



BRITISH COLUMBIA'S
PROVINCIAL PUBLIC HEALTH LABORATORY

Laboratory Program Highlights 2008-2010

PHSA Laboratories

A service of the Provincial Health Services Authority

PUBLIC HEALTH MICROBIOLOGY & REFERENCE LABORATORY

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Cover Photo Credit:

*Benny Hoy
Medical Laboratory Technologist,
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2010*

LABORATORY LEADERS - MEDICAL & OPERATIONS

Dr. Judy Isaac-Renton

Public Health Laboratory Director (PHLD)

Dr. Isaac-Renton provides overall leadership to ensure that testing priorities and best practices for the Public Health Microbiology and Reference Laboratory (PHMRL) are met, linking the provincial lab with national and international public health systems. She is a Medical Microbiologist, the Program Head for the Parasitology and Environmental Microbiology Programs, and a Professor in the Department of Pathology and Laboratory Medicine at the University of British Columbia (UBC).

Dr. Mel Krajden

Associate Laboratory Director

Dr. Krajden supports the PHLD in laboratory leadership and was the Director of Hepatitis Services at the BC Centre for Disease Control (BCCDC). He is a Medical Microbiologist and Professor in the Department of Pathology and Laboratory Medicine at UBC.

Jeff Stott/Kathy Kelemen

Operations Directors

Jeff led laboratory operations from 2008 to 2009, including financial oversight, management and human resources, and ensuring business requirements were met. Kathy Kelemen assumed the role of Multi-Site Operations Director in 2010, leading operations for the PHMRL as well as for hospital laboratories in the Fraser Health Authority (FHA).

Amelia Trinidad

Chief Technologist

Amelia is second-in-command to the Operations Director and is responsible for supporting the operation of all laboratory programs. During 2008-2009 she worked closely with Peggy Tsang but more recently has assumed responsibility for both of the public health laboratory sites at BCCDC, including Central Processing & Receiving.

Peggy Tsang

Chief Technologist, Central Processing & Receiving

Peggy was responsible for supporting operations in the Central Processing & Receiving Program in 2008-2009. She has now moved to the BC Cancer Agency.

Dr. Martin Petric

Clinical Virologist

Dr. Petric served as Clinical Virologist, providing expertise to the Virology Program from 2002 until late 2010 when he retired. He was also a Professor in the Department of Pathology and Laboratory Medicine at UBC.

Dr. Muhammad Morshed

Clinical Microbiologist

Dr. Morshed is the Program Head and Clinical Microbiologist for the Zoonotic Diseases & Emerging Pathogens Program. He is a Clinical Professor in the Department of Pathology and Laboratory Medicine at UBC.

Dr. Linda Hoang

Medical Microbiologist

Dr. Hoang is the Program Head for the Bacteriology & Mycology Program. She is a Clinical Assistant Professor in the Department of Pathology and Laboratory Medicine at UBC.

Dr. Patrick Tang

Medical Microbiologist

Dr. Tang is the Program Head for both the Tuberculosis (TB)/Mycobacteriology and Molecular Microbiology & Genomics Programs. He is Clinical Assistant Professor in the Department of Pathology and Laboratory Medicine at UBC.

LABORATORY LEADERS - TECHNICAL SPECIALISTS

John Chan

Section Head,
Central Processing &
Receiving (Pre-Analytical)
and
Technical Support Program

Neil Chin

Lead,
Biosafety Biosecurity
Biohazard Containment
Program

Joe Fung

Section Head,
Environmental Microbiology
(Water & Food) Program

Annie Mak

Section Head,
High Volume Serology
Program

Alan McNabb

Section Head,
Molecular Microbiology &
Genomics Program
and
Virology Program

Ana Paccagnella

Section Head,
Bacteriology & Mycology
Program

Dr. Mabel Rodrigues

Section Head,
Tuberculosis/
Mycobacteriology Program

Quantine Wong

Section Head,
Parasitology Program
and
Zoonotic Diseases &
Emerging Pathogens
Program

Surveillance & Outbreak Response

Yin Chang, **Laboratory Surveillance & Outbreak Coordinator**
Kim Macdonald, **Laboratory Liaison Technical Officer**

Laboratory Information Management Team

Rob MacDougall, **Laboratory Information Management Coordinator**
Peter Ng, **Laboratory Information Management Coordinator**

Administrative Team

Kitty Liu, **Executive Assistant to the PHLD**
Yvonne Santa Cruz, **Administrative Assistant, Operations**
Cora Yee, **Healthy Water Coordinator, Enhanced Water Quality Assurance (EWQA)**

REPORT PURPOSE

This report highlights some of the events, achievements, and improvements that occurred during 2008, 2009 and 2010 at the Provincial Health Services Authority (PHSA) Public Health Microbiology & Reference Laboratory (PHMRL).

PHMRL is housed at the British Columbia (BC) Centre for Disease Control (BCCDC) and provides services for BC via seven service delivery programs. The service delivery programs in turn rely on seven cross-cutting core functions such as information management, emergency response, and quality management.

The PHMRL is a leader of, and coordinator for, the provincial network for the detection of microbes causing communicable diseases. Working alongside partners in acute care medical microbiology and infection control, PHMRL provides unique provincial public health programs to workers at the local, provincial, national and even international levels. In the last five years, almost all programs have provided services 6 days a week with on call service for urgent 24/7 response. Some services provide 7 day/week services with further client review underway. Our aim is to continually improve our programs to protect our communities.

