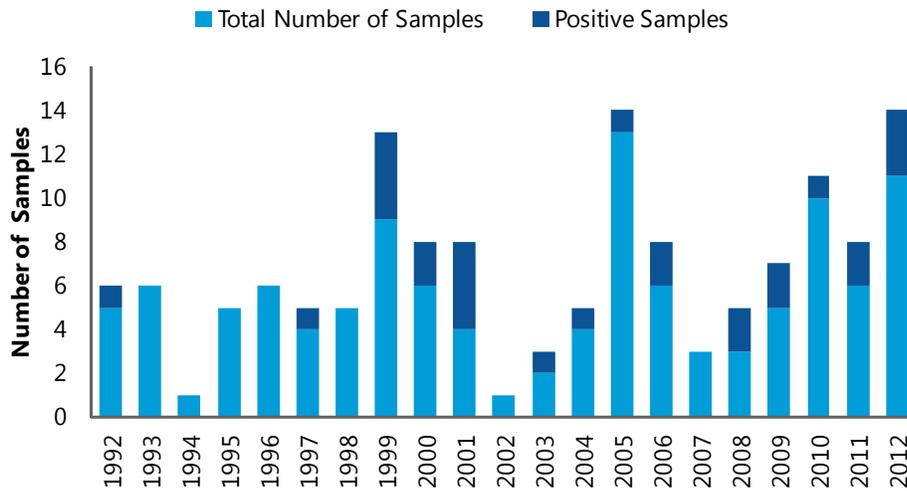
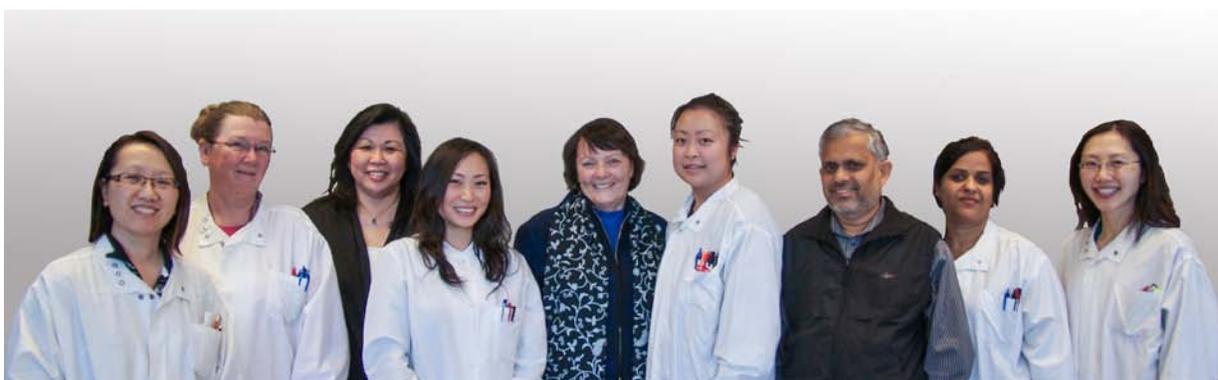


Figure 17. *Leishmania* samples submitted to BCPHML, 1991-2012.

### Telepathology Service

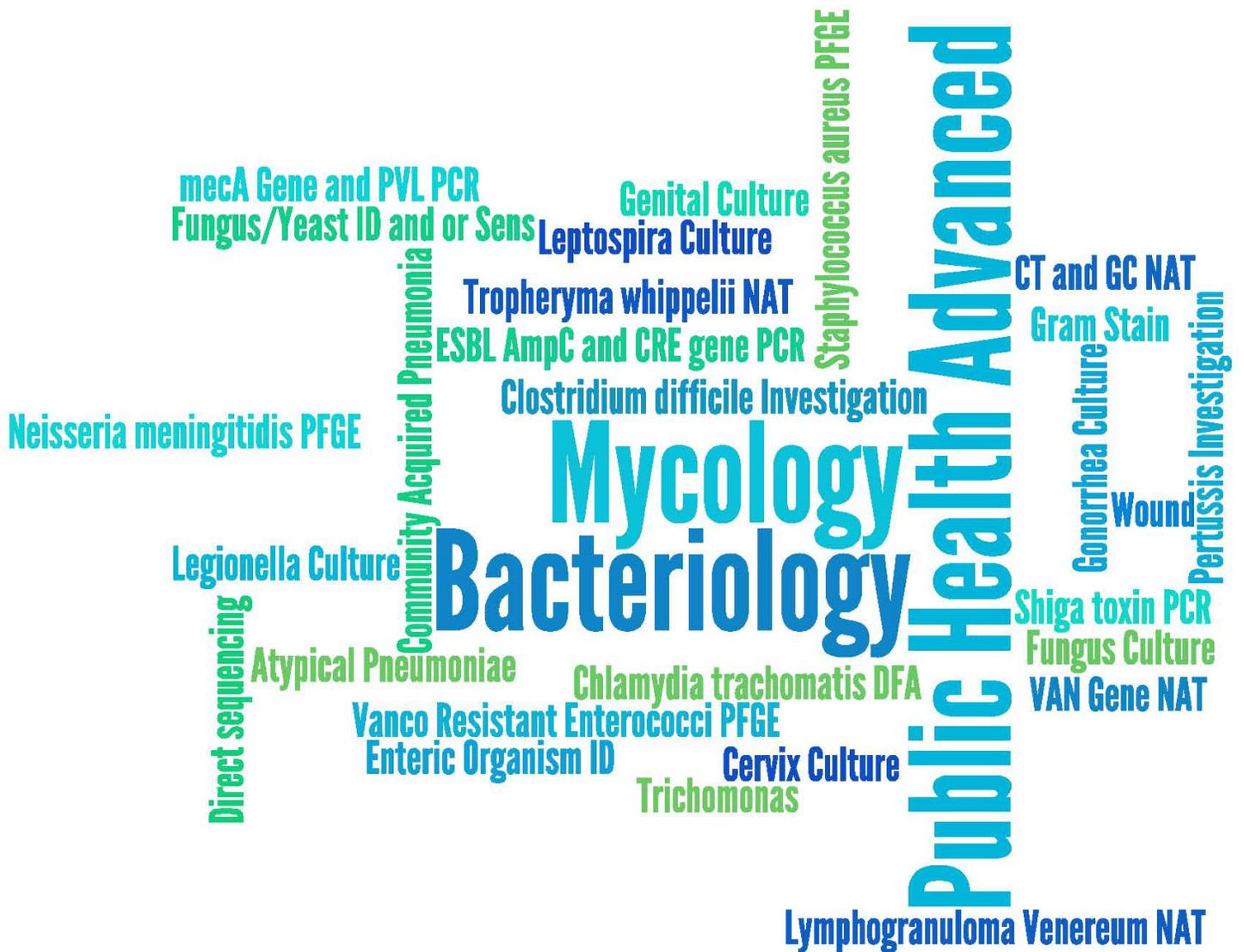
The Parasitology Program has been developing a parasitic telepathology service to aid in the diagnosis of parasitic infections. Telecommunications technology facilitates the transfer of image-rich pathology data between distant sites for the purposes of diagnosis, education and research. Implementation is planned for 2013.

Images can be emailed to [TeleParasitology@phsa.ca](mailto:TeleParasitology@phsa.ca). A completed Parasitology requisition must be scanned/emailed along with the images or faxed to the Parasitology Program so that a report can be generated; pertinent patient history must also be included. For further information on this service, the Parasitology staff can be contacted at (604)707-2629.



## Parasitology Telepathology Service

BC Public Health Microbiology and Reference Laboratory



# Public Health Advanced Bacteriology & Mycology



**DR. LINDA HOANG**

Program Head,  
Medical Microbiologist



**ANA  
PACCAGNELLA**

Section Head

The PHABM Program provides provincial public health and reference diagnostic bacteriology and mycology services. The Program confirms and further characterizes bacterial and fungal organisms responsible for enteric, respiratory, sexually transmitted and health care associated infections using a variety of culture-based and molecular diagnostic methods. Characterization by many molecular fingerprinting techniques is performed for outbreak detection and management, and for public health and infection control purposes.

Reference bacteriology and mycology services are also widely used by laboratory partners in BC. This was the first public health laboratory in Canada to be certified under the CLRN, providing diagnostic testing on high containment level agents of concern such as anthrax and tularemia. The laboratory also actively engages in research and training up to the post-graduate level.

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## NAT Detection of STEC

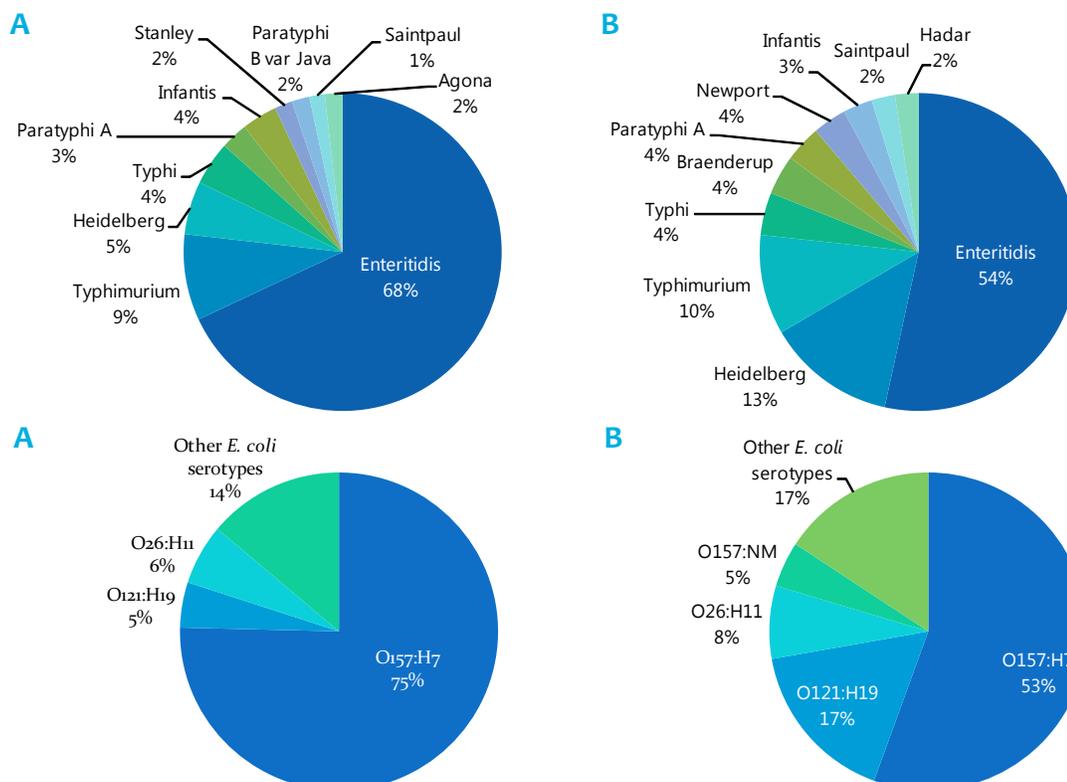
In mid-June 2012, the PHABM Program began using NAT for the detection of toxin genes of STEC in place of the vero-cell assay. Assay development was carried out in partnership with the MMG Program. It improves on test sensitivity and specificity, significantly decreases turnaround time and simplifies processes (i.e., no cell cultures). All submitted stool samples for enteric pathogen testing are now screened using STEC PCR with additional isolation of STEC for serotyping and PFGE.



## Enteric Surveillance

Defined enteric *Salmonella*, *Shigella* and Shiga-toxin producing *E. coli* isolates forwarded to the PHABM Program by frontline laboratories are subtyped and fingerprinted. Observations in 2011 and 2012:

- *Salmonella* was the primary enteric pathogen identified with 1131 cases in 2011 and 933 cases in 2012. *Campylobacter* was the second most common but the highest province-wide cause of enteric bacterial illness.
- In 2011, *S. Enteritidis* accounted for 52% of all *Salmonella* species isolated or received at the BCPHMRL and constituted 68% of all enterica serovars (Figure 18A). The next most common serovar was *S. Typhimurium* (9%); this is in contrast to 2012 where *S. Heidelberg* was the second most common serovar (13%). *S. Enteritidis* only accounted for about 37% of all *Salmonella* species isolated or received at the BCPHMRL in 2012 and constituted 54% of all enterica serovars (Figure 18B).
- There were 129 cases of *E. coli* in 2011 and 192 cases of *E. coli* in 2012. *E. coli* O157:H7 was the predominant serotype, representing about 75% all *E. coli* subtyped in 2011 and 53% in 2012 (Figure 19). Non-O157 serotypes accounted for 20% (2011) and 40% (2012) of cases.



**Figure 18.** Top 10 *Salmonella* enterica serovars identified from clinical samples in 2011 (A) and 2012 (B).

**Figure 19.** *E. coli* serotypes identified from clinical samples in 2011 (A) and 2012 (B).

### Streptococcus Surveillance

*Streptococcus pneumoniae* isolates causing invasive disease (IPD) are routinely forwarded by frontline microbiology laboratories to the BCPHMRL for initial serotyping and then sent to NML. Age groups at highest risk of pneumococcal disease are children and older adults, as evidenced in Figure 20. More than 90 known *S. pneumoniae* serotypes can cause invasive pneumococcal disease (IPD). Serotype 19A was the leading serogroup in 2011-12, followed by 22F, 3 and 7F (Figure 21). Inclusion of 19A in the PCV 13 vaccine should manifest in fewer cases of IPD of this serotype in coming years.

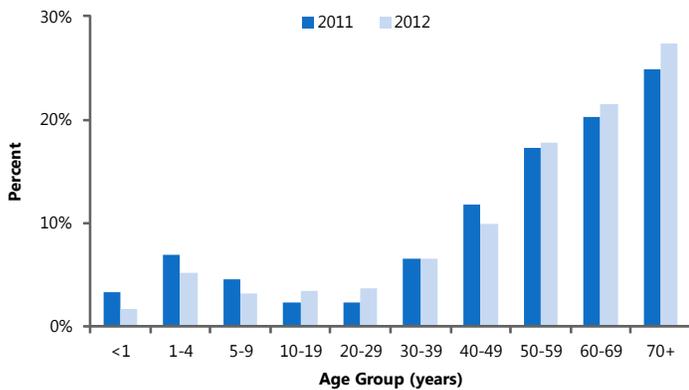


Figure 20. Ages of invasive pneumococcal disease cases submitted to the Public Health Advanced Bacteriology & Mycology Program, PHMRL, 2011-2012.

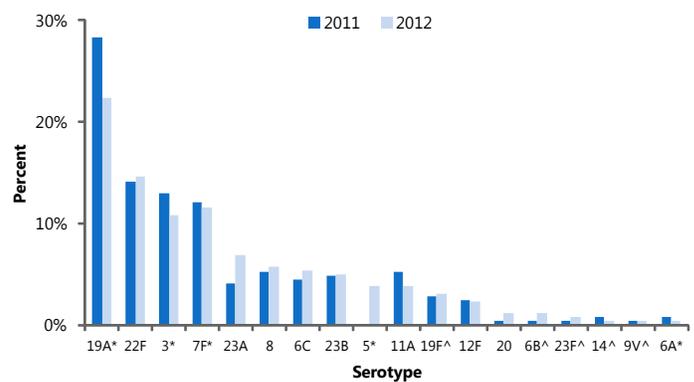


Figure 21. Occurrence of top *Streptococcus pneumoniae* serotypes, 2011-2012. PCV 7 vaccine (implemented in 2003) covers serotypes 4, 6B, 9V, 14, 18C, 19F and 23F and PCV 13 vaccine (implemented in 2010) covers serotypes 1, 3, 5, 6A, 7F and 19A in addition to PCV 7 serotypes.

Serotyping of *Streptococcus pyogenes* by NML is based on both the M protein virulence factor and by the surface T antigen, also known as emm typing and T-typing. There are over 100 emm types and 20 T-types known. The most common serotypes seen in BC are as shown in Figures 22 and 23. About 35% of the iGAS isolates submitted in 2011 and 2012 have been emm type 1 and T-type 1.

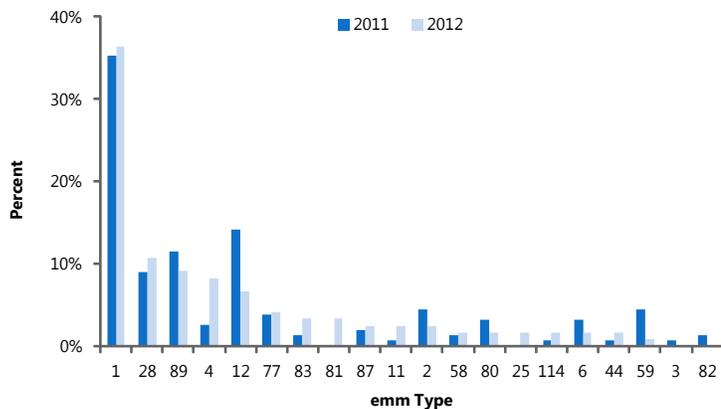


Figure 22. Top *Streptococcus pyogenes* (iGAS) emm serotypes, 2011-2012.

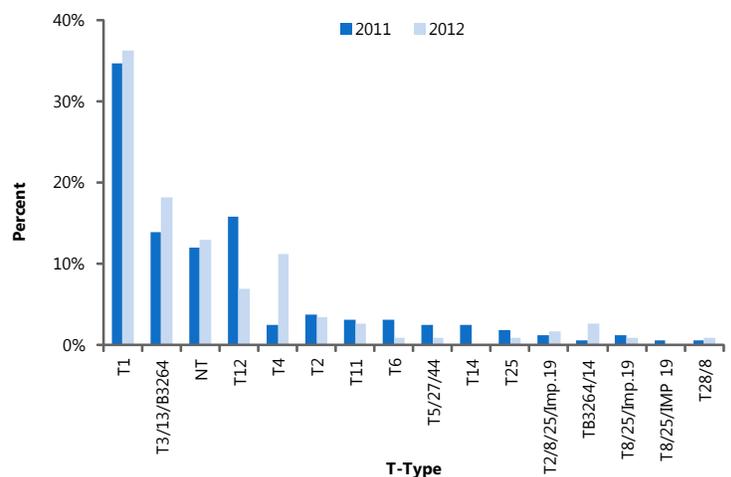


Figure 23. Top *Streptococcus pyogenes* (iGAS) T serotypes, 2011-2012.

## Sexually Transmitted Infections (STI) Surveillance

### Lymphogranulomatous Venereum (LGV)

LGV, a serovar of *Chlamydia trachomatis*, is classically associated with inguinal lymphadenopathy and invasive disease in both men and women although BC cases have been associated with MSM, presenting as proctitis. To diagnose LGV, rectal swabs and urine samples positive for *C. trachomatis* are sent to the PHABM Program for confirmation and then forwarded to NML for sequencing to determine the serovar of *C. trachomatis*. There were increased numbers of LGV detected in 2011 (21 cases) and 2012 (15 cases) compared to the previous 5 years where there had been from 2 to 6 cases annually.



### *Neisseria gonorrhoeae* Susceptibility Testing Trends

Gonorrhoea is the second most reported STI after chlamydia and since the 1990s, rates of infection have been gradually increasing. Most endocervical, urethral swabs and urine samples are tested using NAT (Figure 24). This shift away from culture means fewer isolates are available for antimicrobial susceptibility testing; culture is done on defined isolates, an important surveillance tool to monitor resistance trends that informs treatment practices. Susceptibility testing is carried out against first-line and alternative treatment antimicrobials for all positive *N. gonorrhoeae* cultures. Since 2008, increasing minimum inhibitory concentration (MIC) trends for cephalosporins (cefixime and ceftriaxone) were a cause for concern as these antimicrobials are the recommended treatment options. However, unlike

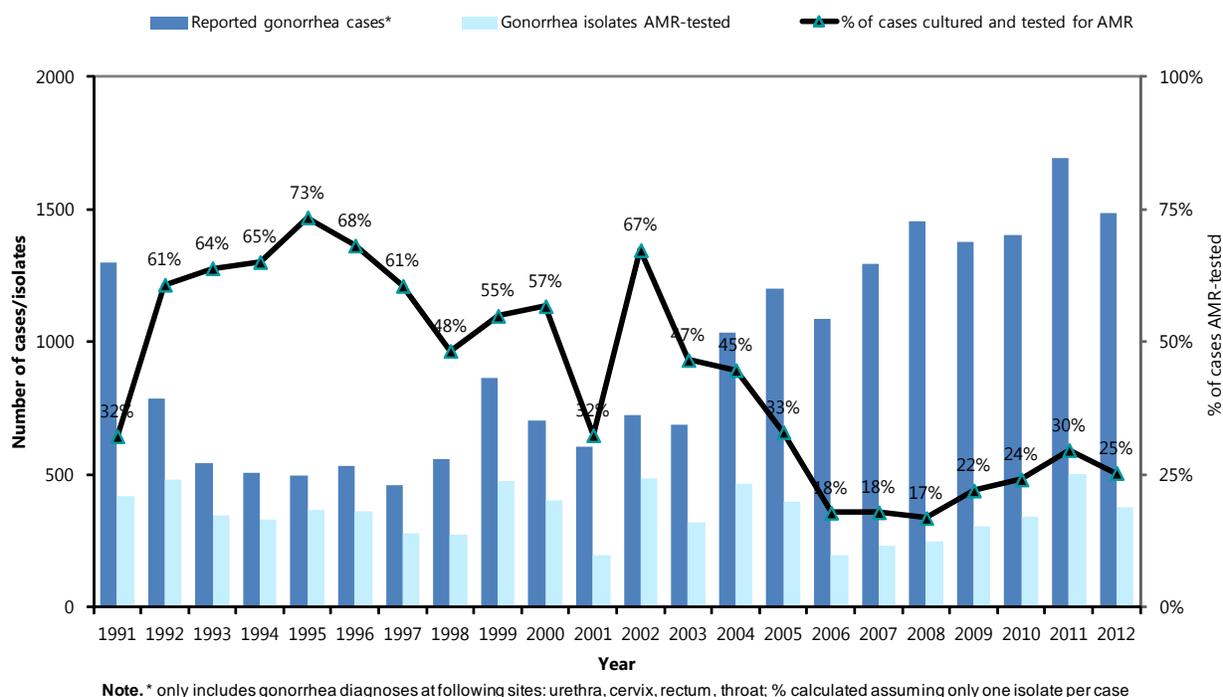
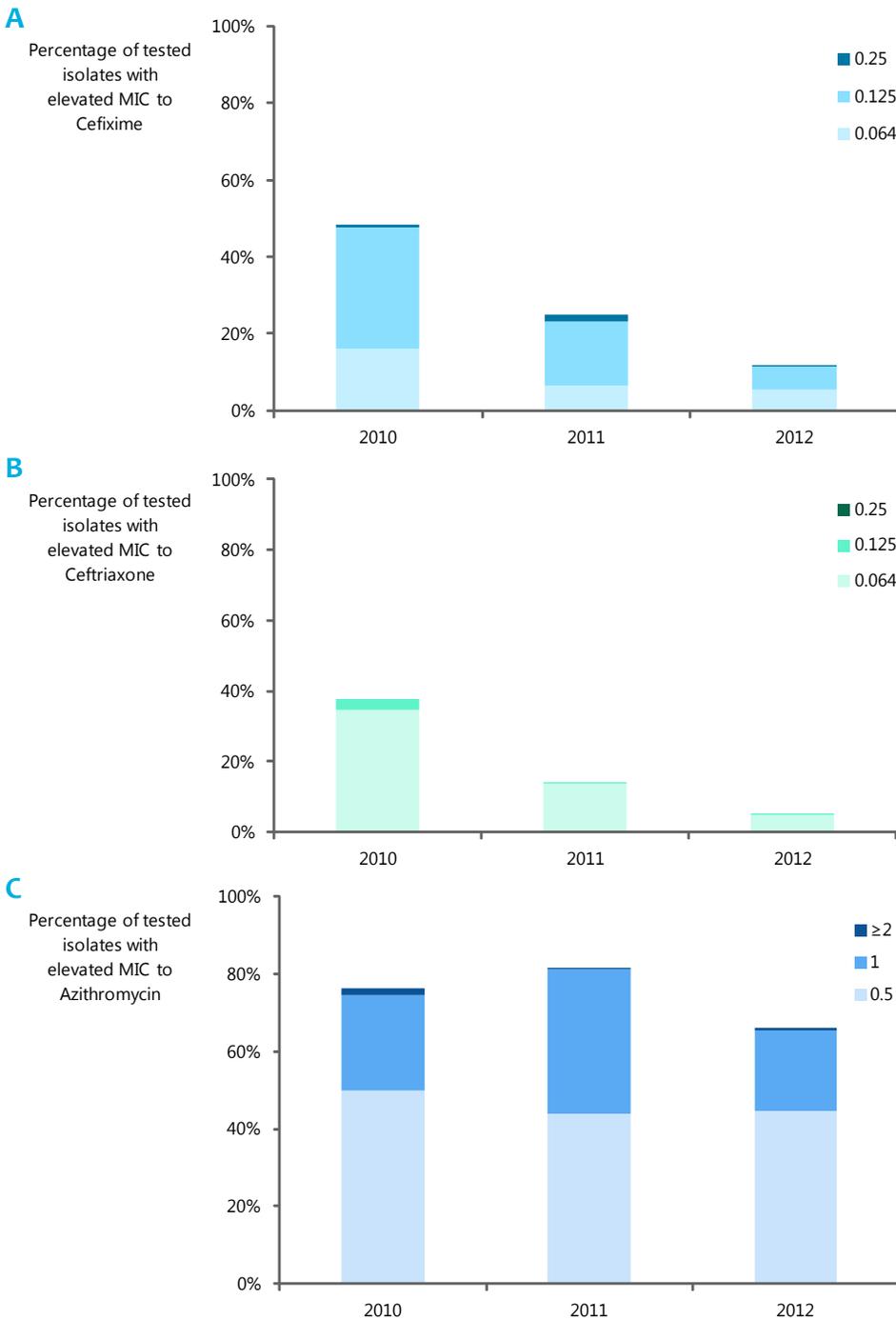