WORDS OF APPRECIATION

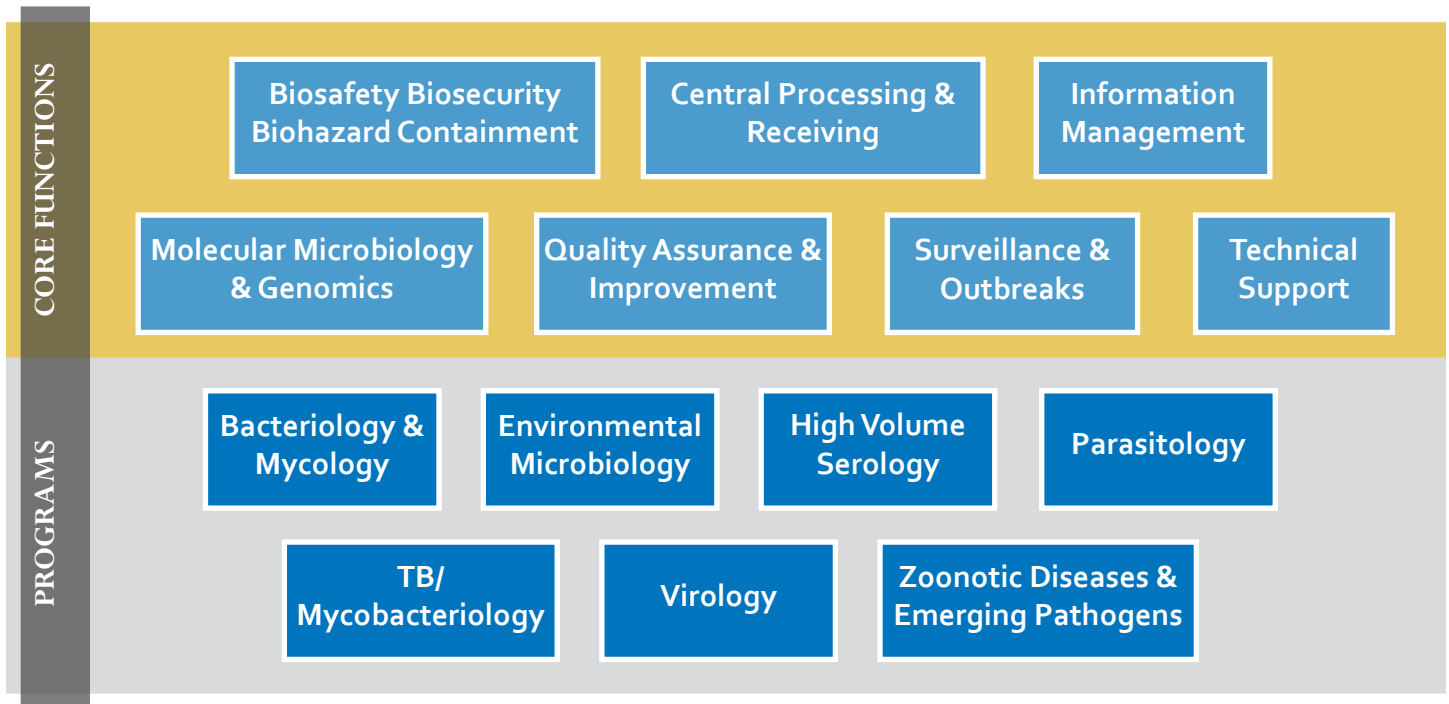
PHMRL staff members acknowledge the ongoing support of, and direction from, our colleagues throughout BC and from colleagues in the Canadian Public Health Laboratory Network (CPHLN).

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ORGANIZATIONAL OVERVIEW

ORGANIZATIONAL FRAMEWORK



OUR VISION

- We strive to be a competitive, knowledge-based team, committed to improving community health through innovation, education and research.
- We value our people and their exceptional contributions.
- We aspire to provide services in an accountable manner.

OUR MISSION

To provide leadership in public health reference microbiology laboratory services for the detection and control of communicable diseases through learning, sharing information and developing policy.

LABORATORY NETWORKS

BC PUBLIC HEALTH LABORATORY NETWORK AND MOLECULAR MICROBIOLOGY NETWORK

These Networks are informal collaborations of laboratory experts working together to prevent and control infectious diseases of public health importance. The PHMRL partners, as appropriate, with its Health Authority (HA) colleagues to share best practices and technologies and to provide training and education. The value of the BC PHLN for surge capacity was seen during the 2009 H1N1 influenza pandemic when new standard operating procedures developed by PHMRL for the novel virus were rapidly shared with other laboratories such as Virology for Providence Health Care and Virology at the Children’s and Women’s Health Centre of BC. Regional laboratories were also trained by PHMRL staff to perform new rapid molecular influenza testing.

CPHLN

CPHLN is a nation-wide network of public health laboratory leaders. The CPHLN fosters knowledge transfer and champions coordinated laboratory response to emerging and re-emerging communicable disease threats. Collaborations with the Public Health Agency of Canada (PHAC) have lead to the following initiatives:

- Canadian Laboratory Response Network (CLRN)
- Canadian Network for Public Health Intelligence (CNPHI)
- Laboratory Liaison Technical Officer (LLTO) Program

The National Microbiology Laboratory (NML) in Winnipeg also provides leadership through CPHLN for:

- National Enteric Surveillance Program (NESP)
- PulseNet Canada
- Canadian Laboratory Response Network (CLRN)
- Various subcommittees – see www.cphln.ca for further details.



CANADIAN FOOD INSPECTION AGENCY

The PHMRL works closely with the Canadian Food Inspection Agency (CFIA) for outbreak coordination and food sample testing. In particular, CFIA provides support during outbreaks of botulism and performs fish testing through its Fish Inspection Program. As a laboratory that handles animal and zoonotic pathogens, CFIA also mandates Containment Level 2 (CL2) compliance for importation permits and provides certification for the Containment Level 3 (CL3) facilities at the PHMRL.

CROSS BORDER NETWORKS

Cross border collaboration is important for improving communication within the geographic region, sharing response and preparedness plans for public health emergencies, and formalizing agreements for sharing resources.

- Since 2004, the Washington State Department of Health and the BC Ministry of Health Services (MOHS) have jointly sponsored an annual Pacific North West Cross Border Public Health Workshop on emerging public health issues.
- In 2008, the Pacific North West Border Health Alliance was formed including American and Canadian representation from BC, Saskatchewan, the Yukon Territory, Washington, Oregon, Idaho, Montana, and Alaska. Alberta and North Dakota have recently been invited to participate.
- In 2010, after years of working together, the BC MOHS signed a Memorandum of Agreement (MOA) with the Washington State Department of Health to share public health laboratory services. The MOA facilitates mutual aid and cooperation during an outbreak of disease, foodborne contamination, or suspected biological or chemical terrorism by sharing capacity and expertise when required.



CONTINUING EDUCATION

MICROBIOLOGY FOR PUBLIC HEALTH/REFERENCE LABORATORIES (MPHRL) COURSE

A successful series of noon-hour lectures was offered by the Public Health Medical Microbiologists. More than 100 people regularly attended the lectures using video-conferencing for remote attendees. Lectures provided clinical and public health contextual information for public health workers located at PHMRL and for staff at the Public Health Laboratory in Regina, Saskatchewan. The course purpose was to build a foundation for clinical and diagnostic public health microbiology for public health laboratory staff. Many topics were covered including Canadian and global public health laboratory systems, viral pathogens, environmental microbiology, and bioterrorism.

The lecture series (organized in four different blocks) was approved by UBC Division of Continuing Professional Development and Knowledge Translation as an Accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification program of the Royal College of Physicians and Surgeons of Canada. The Canadian Society for Medical Laboratory Science also granted continuing education credit for this 2-year course. The Canadian College of Microbiologists invited successful participants (those who met attendance criteria and passed appropriate examinations) to apply for Registered Microbiologist designation with the College.

- MPHRL- Part 1: January 2008 – July 2008 (Introduction to Clinical Microbiology, Quality Leadership, Virology)
- MPHRL- Part 2: September 2008 – January 2009 (Bacteriology)
- MPHRL- Part 3: January 2009 – July 2009 (TB, Zoonotic and Vector-Borne Pathogens, Parasites, Environmental Microbiology)
- MPHRL- Part 4: September 2009 – February 2010 (Mycology, Community Outbreaks, Health Care Acquired Infections, Bioinformatics)

LABORATORY CORE FUNCTIONS

All PHMRL Programs rely on Laboratory Core Function teams. Their functions and deliverables ensure continued optimal work – they are essential to service delivery due to their highly specialized troubleshooting and fundamental support expertise. The Core Function Teams provide a framework of essential services and act as the “van guard” for validation and implementation of required cutting edge program operations and they provide focused leadership in maintaining best reference laboratory practices.