Figure 24. Number of gonorrhoea case reports and number of isolates tested for antimicrobial resistance in BC, 1991-2012. Data sources: STI-IS data cube version 2013-May-13 and PHABM Program.

trends observed in other parts of Canada and globally, cephalosporin MICs have decreased in 2011 and 2012 (Figure 25). Azithromycin MICs have also decreased slightly from 2010 at the 0.5 µg/mL breakpoint in both 2011 and 2012 (Figure 25). This trend is suggestive of differential susceptibility profiles that are localized, perhaps only to BC, and may impact treatment guidelines. Continued surveillance work by PHABM and with partners at the BCCDC STI Clinics is important in monitoring these resistance trends.



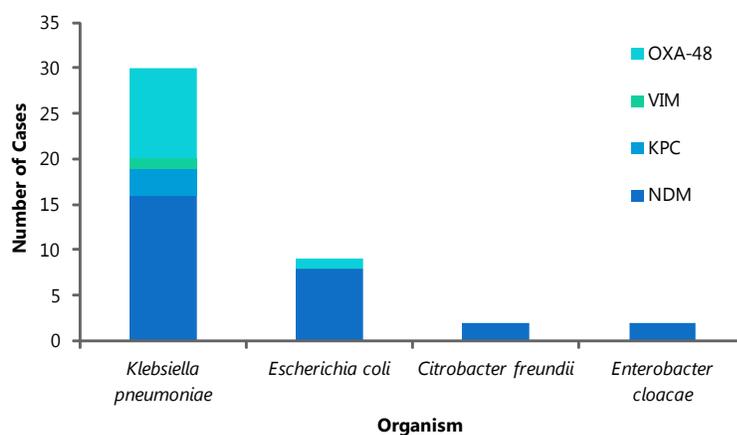
**Figure 25.** Percentage of tested *N. gonorrhoeae* isolates with elevated minimum inhibitory concentrations (MICs) to cefixime (A), ceftriaxone (B), and azithromycin (C) from 2010-2012. MIC units are in µg/mL.

### Health Care Acquired: Carbapenem-Resistant *Enterobacteriaceae*

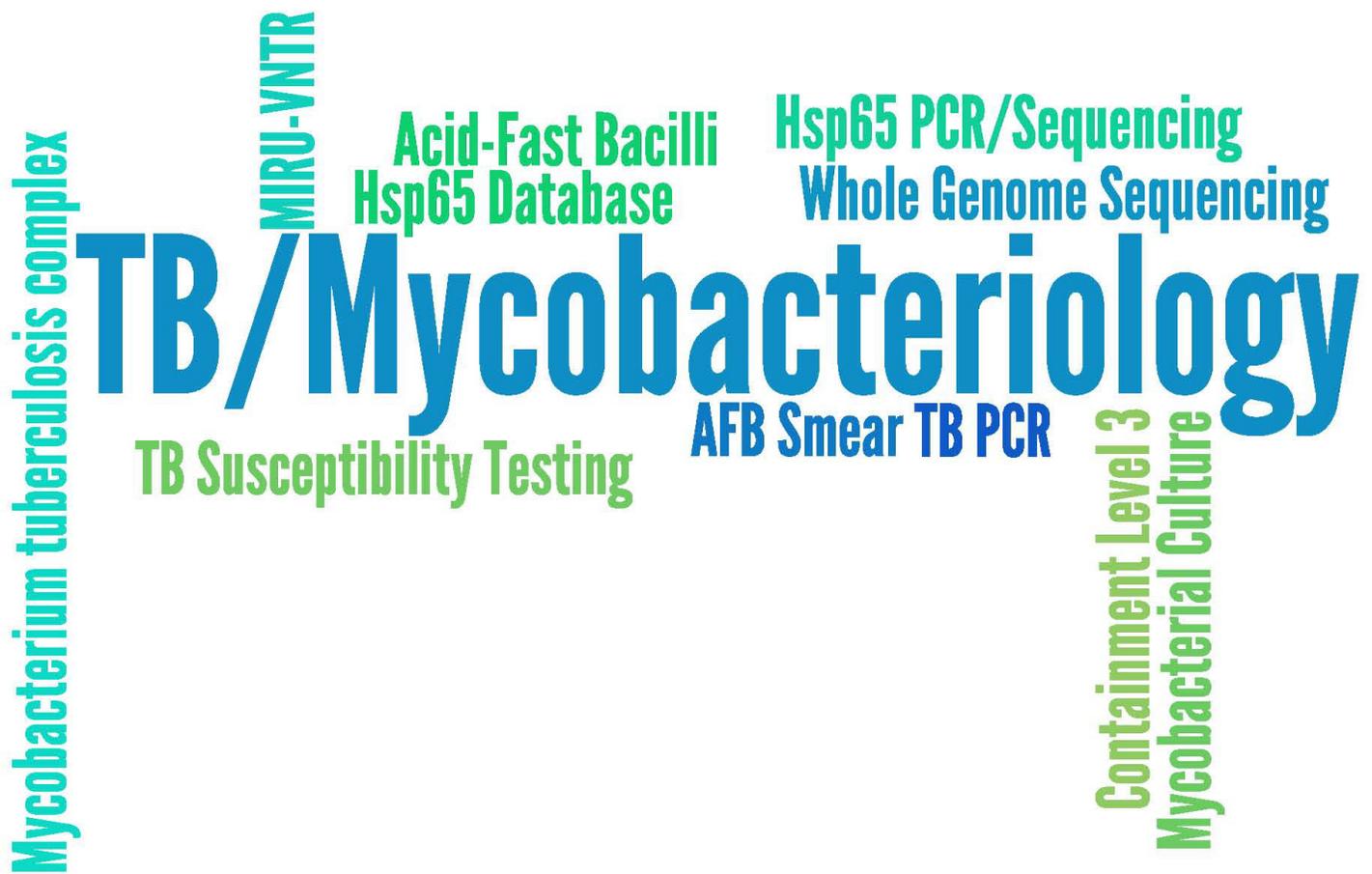
PHABM's health care associated infection work includes genotypic analysis of carbapenem-resistant *Enterobacteriaceae* (CRE). Isolates forwarded from partners in microbiology laboratories have been tested and trends monitored since 2010. The PCR multiplex assay screen isolates for the plasmid-mediated genes including the New Delhi Metallo- $\beta$ -lactamase-1 gene (NDM-1) endemic in South Asia, *Klebsiella pneumoniae* carbapenem (KPC) and *Enterobacteriaceae* that produce either a Verona integron-encoded metallo-beta-lactamase (VIM) or IMP-type  $\beta$ -lactamase. The emerging OXA-48 gene is screened by NML. Up to the end of 2012, 36 patients with carbapenem-resistant organisms were reported: 21 harboured the New Delhi NDM-1, nine had oxacillinase (OXA)-48 carbapenemase and two had KPC; some patients had multiple resistance factors including two patients with NDM-1 and OXA-48 carbapenemase and one other case with the KPC  $\beta$ -lactamase gene as well as a VIM gene (Table 2). Travel to South Asia was identified as the predominant risk factor. The age range of patients with carbapenem-resistance was 23 to 97 years, with the majority (86%) older than 60 years. A variety of CRE organisms were isolated, including *Klebsiella pneumoniae* (70%), *E. coli* (20%), *Citrobacter freundii* (5%), and *Enterobacter cloacae* (5%) (Figure 26).

**Table 2.** Carbapenem-resistant *Enterobacteriaceae* detected since 2010. Counts include one patient\* with KPC and VIM, two patients^ with NDM-1 and OXA-48 in the same year and one patient<sup>§</sup> with NDM in 2008 and 2009 (n=36).

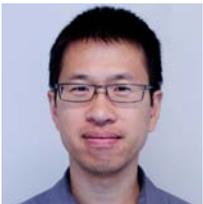
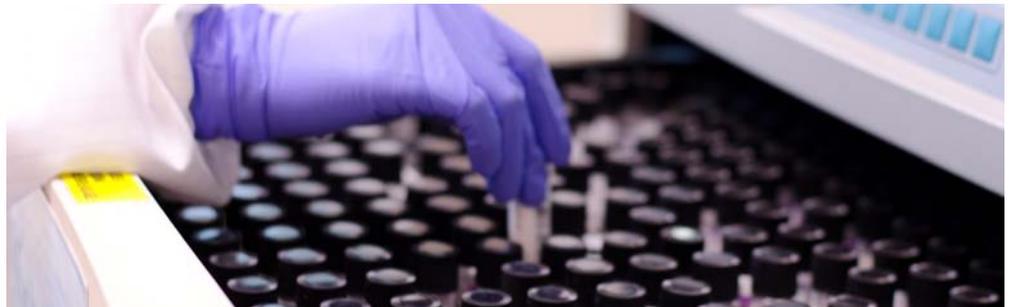
Type	Collection Year				
	2008	2009	2010	2011	2012
NDM-1	1 <sup>§</sup>	1 <sup>§</sup>	3	7	13 <sup>^</sup>
KPC			1*	1	1
VIM			1*		
IMP					
OXA-48				1	10 <sup>^</sup>



**Figure 26.** Species and resistance genes distribution of carbapenemase-producing *Enterobacteriaceae* cases, collected 2008-2012 (n=43). Four patients had more than one organism isolated and three patients had more than one resistance factor.



# Tuberculosis/ Mycobacteriology



**DR. PATRICK TANG**

Program Head



**DR. MABEL  
RODRIGUES**

Section Head

The TB/Mycobacteriology Program is the diagnostic and reference laboratory for *Mycobacterium tuberculosis* (MTB) and non-tuberculosis mycobacteria (NTM) in BC and the Yukon. This work includes examining acid-fast smears, culturing mycobacteria, identifying isolated mycobacterial organisms by genetic methods, and performing antimicrobial susceptibility tests. The program supports microbiology laboratories across the province for TB confirmation, shows leadership through national TB networks and is committed to public health research and training for mycobacteriology.