The Core Function Programs are small and diverse but critical to the daily work of PHMRL. They include:

- Biosafety Biosecurity Biohazard Containment
- Public Health Central Processing & Receiving
- Information Management
- Molecular Microbiology & Genomics
- Surveillance & Outbreaks
- Quality Assurance & Improvement
- Technical Support

BIOSAFETY BIOSECURITY BIOHAZARD CONTAINMENT(BBBC) maintains the continued operation of the CL2 and 3 facilities that constitute the PHMRL. This includes successful annual Health Canada CL3 certification of three facilities (on three floors), education and training for CL2 and CL3 staff to meet national standards, and expertise in laboratory safety and biohazard containment response. Leaders during public health emergencies, members of this two-man team are prepared to respond to events such as threats from the intentional misuse of biological agents. The next few years will also see their leadership in biosecurity to ensure that the PHMRL meets requirements related to the new federal *Human Pathogens and Toxins Act* (HPTA).



John Tansey, Assistant Biosafety Officer and Neil Chin, BBBC Program Public Health Lead and Biosafety Officer

HIGHLIGHTS INCLUDE:

- Achieving successful annual certification of CL3 laboratories by Health Canada and CFIA (since 2001).
- Leading the planning for laboratory readiness to comply with HPTA.
- Leading staff in CL2 and CL3 Programs in best practices in biosafety, biosecurity and biohazard containment.
- Sustaining national membership in the Biosafety Officers Network (provincial and federal public health laboratories).
- Maintaining certification by the Emergency Response Assistance Program (ERAP) (Containment Level 4 pathogen response).
- Developing import export permits for the Cross Border MOA.

PUBLIC HEALTH CENTRAL PROCESSING & RECEIVING (CPR)

The pre-analytical receiving and triaging for all laboratories at the PHMRL, CPR is the first point of contact for both human and environmental samples collected from all over the province. More than 5000 samples arrive daily. Staff members in this area sort and process complex samples arriving from a number of clients. CPR also manages the Client Services Line, responding to enquiries from health care and public health clients for all PHSA laboratories.



HIGHLIGHTS INCLUDE:

- Completing three Lean imPROVE projects, resulting in one-piece flow and other significant efficiencies
- Achieving a rapid sample sorting time goal by clearly identifying, separating and routing water sample coolers
- Improving the work flow at the sorting bench, also positively impacting other PHMRL Sections
- Streamlining of other "imPROVE" processes, e.g., sorting, data entry, labelling, and batching
- Improving laboratory safety practices related to packaging disparities
- Enhancing security related to the large numbers of delivery people entering CPR

INFORMATION MANAGEMENT (IM)

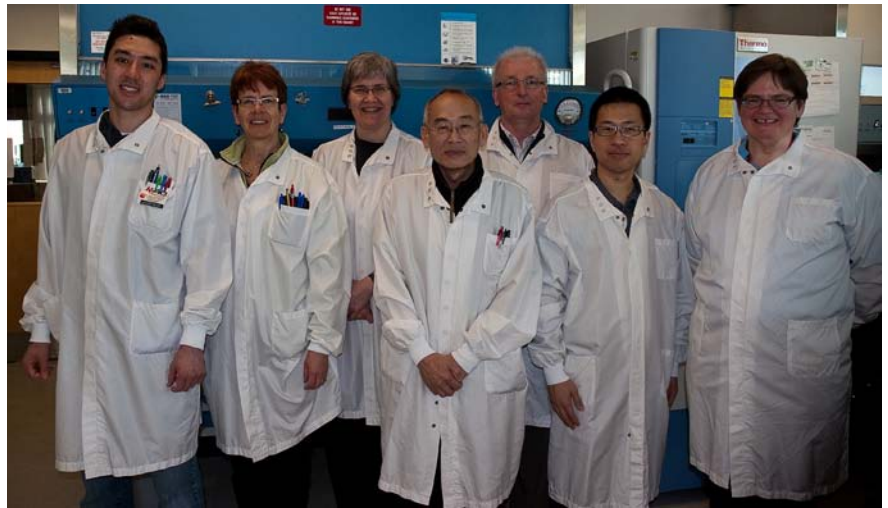
The IM Team maintains a robust information system for the PHMRL and is leading integration across systems. The two data administrators work to ensure timely dissemination of laboratory data used to make public health, patient care and disease management decisions. Ensuring interoperability of consolidated and linked systems is a key area of focus as the PHMRL works with HAS, the Provincial Laboratory Information Solution (PLIS), and nationally on the PANORAMA stage.

HIGHLIGHTS INCLUDE:

- Early adopting of the PLIS, providing consolidated test results (first site to do so).
- Participating in the Logical Observations Identifiers Names and Codes (LOINC) project for provincially standardizing order codes as part of PLIS activities.
- Partnering on the development, validation and implementation of a bidirectional laboratory interface with FHA, enabling faster, more reliable transmission of test requests and results.
- Initiating ongoing improvements in electronic Reportable Communicable Disease (RCD) programs.
- Collaborating with the PHSA to support linked databases and information systems in the Public Health Repository Data Warehouse (in previous iterations known as the Laboratory Database Management System) with Enteric and Virology datamarts completed.
- Automating RCD reports within the Sunquest Laboratory Information System (LIS) environment.
- Leading training on bionumerics application for isolate characterization.
- Leading consideration of water laboratory IM options.

MOLECULAR MICROBIOLOGY & GENOMICS

This small but highly essential team supports all other PHMRL programs. Identifying and characterizing novel and emerging new microbes is a crucial component of laboratory services. Molecular methods are increasingly relied on with short turnaround times and better sensitivities. The current PHMRL molecular capacity would not be possible without the day-to-day leadership and troubleshooting provided by these experts. Staff members work closely with all other areas in the PHMRL on polymerase chain reaction (PCR) testing and genomic testing problems, on molecular quality assurance (QA) activities such as internal proficiency testing (PT) and QA for molecular tests. They also train and provide competency assessments in molecular assays, as well as partnering with service program leaders to design, validate and implement new molecular tests. This team is also critical to the PHMRL rapid response to emerging and novel pathogens and for rapid detection of bioterrorism agents. Clearly a unique and fundamental team!



Molecular Microbiology & Genomics Team (L-R): Mark McCabe, Glenna Geddes, Diane Eisler, Rueben Chen, Alan McNabb, Dr. Patrick Tang, Kathy Adie.