This team works closely with the BCCDC TB Control Division and with all Health Authorities in *M. tuberculosis* surveillance, prevention, outbreak/cluster identification and control. STAT (24/7) services are offered through the Medical Microbiologist on call.

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# TB/Mycobacteriology



## TB Services

**Table 3.** Testing Volumes

Year	Samples	Referred-in Cultures
2011	24,139	417
2012	24,543	408

**Table 4.** Positivity Rates

Year	AFB Smears	Culture
2011	1279 (5%)	2007 (8%)
2012	1426 (6%)	1903 (9%)

**Table 5.** Molecular and Susceptibility Testing Volumes

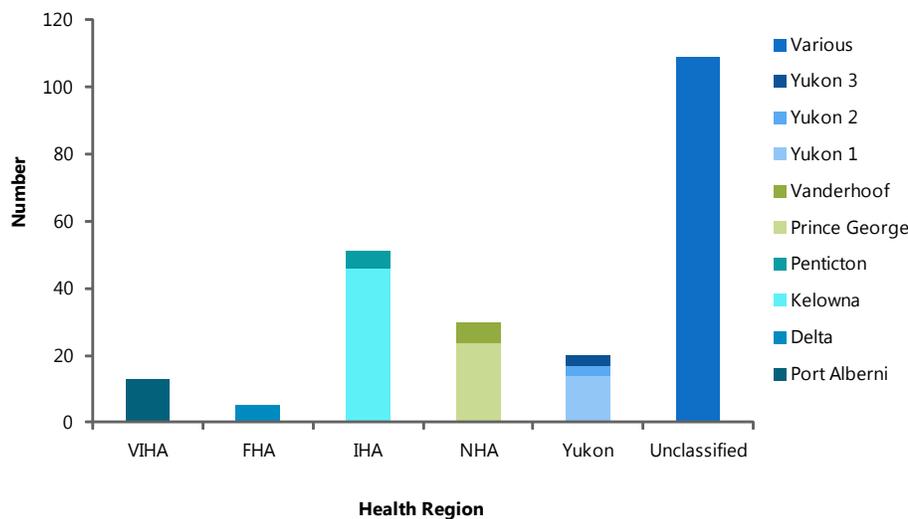
Year	MTB NAT	HSP65 PCR	MTB sens	MAC sens (performed by NRCM)
2011	589*	571	498	38
2012	899	622	492	32

\*TBqPCR introduced in 2011

The Program receives more than 24,000 samples and 400 referred-in cultures annually (Table 3) with positivity rates of 5-6% and 8-9% for smears and cultures, respectively (Table 4). A variety of molecular characterization techniques such as real-time PCR for *M. tuberculosis* complex and heatshock protein-65 (hsp65) are employed for direct detection of mycobacteria in samples. In addition, sensitivity testing to first-line antituberculosis drugs are performed in our CL3 laboratory (Table 5).

## Outbreaks

The Program plays a central role in controlling the spread of TB in BC. The laboratory works with regional Health Authorities and BCCDC TB Control to track outbreaks. Using a genotyping method called Mycobacterial interspersed repetitive unit-variable-number tandem-repeat (MIRU-VNTR), we are able to identify clusters of potentially related TB cases. Nine distinct TB outbreaks were documented in five BC Health Authorities and one in the Yukon including Port Alberni, Victoria, Delta, Vancouver, Kelowna, Penticton, Vanderhoof, Prince George and Whitehorse. Two different MIRU-VNTR patterns were observed in the Prince George outbreak while there were three patterns in the Yukon (Figure 27).



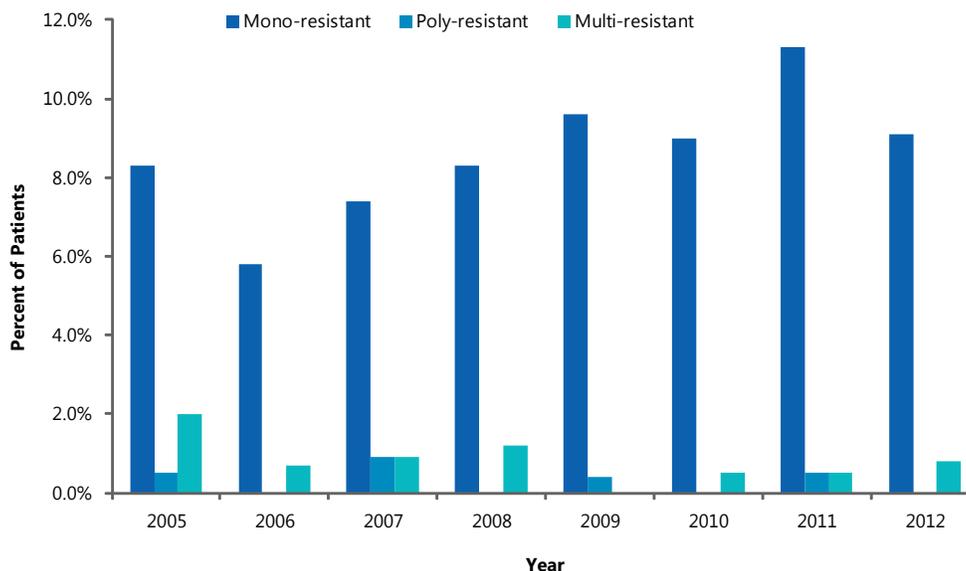
Whole genome sequencing is now used to further define known TB clusters. One cluster consisted of not one but two clades of TB using whole genome sequencing; this work was reported in an article in the New England Journal of Medicine (Gardy et al, 2011).

**Figure 27.** Number of isolates with MIRU-VNTR outbreak patterns identified since 2009.

## Tuberculosis Susceptibility Testing for BC

First-line anti-TB drug testing is performed routinely using the BACTEC® 960 fluorometric proportion method. Isolates are tested against critical concentration levels of isoniazid (INH), rifampin (RMP) and ethambutol (EMB); pyrazinamide (PZA) testing is performed on isolates showing resistance to INH and/or RMP and also when requested. 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 first-line drugs not including the combination of INH and RMP); and, multidrug-resistant TB (MDR-TB) (resistance to at least the two best first-line anti-TB drugs, INH and RMP, but not meeting the definition of extensively drug-resistant TB).

*Mycobacterium tuberculosis* complex (MTBC) drug susceptibility testing results are reported to the Canadian Tuberculosis Laboratory Surveillance System (CTBLSS) annually. Resistance patterns of MTBC patient isolates from 2005 to 2012 are shown in Figure 28. Mono-resistance peaked from about 6% in 2006 to 11% of isolates in 2011 and decreased to 9% in 2012. Poly-resistance has varied from 0% to about 1% while multi-resistance has varied from 0% to 2% during this period. Since 2008, the level of mono-resistance has been greater than that of the Canadian average as reported by the CTBLSS (data up to 2010). Most mono-resistance has been to INH. Data for MDR-TB rates in BC have either been the same or below national rates from 2005–2010 as reported by the CTBLSS.



**Figure 28.** Percent of *M. tuberculosis* complex patients that are mono-resistant, poly-resistant and multi-resistant in British Columbia, 2005-2012.

## Lean Initiatives

Processes and procedures for enhancing service delivery are continuously evaluated. Initiatives in 2011-2012 included applying lean methodologies to improve turnaround times, e.g., review of workflow revealed the need to perform the TB PCR test on a daily basis and improvements in the reading of smears have also resulted in more timely smear and molecular results. The 2012 upgrade of the LIS to Sunquest version 6.4.2 has enabled better sample tracking and immediate result delivery to VCHA and PHC.

## New Molecular Tests in the TB/Mycobacteriology Program

New molecular methods for the early detection of *M. tuberculosis* and drug resistance continue to be explored. An in-house-developed real-time PCR assay for the detection of MTBC was implemented in 2011. The Cepheid GeneXpert system was also evaluated for the rapid detection of TB and MDR-TB. The MMG Program has been working closely with the TB/Mycobacteriology Program in the implementation of the mycobacterial interspersed repetitive unit-variable-number tandem-repeat (MIRU-VNTR) fingerprinting for *M. tuberculosis* isolates. Use of Whole Genome Sequencing (WGS) was used to examine and resolve transmission of TB. More recently, funded by the BCCDC Foundation for Population & Public Health, a study using WGS for fingerprinting isolates will be carried out. Improvement in existing molecular methods for mycobacteria detection and speciation is another dedicated area of work. A project is underway to develop and validate a new assay to detect *M. avium-M. intracellulare* complex (MAC) in clinical specimens. We are also continually updating our hsp65 sequence databases to ensure that our mycobacterial speciation is accurate and up to date.



## Canadian Tuberculosis Laboratory Technical Network

The Canadian Tuberculosis Laboratory Technical Network (CTLTN) is a national network made up of technical heads from each provincial or territorial laboratory that performs Mycobacteriology testing; Dr. Mabel Rodrigues is the BC and Yukon Territory representative. Representatives from the National Reference Centre for Mycobacteriology and PHAC and a designee from the Tuberculosis Prevention and Control at PHAC are also members.

The goals of the CTLTN are:

- Standardization of methodologies (conventional and state-of-the-art)
- Better biosafety operational practices and physical requirements
- Implementation of biosafety guidelines
- Participation in the national surveillance and proficiency programs
- Exchange of services and information regarding new technologies

A key 2011-2012 initiative was to provide consultation and input into the draft PHAC Biosafety Directive for laboratories handling pathogens in the MTBC. This Directive provides a stratified approach to the containment of MTBC according to the specimen type and procedures used. It provides a list of activities that can be safely performed at a lower containment level than CL3 and a list of the operational practices from the *Laboratory Biosafety Guidelines* required to mitigate the risk of working with MTBC at lower containment levels.

# Virology



# Virology



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Program Head,  
Medical Microbiologist



**DR. MARTIN PETRIC**

Clinical Virologist



**ALAN MCNABB**

Section Head



The Virology Program provides province-wide leadership, with national and international linkages. It provides diagnostic and reference services, primarily using advanced molecular methods. As the provincial virology reference laboratory it also maintains virus isolation in cell culture and immunofluorescence microscopy. The laboratory provides rapid diagnosis of over 16 respiratory viruses simultaneously for sentinel surveillance purposes and during outbreaks. Typing and subtyping by RT-PCR and nucleic acid sequencing and genotypic antiviral resistance testing are performed for influenza A viruses and multiplex nucleic acid testing (Luminex) for other respiratory viruses.

The Virology Program together with MMG provides expertise in the national framework for response to pandemic influenza through the Pandemic Influenza Laboratory Preparedness Network of CPHLN. Additional roles in outbreak detection and management include testing for enteroviruses and vaccine-preventable diseases such as measles and mumps. Molecular tests for hepatitis, HSV, VZV and West Nile virus are also performed.

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## Virus Isolation: Time to Change the Name

Laboratories at the BCPHMRL occasionally change their names to reflect a change in function or organization. The Virus Isolation Laboratory is a case in point. The name, Virus Isolation or VI for short, was well deserved when BCPHMRL was established decades ago. At that time there were only two ways of performing the laboratory diagnosis for virus infection: isolating the virus in cell cultures, embryonated hen eggs or suckling mice; and demonstrating an immune response in the patient's serum. These were respectively performed in the Virus Isolation Laboratory and the Virus Serology Laboratory. Over time, viral serology platforms evolved into automated EIA while Virus Isolation underwent a more complex and slower evolution. Over the past decade, NAT in the form of RT-PCR, has been widely implemented and has now become the predominant assay format in virology.

Currently, the diagnosis of all respiratory viruses, HSV and VZV, enteroviruses, hepatitis C and HIV, measles, mumps and West Nile viruses, once only detected by virus isolation, are carried out by well validated, often locally developed, RT-PCR assays. The Virology Program has led the way nationally in the implementation of NAT for pandemic influenza in 2009 and is now fully prepared to implement this technology for the diagnosis of the novel H7N9 influenza A virus and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV).

These developments have taken place through the close collaboration between MMG and the Virology Program with both laboratories participating in the validation processes. Assay development has substantially increased the sensitivities of the assays, decreased turnaround times, and decreased costs.

Since the vast majority of the work in virology is now based on the NAT platform, the term Virus Isolation Laboratory is a misnomer and should firmly be recast as the Virology Program.

## Towards Standardization of Real-Time PCR Assays

During the last 2 years, the Virology and MMG Programs have been standardizing assay conditions for a number of PCR assays performed by the Virology Program. Currently the two laboratories have standardized and validated PCR assays for enterovirus, Epstein-Barr virus, West Nile virus, herpes virus, adenovirus, measles, and mumps using the same thermocycling parameters. This allows the laboratory to test for these viruses using a single PCR run which saves the laboratory several hours a day in testing samples, allows assays to be run in a day that would normally require a span of several days to accomplish, and captures a small savings by decreasing related consumables.



Moving forward, the two laboratories intend to explore further standardization of current assays and development of new assays using the same master mix and cycling parameters. The intent is to extend this standardized concept to other laboratories so that multiple assays can be run at the same time thereby reducing workload and decreasing turnaround times for all PCR testing done by the BCPHMRL.

## Optimizing Detection of Respiratory Viruses Circulating in BC

The Virology Program is changing to meet client demands. The initiation of any new in-house developed or commercially available test is evaluated based on our standardized validation and implementation process and procedures including assessing sensitivity, specificity, precision, and cost (the latter being a major factor in implementing an assay).

During the 2010/2011 respiratory season the laboratory used a commercial Luminex xTAG RVP fast assay to detect the presence of respiratory viruses in all samples submitted for testing. During the course of that respiratory season, a new in-house 4-plex RT-PCR assay for the detection of influenza A/B and Respiratory Syncytial virus (RSV) was developed and validated. This MMG-partnership work was done due to issues with the commercial assay including suboptimal sensitivity and high cost. The Luminex xTAG assay was further evaluated for sensitivity issues for respiratory viruses other than influenza/RSV and performed well. The testing protocol was then modified for the 2011/2012 and 2012/2013 respiratory seasons with a primary RT-PCR screening of influenza and RSV followed by the Luminex xTAG assay only on selected samples. This new algorithm approach appears to be working.

The respiratory season in Canada runs from September to August with activity usually peaking in December-January. In BC in 2011 and 2012, this pattern was reflected in the number of tests requested although the 2011 testing peak occurred in February to March. Detection rates for influenza A(pH1N1) peaked in January 2011 (13%), decreasing over February-April, becoming undetected, then reappearing in January 2012 for a few months and disappearing again. Influenza A(sH3N2) detection rates peaked December 2011-February 2012 (11-19%) and remained present in the community until about June. In the 2012/13 season, influenza A(sH3N2) returned in October and was responsible for a heavy influenza season with high detection rates (up to 27% in December) up through early 2013. Influenza B typically appears later in the season, peaking in March 2011 (10%) before subsiding and returning at low levels in October 2012 before peaking in March-May (7-8%) again. RSV detection rates also followed seasonal trends with peaks in February-April in 2011 (11-14%) and 2012 (9-13%) (Figure 29).

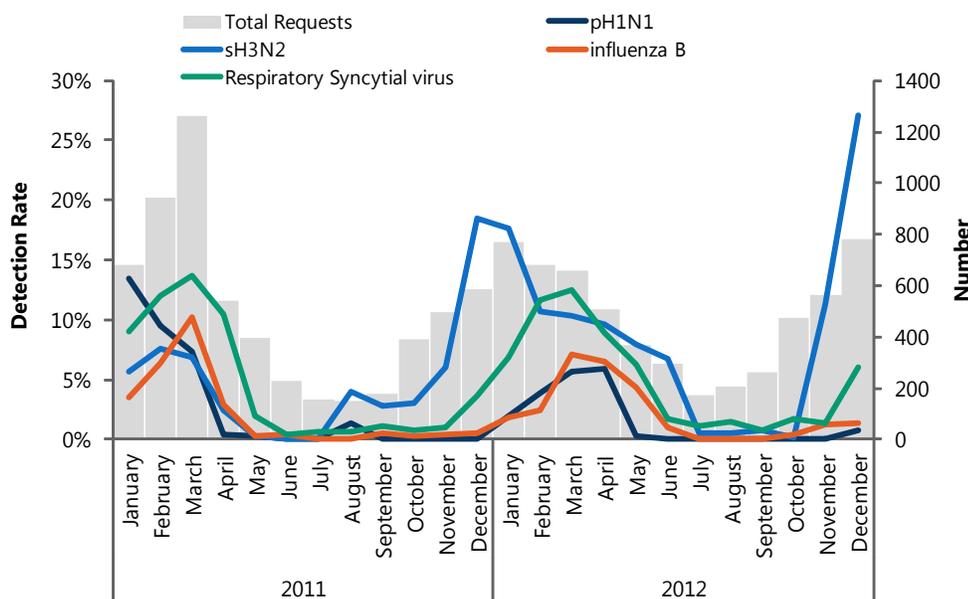


Figure 29. Influenza A, B and RSV testing and detection rates, 2011-2012.

### Adenovirus/Rotavirus Testing

Rotavirus causes gastroenteritis and is a major cause of severe diarrhea among infants and young children. Currently adenovirus and rotavirus are detected in stools using a commercial rapid diagnostic antigen detection test, with results in less than thirty minutes. Although both the sensitivity and specificity of this test are high the Virology Program is investigating replacing this combo assay with a duplexed PCR to ensure that the detection of these viral agents is maximized. The laboratory has already validated a PCR for adenovirus and will shortly design, generate and duplex a rotavirus assay with the adenovirus assay.



Seasonal trends are apparent for rotavirus detection (Figure 30). Rotavirus activity peaked in April 2011 with 21% of submitted samples being positive for the rotavirus antigen. In 2012, the peak occurred in April-May with 15-16% of samples testing positive for the virus.

Seasonal trends are less apparent for enteric adenovirus detection. Detection rates averaged 2.5% over 2011 with a slight peak in December (5.6% adenovirus antigen detection). Detection rates averaged 2.3% in the months of 2012 with a slight peak of 6.1% positivity in November (Figure 30).

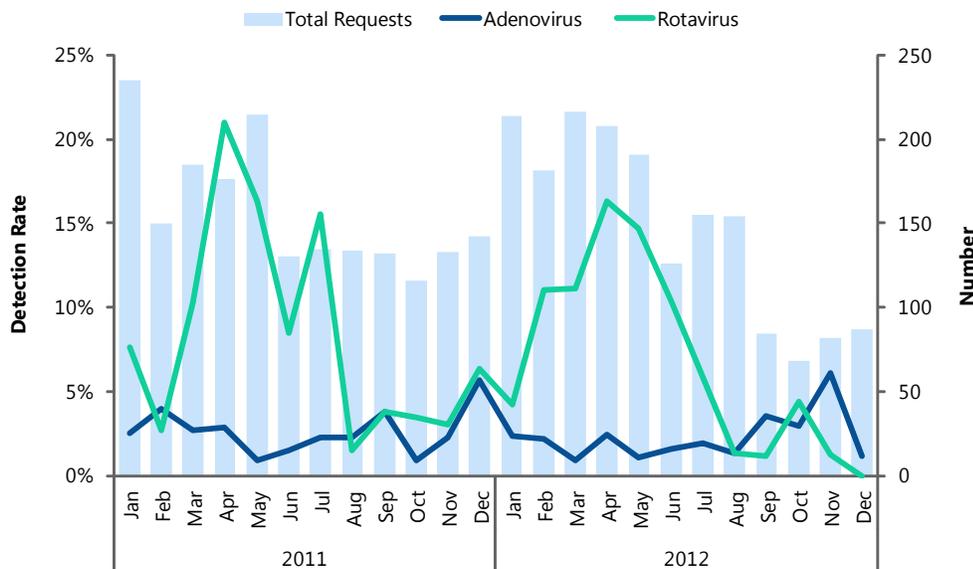


Figure 30. Adenovirus and rotavirus testing and detection rates, 2011-2012.

## Molecular Detection and Epidemiology of Enteroviral Meningitis

Human enteroviruses, widely recognized as the causative agents of aseptic meningitis, are responsible for a wide spectrum of diseases that include hand-foot-mouth disease, conjunctivitis, myocarditis and respiratory illness. Enterovirus infections have a seasonal pattern, typically occurring in the summer and fall. They are the most common cause of viral meningitis, occasionally occurring as outbreaks. Until recently, virus culture was the most common method for detection, but this method is slow and insensitive. The introduction of RT-PCR enterovirus detection has increased the detection rate and reduced costs and time to detection.



In early 2010, the BCPHML modified and validated a published RT-PCR assay for the detection of enteroviruses. This assay was demonstrated to reliably detect down to 5,000 virus copies/mL of CSF. Although not performing all testing for the detection of enterovirus in BC, the Virology Program received 820 CSF samples for enterovirus testing; enterovirus RNA was detected in 13%. Due to the quantitative nature of our RT-PCR assay it was possible to estimate the viral copy numbers present in the CSF with results showing fewer than 500,000 virus copies/mL in CSF although stool samples revealed much higher titres.

In 2011, enterovirus detection rates peaked in February (15%) and then followed the typical season of summer and fall activity with another peak in September 2011 (9%). In 2012 the peak occurred in August (9%). The average monthly detection rates have been 4.4% (2011) and 4.1% (2012) (Figure 31).

Enteroviruses were traditionally identified and typed by serological methods but now partial sequencing of the Viral Protein 1 (VP1) gene is the preferred method. Partial sequencing of the VP1 gene of positive samples indicated that a limited number of enterovirus species was circulating in BC: Coxsackie A9, Echovirus 4-related species, Echovirus 9, Echovirus 14, Echovirus 30 and Echovirus 39. Coxsackie A9 was the most prevalent enterovirus followed by Enterovirus 30 during the study period. Even though a limited number of species is circulating in the province there appeared to be significant variation within intra-species sequences, possibly indicating that several strains of the same species are causing disease in our population. Review of patient demographics of positive samples showed that infections are spread throughout the province, with increased concentration in some regions. As expected, most positive samples came from larger population centres.

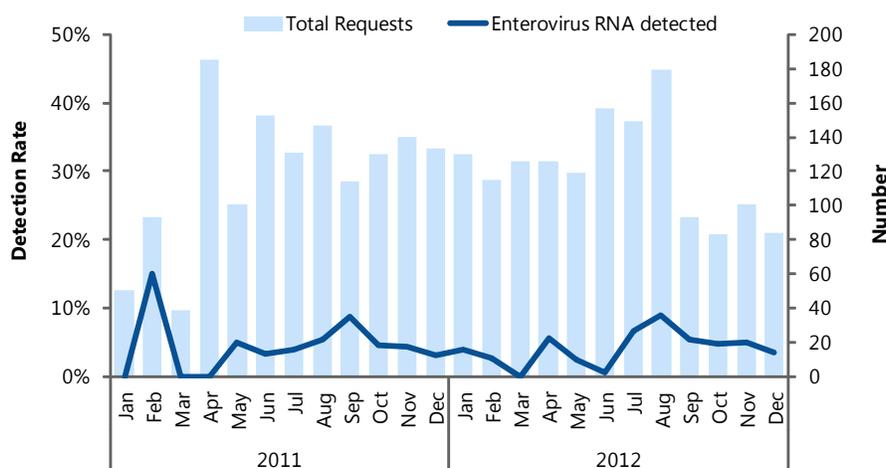


Figure 31. Enterovirus testing and detection rates, 2011-2012.