HIGHLIGHTS INCLUDE:

- Leading an Internal Quality Audit (IQA) of all molecular assays in all programs at PHMRL.
- Introducing rapid DNA sequencing to detect the novel H1N1 influenza virus.
- Rapidly developing and validating a reverse-transcriptase PCR (RT-PCR) assay for detecting the new pandemic virus.
- Sharing our multiplex PCR for the pandemic virus with Providence Health Care (PHC), Children's and Women's Health Centre, and hospitals in Victoria.
- Partnering with Virology staff to develop, validate and implement better molecular assays for herpes simplex virus, adenovirus, and measles.
- Partnering with Bacteriology & Mycology (BAM) staff to develop, validate and implement a new pertussis assay.
- Partnering with BAM for direct 16S sequencing of isolates.
- Supporting BAM and CLRN staff in developing molecular assays for bioterrorism agents.
- Partnering with BAM staff in developing a universal methodology for extracting fungal DNA.
- Partnering with BAM staff on multiplex PCR detection of the nuc, mecA and PVL genes in Methicillin-resistant *Staphylococcus aureus* (MRSA) strains.
- Partnering with Environmental Microbiology (EM) staff to develop, validate and implement sapovirus and STEC molecular assays.
- Partnering with EM staff on speciation of *Campylobacter* species and assisting with the transition of Norovirus conventional PCR detection assays to real-time PCR.
- Partnering with tuberculosis (TB)/Mycobacteriology staff to develop, validate and implement a faster and cheaper IS6110/MPT64 assay for the direct detection of *Mycobacterium tuberculosis*.
- Partnering with TB staff to develop direct hsp65 sequencing for detecting and identifying *Mycobacterium* species directly from patient samples and sharing this work with the microbiology lab at PHC.

The **SURVEILLANCE & OUTBREAKS** Program improves internal and external linkages for rapid emergency response. The two staff members (one a federal LLTO staff member) coordinate and manage outbreak-related events for emergency responses and ongoing surveillance. Other key duties include internal and external communications, work with the BBBC Program and internal quality initiatives. Partners are colleagues at BCCDC, BC's HAs and the CPHLN. Figure 1 demonstrates the variation in the number of outbreak events over 2008-2010; 2009 was particularly busy with the pandemic H1N1 causing many facility outbreaks across the province.

HIGHLIGHTS INCLUDE:

- Providing coordination and support for the following outbreaks:
 - 2008 mumps outbreak in a vaccine-resistor community (more than 100 cases).
 - 2009 pandemic H1N1 influenza outbreak in two waves.
 - 2009 *E. coli* 0157:H7 related to a petting zoo (41 cases).
 - 2010 post-Olympics measles virus outbreak (75 cases).
 - 2010 rubella virus outbreak (8 cases).
 - 2010 *Salmonella* Chester outbreak from consumption of contaminated food (31 cases).
 - 2010 *Campylobacter jejuni* outbreak from consumption of contaminated food (8 cases).
- Preparing for testing, communications and enhanced surveillance for the Olympic and Paralympic Winter Games, February-March, 2010.
- Partnering with the NML to pilot Measles and Rubella Surveillance (MARS).
- Participating in a standardized outbreak identification project within the LIS.
- Integrating a new federally-sponsored LLTO position into the team to improve provincial-federal surveillance activities.
- Participating in a modelling project with the UBC Sauder School Centre for Operations Excellence (laboratory operations during the pH1N1 outbreak).
- Participating in modelling work with CPHLN and USA Centers for Disease Control and Prevention (CDC) on public health laboratory surge capacity.
- Optimizing and assisting in validation of Comparative Genomic Fingerprinting (CGF) for *Campylobacter*.

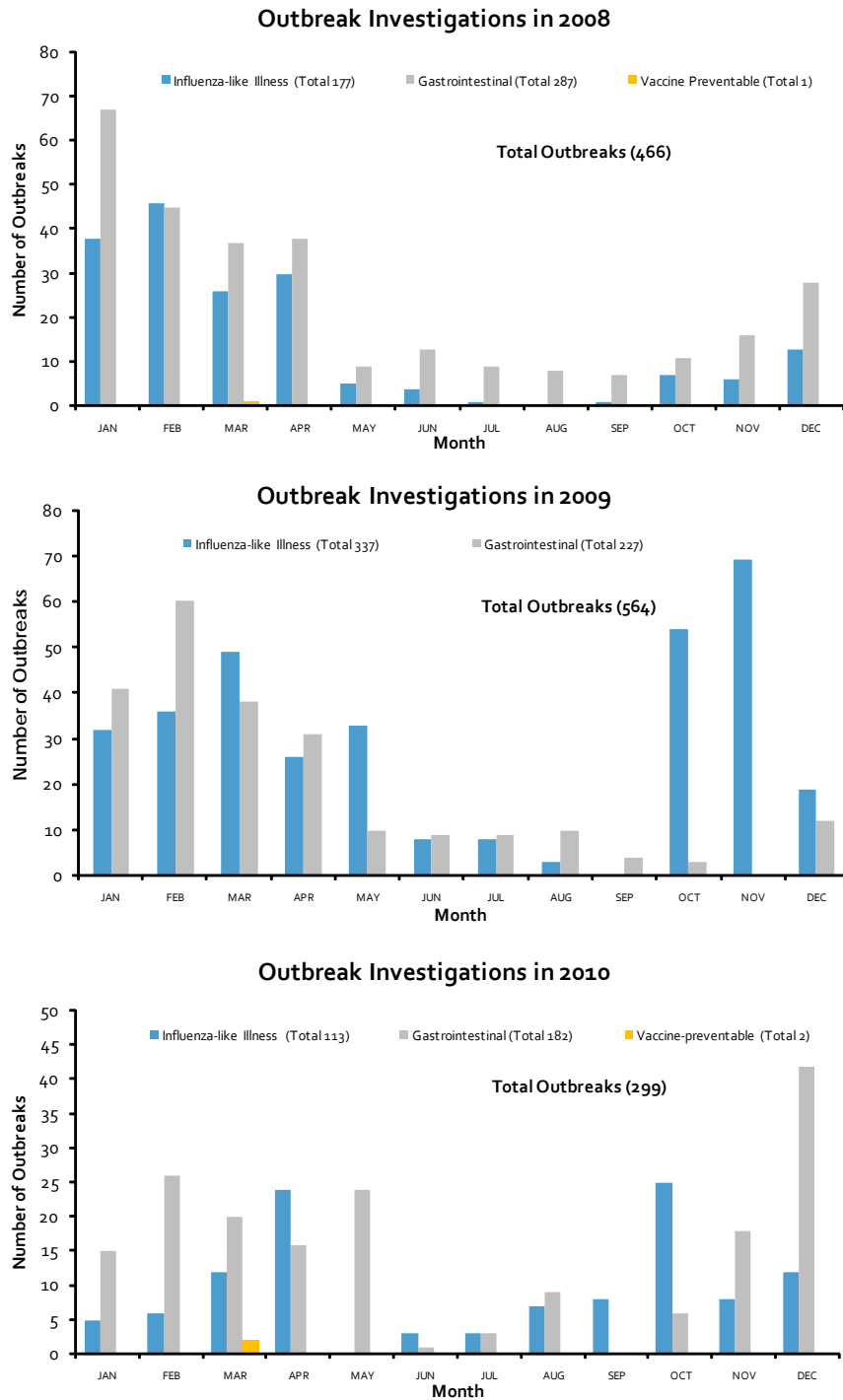


Figure 1. Outbreak investigations from 2008-2010.