## Preparing for the Molecular Detection of Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

In April 2012, the emergence of a novel MERS-CoV causing severe respiratory infections in Amman, Jordan and in October, 2012 in Saudi Arabia prompted the Virology Program to acquire detection capabilities for this virus. The MMG Program tested an RT-PCR using currently available primers but these were not able to detect the novel coronavirus. Primers and probes were then designed and tested to detect the newly emerged agent; they proved capable of detecting a nucleic acid construct that simulated the areas targeted by the newly developed assays. This gave the Virology Program immediate capability to detect this agent's presence in BC. Subsequently, the assay was shown to work on novel coronavirus RNA sent from the NML in Winnipeg, confirming the accuracy and efficiency of the assay using our primers. The Virology Program then adopted the World Health Organization (WHO)-recommended diagnostic protocol that targets the region upstream from the E gene (upE gene assay) followed by a confirmatory assay targeting the ORF1b region and sequencing of the amplified products. A 1-week trial study was done to screen for the presence of the novel coronavirus in all respiratory samples submitted for routine respiratory virus testing; no MERS-CoV RNA was detected. Testing for MERS-CoV is only performed upon a direct request of the physician after consultation with a Medical Microbiologist.

## Conversion to Hepatitis C PCR Quantitative Testing Only

The Virology Program performs approximately 20,000 hepatitis C virus (HCV) RNA tests each year including 17,500 qualitative tests to detect active/current HCV infection and 2,500 quantitative tests to predict and monitor antiviral treatment response. As the quantitative and qualitative tests are equally sensitive and cost effective, the Virology Program adopted a "quantitative only" HCV RNA testing algorithm in 2012 that allows the laboratory to provide one test for diagnosis or monitoring, thus simplifying test accessioning and shortening turnaround times.

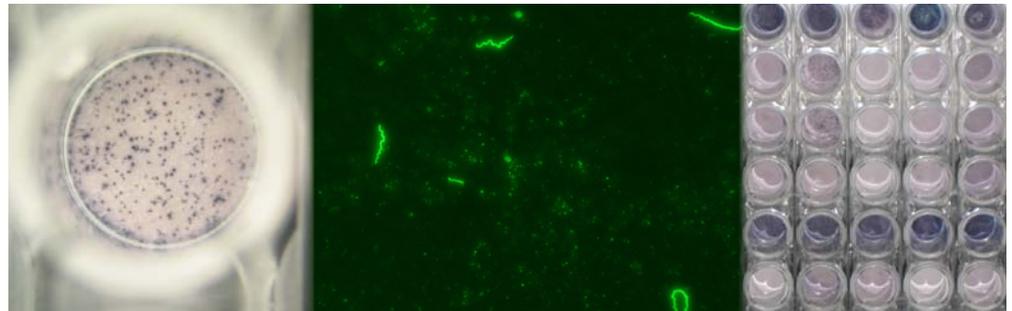
## Improving the Accuracy of Hepatitis C Genotyping

Prior to conversion to HCV quantitative-only testing by the Virology Program, HCV genotyping and subtyping were performed using the amplified product from the qualitative detection assay. This assay detected HCV in patient samples by amplifying a portion of the 5' untranslated region of the virus. The amplified product was then tested with a commercial line blot assay (Inno-LIPA) to determine the genotype and subtype of the strain. With the conversion to quantitative-only testing the Virology Program amplified a commercial product instead, improving the accuracy of genotyping and subtyping as the commercial assay amplified and utilized both the 5' untranslated region and core regions of the virus, allowing for more accurate differentiation of subtypes 1a versus 1b and subtypes 6 c to l.





# Zoonotic Diseases & Emerging Pathogens



**DR. MUHAMMAD MORSHED**

Program Head



**QUANTINE WONG**

Section Head

The Zoonotic Diseases & Emerging Pathogens (ZEP) Program provides testing and consultation services for a variety of bacterial, parasitic, fungal and viral diseases of public health importance. The Program performs high volume spirochete testing (syphilis, *Helicobacter pylori*) and detection of Lyme disease, *Toxoplasma*, *Cryptococcus*, West Nile virus, Dengue virus, *Bartonella* and Group A Streptococcal infections. The ZEP Team leads the province-wide Interferon-Gamma Release Assay (IGRA) program,

a cell-mediated immune response serological assay to detect latent TB. The Program also acts as the reference centre for other infectious agents including Hantavirus, *Legionella*, relapsing fever, and exotic and rare parasitic and rickettsial pathogens. Its staff members are recognized as national leaders, collaborating with the NML and US Centers for Disease Control in spirochaetal diseases such as Lyme disease and syphilis.

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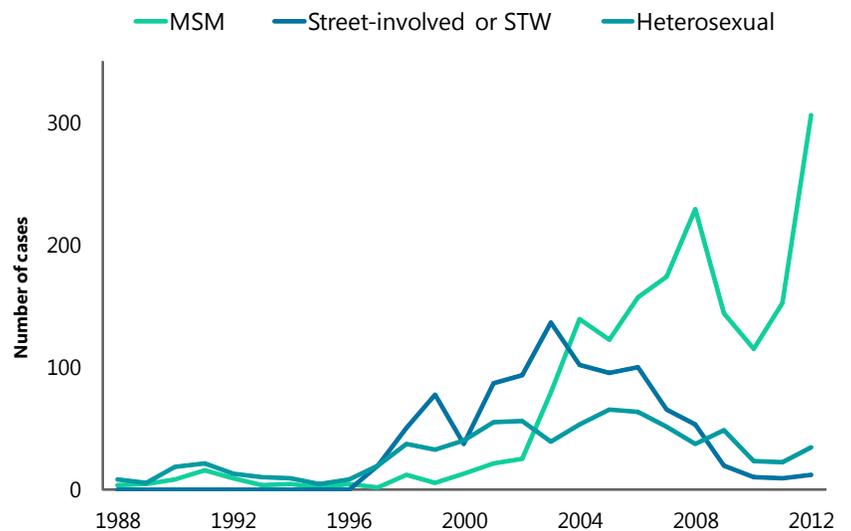
604-707-2602

## Zoonotic Diseases & Emerging Pathogens

### Syphilis Surveillance

Syphilis testing is centralized in BC with all samples tested by the ZEP Program. Since *Treponema pallidum* cannot be cultured, a series of serological tests following a specific algorithm is commonly used to diagnose syphilis infections. The rapid plasma reagin (RPR) screening assay is first used; when positive, results are confirmed using tests such as the *Treponema pallidum* Particle Agglutination (TPPA), Fluorescent treponemal antibody (FTA) and line immunoassays (LIA). *T. pallidum* can be seen under the microscope from appropriate clinical samples such as ulcer or cancre exudates; however, the sensitivity of this direct test is very low. *T. pallidum* DNA may also be detected by NAT from appropriate samples such as ulcer fluid, CSF, and biopsy tissue, but again test sensitivity is very low.

Syphilis rates in BC have been on the rise since the mid to late 1990s. A large constituent of infections at this time was due to the heterosexual sex trade in the Downtown Eastside of Vancouver. In the 2000s, however, syphilis prevalence was overtaken by the MSM community, increasing to its current, record number of 372 cases in 2012 (Figure 32).



**Figure 32.** Infectious syphilis cases by exposure category, British Columbia, 1988-2012. MSM = men who have sex with men; STW= sex trade worker. Figure provided by BCCDC Clinical Prevention Services.

### *Treponema pallidum* New Antigen Evaluation

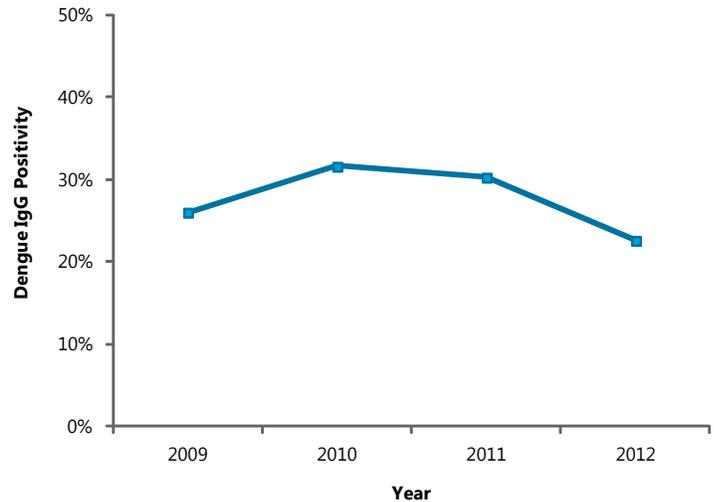
Over the last 20 years, four recombinant treponemal proteins (TpN15, TpN17, TpN47, and TpN44) have been designed and used to develop treponemal EIA or POC tests. The ZEP Program carried out an evaluation of these new antigens. To resolve discrepant results, different vendor products with the same antigens were included.

Recently, scientists at the University of Victoria discovered three novel recombinant proteins for potential use as additional markers. The ZEP Program collaborated with these scientists to evaluate the novel proteins (Tp0326, Tp0453, and the Tp0453-Tp0326 chimera) using characterized clinical samples. The sensitivities of Tp0326, Tp0453, and the Tp0453-Tp0326 chimera were found to be 86%, 98%, and 98%, respectively, while the specificities were found to be 99%, 100%, and 99%, respectively. For comparison, the Captia syphilis (*T. pallidum*)-G enzyme immunoassay (Trinity Biotech) was used to screen the same serum samples and was found to have a sensitivity of 98% and a specificity of 90%. In particular, Tp0453 and the chimera exhibited 100% accuracy in classifying analytical false-positive samples compared to 43% for the Captia assay. These findings identify Tp0453 and the Tp0453-Tp0326 chimera as novel syphilis-specific diagnostic candidates that surpass the performance of a currently available diagnostic EIA antigen. Newer antigen development will allow more accurate detection of all stages of syphilis infections. This study was published ahead of print in the Journal of Clinical Microbiology (Smith et al, 2012).

## Zoonotic Diseases & Emerging

### Dengue Surveillance

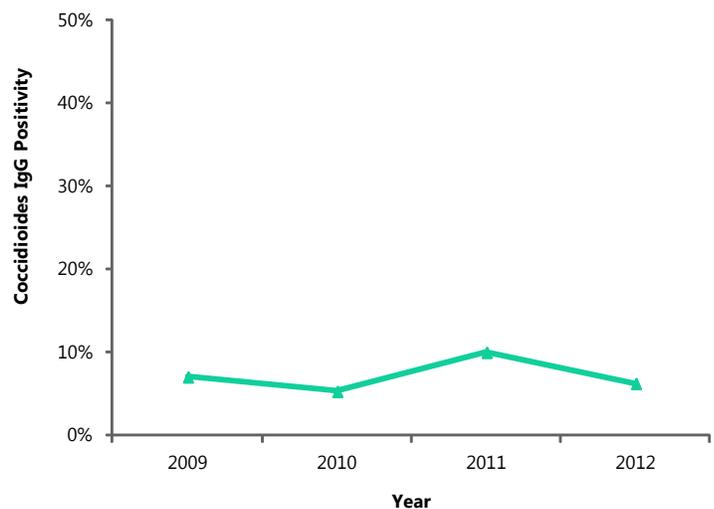
Dengue is a re-emerging arboviral infection in the *Flaviviridae* family. The ZEP Program performs serology to detect IgM and IgG antibodies using EIA on serum samples. This is an indirect method of diagnosing Dengue fever as virus isolation is generally only possible in the first few days of infection during the febrile period. Interpretation of acute versus past infection/exposure is possible using IgM and IgG antibody test results based on acute and convalescent sera. In BC, dengue tests are typically requested for patients who have travelled to tropical/subtropical regions where the mosquito vectors *Aedes aegypti* and *Aedes albopictus*, are prevalent. During the high antibody levels of secondary infection, there is also cross reactivity with other flaviviruses including West Nile virus, St. Louis encephalitis virus, Japanese encephalitis virus and yellow fever virus. Since 2009, dengue IgG positivity in BC (either current or past infection) has ranged from 23% to 32% (Figure 33).



**Figure 33.** Dengue IgG positivity in BC, 2009-2012. Note that the ZEP Program began offering dengue IgG EIA since the latter half of 2009.

### Coccidioidomycosis Summary

Coccidioidomycosis, also known as Valley Fever, is a fungal infection caused by *Coccidioides immitis* or *Coccidioides posadasii*, found in the southwestern US, and Central and South America. Valley Fever is acquired by inhaling one or more airborne spores of the fungus when visiting these endemic areas. Like other serological tests, the early IgM response is useful for detecting acute primary infection while the later IgG response may indicate chronic coccidioidomycosis or past exposure to the organism. Figure 34 reveals that in BC, chronic coccidioidomycosis infection or previous exposure to this pathogen has been found in a portion of the population (travel-related cases or individuals from endemic areas) as suggested by positive IgG results ranging from 5% to 10% over 2009-2012.



**Figure 34.** Coccidioides IgG positivity in BC, 2009-2012.

## Zoonotic Diseases & Emerging Pathogens

### Toxoplasma NAT Development

*Toxoplasma gondii* infection can occur through ingestion of raw or undercooked meat containing *T. gondii* cysts, or from contaminated water, organ transplant, or blood transfusion. It can also be acquired congenitally via maternal-fetal transmission when a mother has had an acute or primary infection. The ZEP Program offers both IgM and IgG tests for *T. gondii* specific serology for the diagnosis of active disease. IgG avidity testing may be done on request when appropriate. In February 2012, the ZEP Program introduced a new prenatal NAT test on amniotic fluid for toxoplasmosis, targeting the B1 gene. This test is offered in select cases with parallel reference laboratory testing for validation purposes.

### Moving from Tick Culture to PCR: Validation of a Real-Time PCR Assay for Detecting *Borrelia burgdorferi* in Ticks

*Borrelia burgdorferi*, the causative agent for Lyme disease, is one of the most fastidious spirochetes found; the spirochete is challenging to grow in the laboratory and culture methods are labour intensive. At the end of 2012, the ZEP Program validated and implemented a real-time PCR test for detecting *B. burgdorferi* from *Ixodes* ticks. Two tests were used to confirm the presence of *B. burgdorferi* I (the screening test detected the 23s ribosomal gene whereas the confirmatory test detected the ospA gene). All culture-positive samples were tested using conventional PCR targeting *B. burgdorferi*. Results of culture and conventional PCR were then compared with the real-time PCR method and statistical sensitivity and specificity were determined. This study demonstrated how changing conventional PCR to real-time PCR improved tick screening as well as passive surveillance for Lyme disease. This new real-time PCR assay has replaced culture of *Borrelia* from ticks with its advantages being higher sensitivity, shorter turnaround time and cost savings.



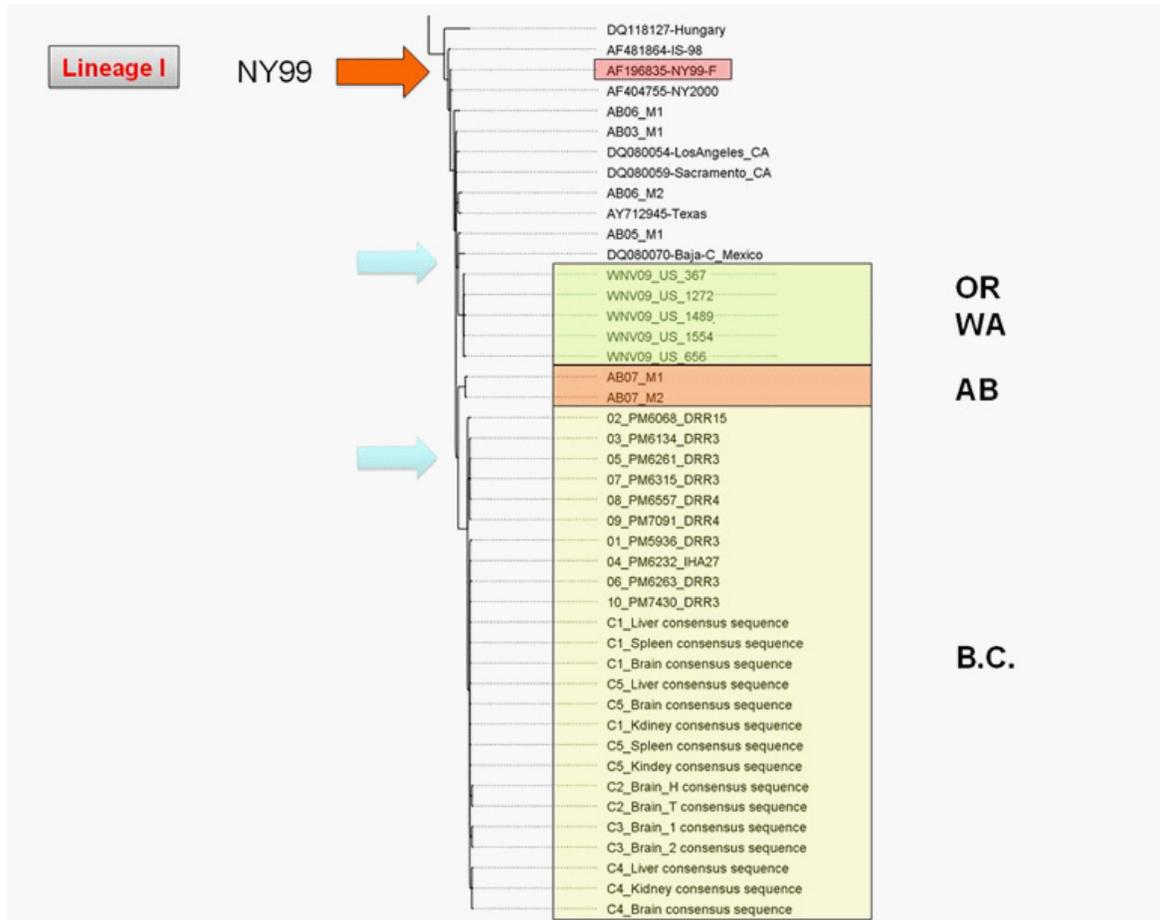
### WHO-Recommended Rapid Syphilis POC Test

The ZEP Program, in conjunction with the BCCDC STI Clinic, evaluated a syphilis POC test for potential use in vulnerable, "difficult to reach" populations. The POC test evaluated was the SD BIOLINE 3.0 which uses the 17 and 15 KDa antigens of *T. pallidum* to detect IgG, IgM and IgA antibodies. POC test requests, following finger-prick by nurses, were compared with results of POC tests on sera, in addition to syphilis confirmatory TPPA test results on sera. The sensitivity of the clinic POC tests versus laboratory TPPA was 85%. When syphilis POC tests using serum in the laboratory were compared with TPPA, the sensitivity was higher (95%). Both clinic and laboratory performed POC tests had an excellent specificity (100%). When the sensitivity of laboratory POC tests was compared to the standard RPR screening test, the sensitivity increased to 98%. The SD BIOLINE 3.0 POC test demonstrated excellent specificity but less-than-ideal sensitivity in the clinical setting; seven treponemal positive cases were missed in samples tested in the clinic. However, despite the lower sensitivity, this test may be useful in high-risk populations who may not consent to submit a blood sample or who may be difficult to locate for treatment.

## Zoonotic Diseases & Emerging Pathogens

### Molecular Characterization of West Nile Virus

To further understand local West Nile virus transmission, BC isolates (with isolates from a neighboring jurisdictions) were sequenced. The BC isolates included 10 positive mosquito pools (2009) and 5 positive birds (2010). The other isolates included mosquito pools from Alberta (6), Washington (3), and Oregon (2) and 162 sequences from GenBank (reference). Sequencing (ABI Genetic Analyzer 3130xl) targeted the pre-membrane protein M, membrane protein M, and the envelope glycoprotein E region. Sequences were assembled and analyzed with Geneious software and a phylogenetic tree constructed with PhyML and MrBayes. Phylogenetic comparisons showed that all isolates from the Pacific Northwest were similar to each other and belonged to Lineage 1 Clade 1a. However, the BC West Nile virus sequences (both 2009 mosquitoes and 2010 birds) were novel and comprised a new subgroup. The closest subgroup was that from two 2007 Alberta isolates (Figure 35). Samples from Washington and Oregon clustered in a separate subgroup. This data suggested that West Nile virus may have reached BC through Alberta.

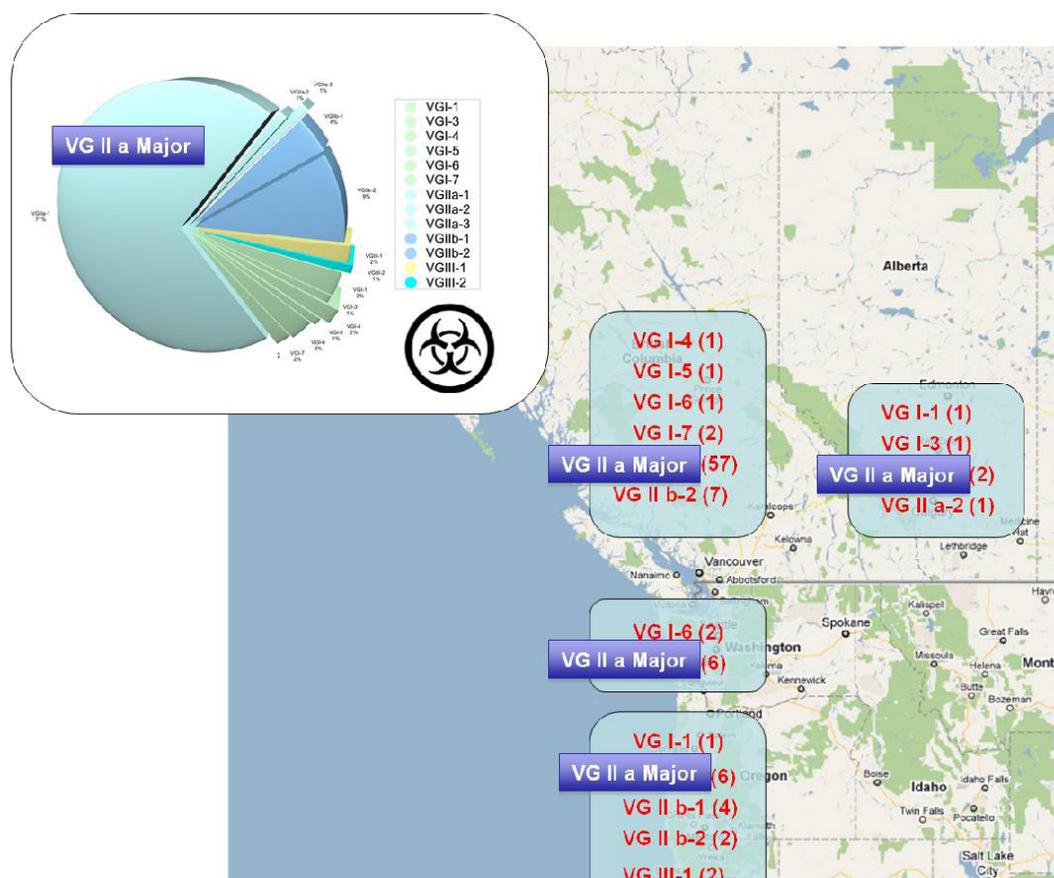


**Figure 35.** This simplified phylogenetic tree of 2,000 bp pre-M, M, and E regions was generated based on the isolates from Western North America. The Western North American WNV strains were clustered in the same lineage as other North American strains but remained distinct from other sequence data published in GenBank. The genetic relationship of BC isolates was closer to the Alberta isolates than the Washington and Oregon isolates.