QUALITY ASSURANCE & IMPROVEMENT

The PHMRL aims to maintain accreditation with the:

- BC Diagnostic Accreditation Program (DAP).
- College of American Pathologists (CAP) for the highest standard of excellence for laboratories (international recognition).
- BC Enhanced Water Quality Assurance (EQWA) Program certification by the Provincial Health Officer (PHO) for drinking water testing.
- Health Canada-required certification for the CL3 laboratories.

The Quality Team, including all program areas, works within the Quality System Essential Framework to ensure that regulatory and public health system requirements are met.

Chaired by the

PHLD, the Team meets monthly, reporting to the PHS Laboratories' Safety and Quality

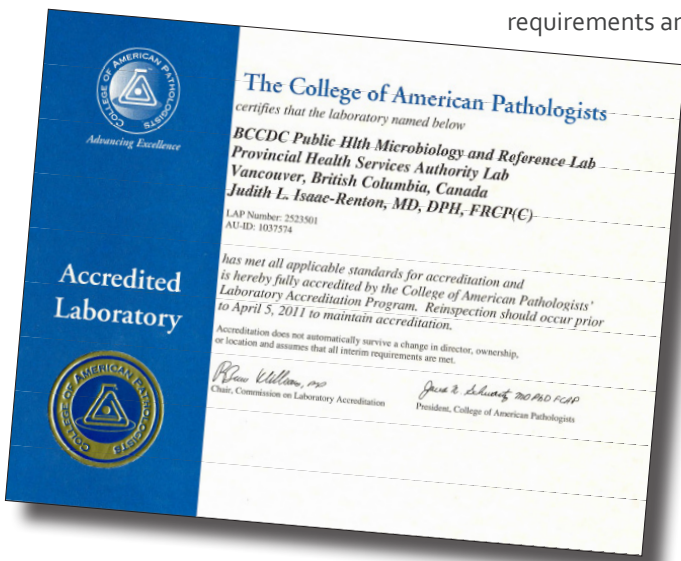
of Medical Care Committee. Besides annual review and approval of more than 1300 standard operating procedures, our programs produce results on 14 external QA/PT areas from seven programs.

The Quality Team has three subcommittees tasked to focus on specific areas of improvement:

- Continuous Quality Improvement (Chair 2008-2010, John Chan)
- Internal QA (Chair 2008-2010, Quantine Wong)
- Staff Development Team (Chair 2008-2010, Alan McNabb).

HIGHLIGHTS INCLUDE:

- Achieving full accreditation with DAP (2007 and 2009), CAP (2007 and 2009), EQWA (water laboratory), and Health Canada (CL3 Laboratories).
- Implementing a new electronic document control system (LabQMS).
- Transitioning to the BC Patient Safety & Learning System (PSLS) from the PHMRL Incident Management System.
- Completing internal QA (Molecular IQA, CAP deficiencies IQA).
- Inspecting other provincial public health laboratories via Audit Teams.



Our **TECHNICAL SUPPORT** Program supplies PHMRL programs with specialized, quality-assured media and reagents and provides sterilization services for laboratory equipment and management of all biological waste products. In 2010, more than 330,000 orders were filled and 275 types of media were provided / quality-assured for PHMRL programs (Table 1). Technical Support also provides specialized sample collection outfits for other clients.

Table 1. Media produced and purchased by the Technical Support Program in 2010.

Section	Media made in 2010	Media purchased in 2010
General Bacteriology	135 120	75 149
Food borne diseases	34 375	4 470
Mycology	12 780	12 166
Water bacteriology	113 271	110 690
Others	3 785	7 070
Grand Total	336 132	209 655
Media Types	275	41

LABORATORY PROGRAMS

The PHMRL is the primary public health and reference diagnostic testing facility for BC. The following pages highlight some of the research, outbreak investigation and new assay development activities of 2008 to 2010 from the seven service delivery programs, including:

- Bacteriology & Mycology
- Environmental Microbiology
- High Volume Serology
- Parasitology
- TB/Mycobacteriology
- Virology
- Zoonotic Diseases & Emerging Pathogens

The Enhanced Water Quality Assurance Program is also administered through the PHMRL.





BACTERIOLOGY & MYCOLOGY

BAM is comprised of three previously integrated laboratories (enteric, reference bacteriology, and mycology), providing provincial public health reference and diagnostic bacteriology and mycology reference services. Using a variety of culture-based and molecular diagnostic methods, the BAM Team confirms and further characterizes bacterial and fungal organisms submitted by frontline microbiology laboratories across BC.

BAM is responsible for providing information on enteric, respiratory, sexually transmitted and health care acquired infections as well as exotic systemic diseases and bioterrorism agents. Characterization by different molecular fingerprinting techniques is performed for outbreak detection and management, and for public health and infection control workers.

PROGRAM HEAD

Dr. Linda Hoang

SECTION HEAD

Ana Paccagnella

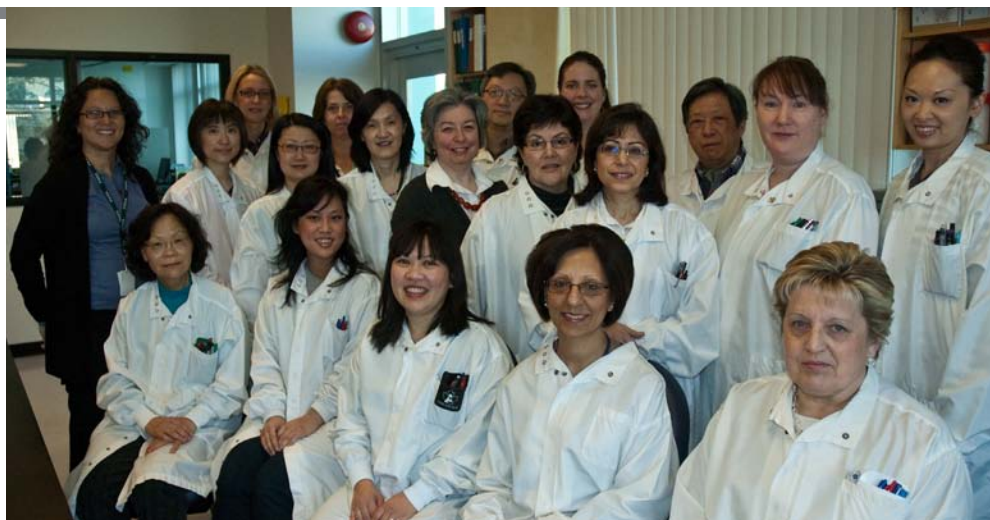
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EMERGENCY CONTACT

604.661.7033 (Med Micro)



HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

CLRN

The PHMRL was the first laboratory in Canada to become a member of CLRN, partnering with our own Molecular Microbiology & Genomics Program (a Core Function Program), BBBC (another of our Core Programs), the CPHLN, the NML and the CDC Laboratory Response Network in the United States. Members of BAM were trained and certified on new rapid molecular methods to detect several CL3 bacterial pathogens to allow for quick response to bioterrorism threats.

CLRN SIMULATION MODELLING PROJECT

This Team worked with the PHMRL Outbreak and Surveillance Team, the CPHLN and the CDC to develop simulation tools for animal and public health laboratories. The pilot project modelled CLRN laboratory testing for CL3 biological agents, evaluating surge capacity and assessing strategies for improved testing efficiency and capacity.

CLOSTRIDIUM DIFFICILE INFECTION PROJECT

Partnering with the Provincial Infection Control Network (PICNet) on a collaborative surveillance program, BAM worked with BC's HAs to measure the incidence of *Clostridium difficile* infection (CDI) in acute care facilities. Two trend reports for 2008-2010 resulted and can be accessed on the PICNet website (www.picnetbc.ca).

CARBAPENEMASE RESISTANCE COLLABORATIONS

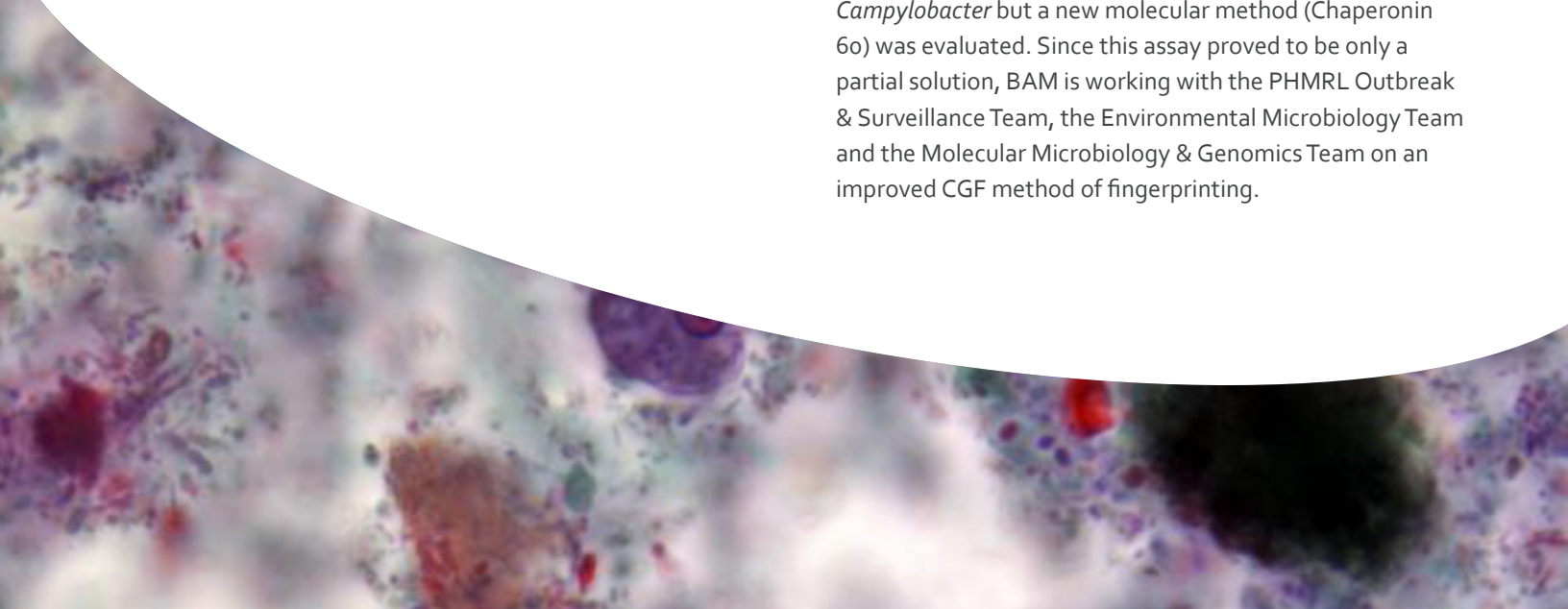
Following the confirmation of a New Delhi Metallo-beta-lactamase gene (NDM) strain in BC, BAM implemented a multiplex PCR test panel to allow detection of important mechanisms of antimicrobial resistance in gram negative bacteria. The PCR panel targets the four carbapenemases: KPC, IMP, VIM and NDM. Collaboration continues with Calgary Laboratory Services, St. Paul's Hospital and the NML. BAM maintains a central repository and surveillance role on behalf of the BC Association of Medical Microbiologists (BCAMM) and works closely with the NML for the timely identification and confirmation of these highly resistant bacteria.

MRSA PCR

MRSA is a major pathogen responsible for significant numbers of health-care-associated infections. Associated with the increased virulence of some strains of *S. aureus* is Pantone-Valentine leukocidin (PVL) which causes severe skin infections. A new real-time PCR technology for detecting MRSA and PVL in partnership with the Molecular Microbiology & Genomics Program was developed, validated and implemented.

CAMPYLOBACTER JEJUNI OUTBREAK

In August 2009, eight cases of *Campylobacter jejuni* were associated with the consumption of contaminated beef buns. Fingerprinting is not available to further characterize *Campylobacter* but a new molecular method (Chaperonin 60) was evaluated. Since this assay proved to be only a partial solution, BAM is working with the PHMRL Outbreak & Surveillance Team, the Environmental Microbiology Team and the Molecular Microbiology & Genomics Team on an improved CGF method of fingerprinting.



HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

OTHER BACTERIAL OUTBREAKS

The BAM Team worked closely with HAs and BCCDC on bacterial outbreaks. A petting zoo was implicated in 17 cases of *E. coli* O157:H7 in 2009. These cases were mostly children whose infections displayed the same pulsed field gel electrophoresis (PFGE) fingerprinting pattern. In 2010, 30 cases of *Salmonella* Chester with the same PFGE pattern were attributed to consumption of contaminated head cheese, resulting in recall of the food. Also, cases of *Salmonella* Enteritidis with the same PFGE patterns were associated with exposures at two restaurants and travel to Mexico in 2010. PFGE is now an aging fingerprinting technology and genomic approaches are currently being evaluated as improved methods.

BORDETELLA PERTUSSIS PCR

B. pertussis (whooping cough) continues to be a significant respiratory disease among unvaccinated children and young adults with waning immunity. PCR improves detection time and is more sensitive than labor intensive culture assay but the PCR method (in use since 1999) needed updating. Partnering with the Molecular Microbiology & Genomics Program, real-time PCR for *B. pertussis* detection (faster and less labour-intensive) was developed and BAM has transitioned to this new assay.