## Zoonotic Diseases & Emerging Pathogens

### Multi-locus Sequence Typing of *Cryptococcus* Isolates

A study evaluated the role of MLST for speciation, as well as its usefulness in determining molecular epidemiological trends in strains of *Cryptococcus* species. *Cryptococcus* strains isolated from humans, animal and environmental samples from BC and the Pacific Northwest (n=107) were isolated using Canavanine-Glycine-Bromothymol agar media. Restriction fragment length polymorphism (RFLP) targeting the URA5 gene was compared to MLST targeting seven housekeeping genes (CAP59, GPD1, LAC1, PLB1, SOD1, URA5 and IGS1 loci). Compared to the previously established RFLP method, MLST not only identified all RFLP genotypes of *Cryptococcus gattii*, but also provided higher fingerprinting resolution. MLST further typed the RFLP genotype VGI into 7 MLST sequence types, VGIIa into 3, VGIIb into 2, and VGIII into 2. MLST sequence type VGIIa\_1 was the predominant strain (clonal in BC) found in the Pacific Northwest, representing over 70% of the human, animal, and environment samples tested. Despite the expensive, time-consuming nature of MLST, it provides greater detail, allowing epidemiological studies that would not be possible with RFLP (Figure 36).



**Figure 36.** The pie chart on the upper left corner shows the proportion of each MLST genotype in the Pacific Northwest. It indicates that the VG IIa is the dominant type in this region (>70%). The map on the lower right provides the distribution information of each MLST type. BC has a higher proportion (up to 82.61%) of VG IIa when compared to Alberta, Washington, and Oregon.

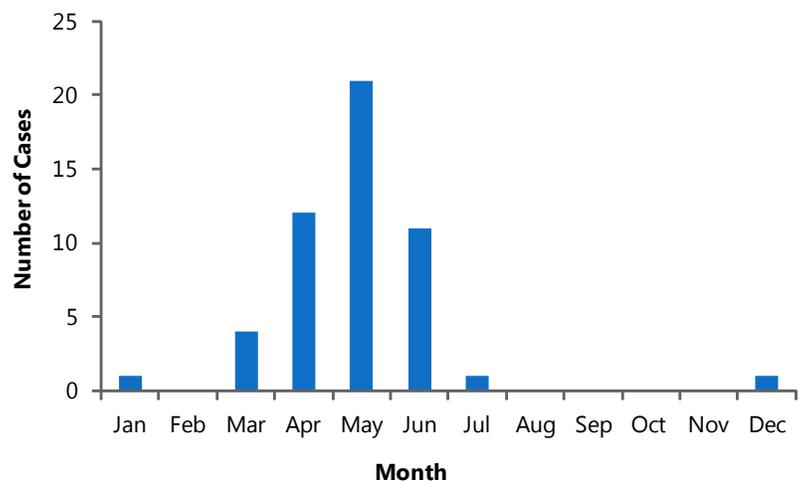
## Zoonotic Diseases & Emerging Pathogens

### Tick Paralysis in British Columbia

Tick paralysis is caused by a neurotoxin found in tick saliva. The neurotoxin (injected by the tick during its blood meal) causes paralysis of skeletal muscles. Although usually not severe, death may occur through respiratory arrest. Nearly 70 species of ticks are capable of inducing paralysis but historical data (1900-1968) indicate *Dermacentor andersoni* as the dominant vector in BC. Data collected from 1990 to 2010 were analyzed to study the transmission of tick paralysis in BC.

There is no test available for tick paralysis; most diagnoses depend on the discovery of embedded ticks and associated symptoms. Case definition for this review was based on tick submission accompanied by a completed BCPHMRL requisition noting symptoms of tick paralysis. All tick species were morphologically identified and clinical data analyzed.

Fifty two infections were identified from four species of ticks (*Ixodes pacificus*, *Rhipicephalus sanguineus*, *Dermacentor albipictus*, and the dominant species, *D. andersoni*). Occurrence distribution was mainly in the BC interior and the southern part of Vancouver Island. Eighty-six percent occurred in the younger (<10 years) and older (>50 years) age groups. Seasonal trends were seen with tick paralysis more common at the onset of warmer weather (Figure 37). Hikers travelling in wooded/bushy areas are advised to take general precautions such as wearing tucked in, light coloured clothing and being aware of tick activity in the area. It is important to remove a tick by pulling it off gently, leaving the tick and its mouth parts intact.



**Figure 37.** Cases of tick paralysis in BC, 1990-2010. Seasonal changes have a substantial impact on the transmission of tick-borne diseases. Tick paralysis becomes most common during warmer weather when adult ticks are most active.



# Grants Awarded

AGENCY	PROJECT TITLE	TOTAL FUNDS	YEARS	PRINCIPLE INVESTIGATOR	CO-INVESTIGATOR
BCCDC Foundation	Surveillance of Lyme Disease Vectors in Select Locations of British Columbia	\$130,659	2012-2014	M. Morshed	D. Patrick, P. Tang, B. Henry, S. Mak
	Etiological Discovery in Chronic Complex Diseases	\$500,000	2011	D. Patrick	M. Morshed et al.
BC Lung Association	Utility of Enhanced TB Molecular Epidemiology	\$60,000	2012-2014	P. Tang	J. Gardy, J. Johnston
Canadian Cancer Society Innovation Research Grants	HPV in Tonsils: Natural History of Infection and Role in Oral Cancers	\$73,225	2012-2015	M. Rosin	M. Krajden et al.
Canadian Institutes of Health Research	Hepatitis C virus Transmission Dynamics Among Injection Drug Users	\$336,569	2011-2014	M. Krajden M/J. Grebley	T. Applegate et al.
	BCCDC Webcasting	\$17,500	2011	D. Patrick	P. Tang, J. Gardy
	Impact of an Integrated Internet-based Testing Program for HIV and Sexually Transmitted Infections in British Columbia	\$349,977	2011-2014	M. Gilbert	J. Isaac-Renton
	Diagnostic Characteristics of Self Collected Specimens for Sexually Transmitted Infections: A Systematic Review	\$98,652	2011	G. Ogilvie, M. Gilbert	L. Hoang, M. Krajden
	Do rats pose a health risk for people living in Vancouver's Downtown Eastside? Understanding the Ecology and Epidemiology of Rat-Associated Zoonoses in Rats and People	\$230,000	2012-2014	D. Patrick	P. Tang et al.
Canadian Water Network	Innovation to Application: Emerging Water Testing Technologies	\$381,435	2011-2014	J. Isaac-Renton, P. Tang	N. Prystajecy et al.
Genome Canada	Applied Metagenomics of the Watershed Microbiome	\$3,236,286	2011-2014	P. Tang, J. Isaac-Renton	N. Prystajecy et al.
Gen-Probe Inc.	Aptima HPV study adjunct to the HPV FOCAL Trial	\$629,400	2011-2016	M. Krajden	A. Coldman et al.
Merck Frosst Canada	Assessment of HPV Pseudovirus Neutralization Assay Limit of Detection vs. Merck cLIA	\$198,749	2012-2014	M. Krajden	
Michael Smith Foundation for Health Research	Quadrivalent vaccine evaluation study (QUEST)	\$220,000 (annually)	2012-2024	G. Ogilvie, M. Krajden	J. Singer et al.
Public Health Agency of Canada	Genomics Research and Development Initiative (GRDI)	\$900,000	2011-2014	M. Gilmour	J. Isaac-Renton
UBC CDC Communal Fund	Characterizing Proportion of Isolates with Community Associated <i>Clostridium difficile</i> : A Feasibility and Pilot Study	\$15,000	2012	B. Henry	L. Hoang, F. Marra, N. Prystajecy
UBC Peter Wall Solutions Initiative (PWSI)	Aboriginal Water Health	\$118,000	2012	M. Mohseni	J. Isaac-Renton, N. Prystajecy et al.



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# Abbreviations & Acronyms

ABI	Applied Biosystems, Inc.
AMMI	Association of Medical Microbiology and Infectious Disease
ASDT	Advanced Skills Development Team
BC	British Columbia
BCCDC	British Columbia Centre for Disease Control
BCPHMRL	BC Public Health Microbiology & Reference Laboratory
BSON	Biosafety Officer Network
CACMID	Canadian Association for Clinical Microbiology and Infectious Diseases
CAP	College of American Pathologists
CPR	Central Processing and Receiving
CGF	Comparative Genomic Fingerprinting
CFIA	Canadian Food Inspection Agency
CL3	Containment Level 3
CLRN	Canadian Laboratory Response Network
CNPHI	Canadian Network for Public Health Intelligence
CPE	Cytopathogenic effect
CPR	Central Processing and Receiving
CPHLN	Canadian Public Health Laboratory Network
CRE	Carbapenem-resistant Enterobacteriaceae
CQI	Continuous Quality Improvement
CSF	Cerebral spinal fluid

# Abbreviations & Acronyms

CTBLSS	Canadian Tuberculosis Laboratory Surveillance System
CTLTN	Canadian Tuberculosis Laboratory Technical Network
CW	BC Children's Hospital and BC Women's Hospital & Health Centre
DSP	Diarrhetic Shellfish Poisoning
EIA	Enzyme immunoassay
EM	Environmental Microbiology
EMB	Ethambutol
ERAP	Emergency Response Assistance Plan
EWQA	Enhanced Water Quality Assurance
FHA	Fraser Health Authority
FTA	Fluorescent treponemal antibody
GI	Gastrointestinal
HCV	Hepatitis C virus
HPTA	Human Pathogens and Toxins Act
HSP	Heat shock protein
HSV	Herpes simplex virus
ILI	Influenza-like illness
Ig	Immunoglobulin
IGRA	Interferon-Gamma Release Assay
INH	Isoniazid
IQA	Internal Quality Assessment

# Abbreviations & Acronyms

IPD	Invasive Pneumococcal Disease
ISDT	Information Skills Development Team
KPC	<i>Klebsiella pneumoniae</i> carbapenemase
LGV	Lymphogranuloma venereum
LIA	Line immunoassay
LIS	Laboratory information system
LIM	Laboratory Information Management
LML	Lower Mainland Laboratories
LLTO	Laboratory Liaison Technical Officer
LSOC	Laboratory Surveillance & Outbreak Coordinator
MAC	<i>M. avium-M. intracellulare</i> complex
MALDI-TOF	Matrix-assisted Laser Desorption/ionization Time of Flight Analysis
MDR-TB	Multi-drug resistant tuberculosis
MERS-CoV	Middle East Respiratory Syndrome Coronavirus
MIC	Minimum inhibitory concentration
MIRU-VNTR	Mycobacterial interspersed repetitive unit-variable-number tandem-repeat
MLST	Multi-Locus Sequence Typing
MLVA	Multi-locus Variable Number Tandem Repeat Analysis
MMG	Molecular Microbiology & Genomics
MSM	Men who have Sex with Men
MTBC	<i>Mycobacterium tuberculosis</i> complex

# Abbreviations & Acronyms

NAT	Nucleic Acid Amplification Test
NDM-1	New Delhi Metallo- $\beta$ -lactamase-1
NGS	Next Generation Sequencing
NML	National Microbiology Laboratory
NTM	Non-tuberculosis mycobacteria
O&P	Ova & Parasite
OXA	Oxacillinase
PCR	Polymerase chain reaction
PFGE	Pulsed-Field Gel Electrophoresis
PHABM	Public Health Advanced Bacteriology and Mycology
PHAC	Public Health Agency of Canada
PHSA	Provincial Health Services Authority
PHC	Providence Health Care
PHO	Provincial Health Officer
POC	Point of Care
PT	Proficiency testing
PZA	Pyrazinamide
QMS	Quality Management System
RFLP	Restriction fragment length polymorphism
RMP	Rifampin
RT-PCR	Reverse transcription polymerase chain reaction

# Abbreviations & Acronyms

RCD	Reportable Communicable Diseases
RPR	Rapid plasma reagin
RSV	Respiratory Syncytial virus
SDT	Staff Development Team
STEC	Shiga Toxin producing <i>E. coli</i>
STI	Sexually transmitted infection
TB	Tuberculosis
TPPA	<i>Treponema pallidum</i> Particle Agglutination
US	United States
VCHA	Vancouver Coastal Health Authority
VIHA	Vancouver Island Health Authority
VIM	Verona integron-encoded metallo- $\beta$ -lactamase
VP1	Viral Protein 1
VZV	Varicella zoster virus
WGS	Whole Genome Sequencing
ZEP	Zoonotic Diseases & Emerging Pathogens

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