IMPROVED FUNGAL IDENTIFICATION METHODS USING GENETIC SEQUENCING

Traditional identification of fungal isolates requires a laborious mixture of expertise in phenotypic and morphologic characteristics. Molecular methods are also limited, particularly when novel fungi continue to be identified as human pathogens. Work is underway with the Molecular Microbiology & Genomics Team for enhanced fungal identification, combining classical phenotypic techniques with newer molecular sequencing genomic microbiology methods.

TEACHING ACTIVITIES

The BAM Program provides teaching and education for public health workers and undergraduate and post-graduate medical trainees. Co-op placements occur frequently. Medical residents for the Dermatology Program routinely rotate through Mycology.

CRITICAL TESTS

- Tests for all CL3 organisms: *B. anthracis*, *Blastomyces*, *Brucella* spp, *Coccidioides*, *F. tularensis*, *Y. pestis*, *Histoplasma*
- Fingerprinting test for outbreaks of bacterial organisms
- Bioterrorism bacterial response assays
- *B. pertussis/parapertussis* PCR and culture (surveillance)
- *Legionella* PCR and culture
- *H. influenzae* serotyping
- *N. meningitidis* serogrouping



ENVIRONMENTAL MICROBIOLOGY

The Environmental Microbiology Team provides testing of clinical, food poisoning and water samples as well as consultation services for public health clients across BC. Working closely with HA Environmental Health Officers, Drinking Water Officers, and Medical Health Officers (MHOs), as well as BCCDC Environmental Health (Food Protection Services), the Team supports the prevention, detection, and management of foodborne and waterborne illness. Drinking water, recreational water and waste water samples from a variety of sources are tested as part of the legislated provincial monitoring program.

The laboratory is the provincial botulism testing site, carrying out highly specialized emergency testing of clinical samples and implicated food sources in this type of food poisoning. It is Canada's first environmental public health team to be certified for rapid molecular detection of botulinum toxin in foods within the CLRN. The Team works with clients province-wide to investigate other types of food poisoning and leads the Food Quality Check Program. Detection and genomics of specific pathogens (*Giardia* sp. and *Cryptosporidium* sp.) are also investigated. Reference environmental pathogens (Ciguatera toxin, scombroid, paralytic shellfish, chemical and mushroom poisoning testing) are expedited for BC through this laboratory.

PROGRAM HEAD

Dr. Judy Isaac-Renton

SECTION HEAD

Joe Fung

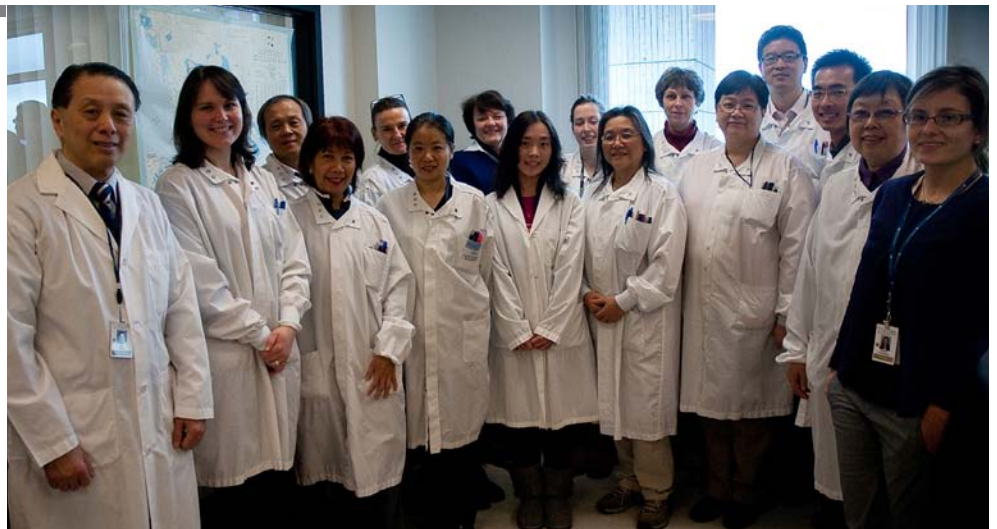
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EMERGENCY CONTACT

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604.707.2620 (Norovirus)



HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

WATER TESTING

Legislated water sample testing increased from 77,694 samples in 2008 to 85,289 samples in 2010 (a 10% increase); 87% of samples were drinking water (Figure 2). To cope with the increase in volumes, a Lean improve event successfully led to improvement in time to results reporting

Water samples must be tested within 30 hours of collection. Geographic challenges and extreme weather conditions mean achieving this goal is difficult for some areas, particularly in BC's interior and northern regions. To reduce the number of rejected water samples, the Team has been working with HAs to set up dedicated coolers to be delivered to the Laboratory overnight, dramatically improving services (Figure 3).

Although the laboratory did not receive water samples from the area affected by flooding in 2008 to 2010, the Team has established a protocol for testing samples from flooded areas or from other emergencies to ensure drinking water is safe.

Proportion of Water Sample Types Tested in PHMRL (2008 - 2010)

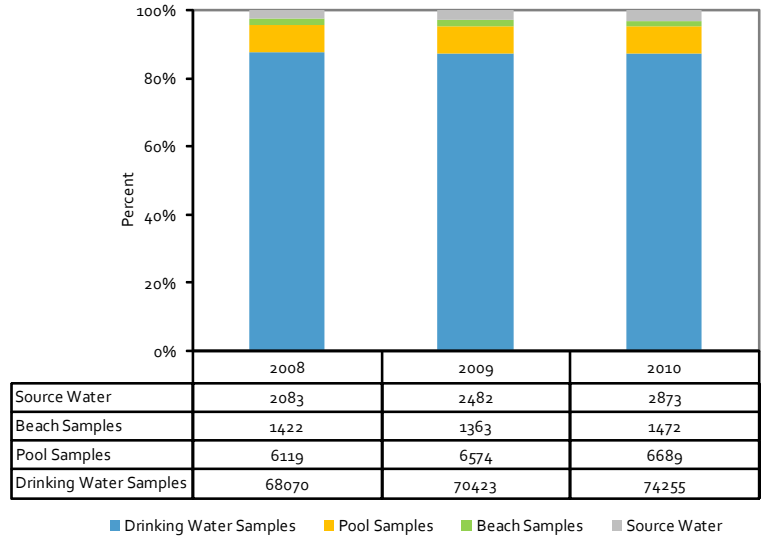


Figure 2. Water sample testing by source, 2008-2010.

WATER MONITORING EVALUATION

Ongoing work with the Health Protection Branch (Ministry of Health) for improving the provincial system of testing was carried out. Besides responding to a BC Ombudsman investigation (Fit to Drink: Challenges in Providing Safe Drinking Water in British Columbia report) projects included: requisition audit and improvement, assessment of predictive value of water testing databases, and evaluation of local "Level C" type testing approaches.

QUANTITATIVE MICROBIAL RISK ASSESSMENT (QMRA) COLLABORATION

QMRA is a new approach used internationally for safer water. This Team worked with others from the Canadian Water Network to assess a framework for health risk assessment using molecular genotyping methods for *Giardia* and *Cryptosporidium*.

Provincial Drinking Water Sample Monitoring

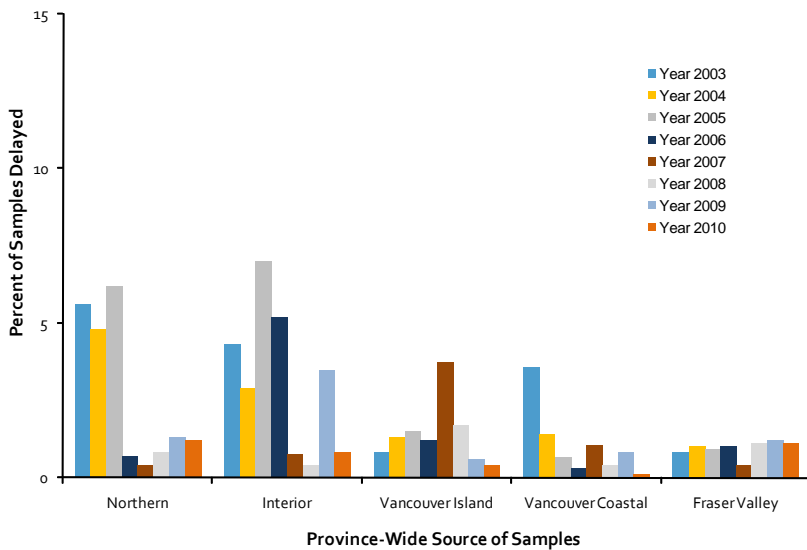


Figure 3. Percent of water samples delayed (and lost to testing) due to transport issues, 2003-2010.

HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

OUTBREAKS

Norovirus is the etiologic agent in 73% of reported gastro-intestinal (GI) outbreaks in BC (Figure 4). During 2008 to 2010 the majority of norovirus outbreaks occurred in residential care (54%) and hospital (32%) settings.

This Program provides RT-PCR for detection of norovirus. In 2009, a real-time RT-PCR method was developed, validated, and implemented in conjunction with the Molecular Microbiology & Genomics Program to provide faster turn-around time (TAT) and genogroup typing. Knowledge of norovirus genogroup can be helpful in GI outbreak investigation especially since norovirus genogroup I has been associated with foodborne or waterborne transmission, while genotype II is more often associated with person-to-person transmission. In BC, for the years 2008 to 2010, the majority of norovirus outbreaks were caused by norovirus genotype GII.4 (85%), while genogroup I caused 4% of all norovirus outbreaks (Figure 5).

The Environmental Microbiology Team also provides molecular microbial genotyping for other outbreak investigations, particularly where foodborne or waterborne spread is suspected. Potential outbreaks of foodborne botulism, *E. coli* O157, *Campylobacter* and *Salmonella* were among the events investigated.

Norovirus Genotypes in BC (2008 - 2010)

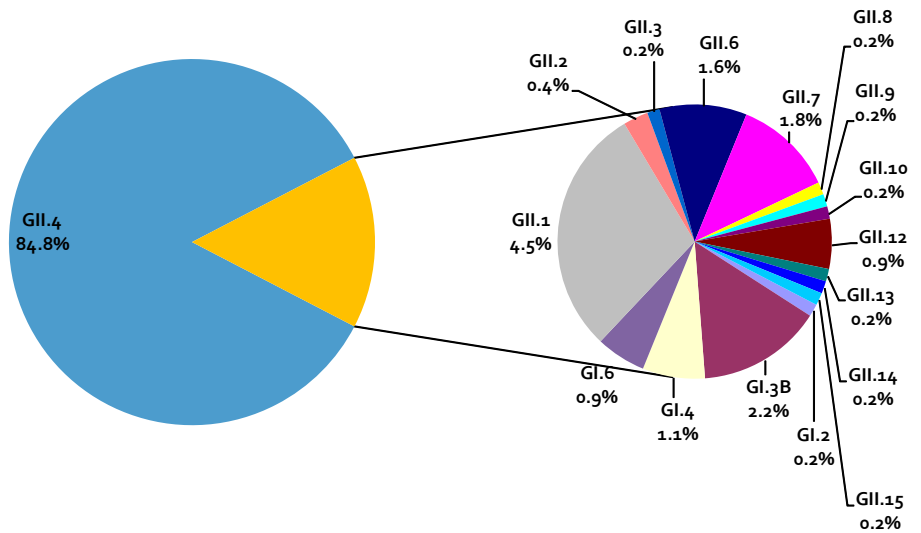


Figure 5. Norovirus genotypes in BC from 2008 to 2010.

Reported Gastrointestinal Outbreaks in BC (2008 - 2010)

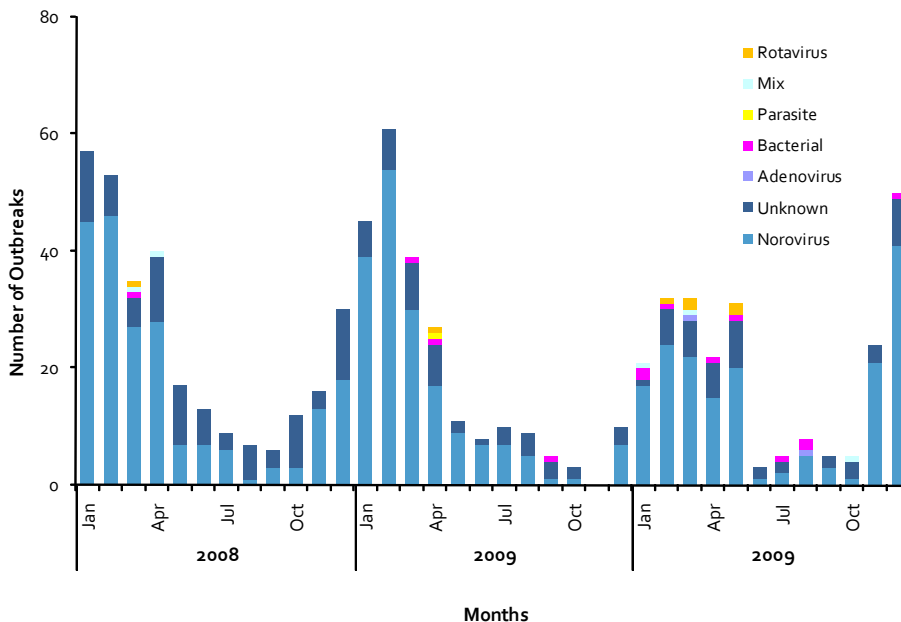


Figure 4. Reported GI outbreak etiologies from 2008 to 2010.

HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

SAPOVIRUS OUTBREAKS

Sapovirus is a recently recognized viral cause of diarrhea. A real-time RT-PCR detection method was developed in partnership with the Molecular Microbiology & Genomics Program. As part of method validation, GI outbreaks with no previously identified etiology were tested for presence of sapovirus over 12 months in 2008-2009. Results showed that during the testing period, sapovirus made up 7% of all reported GI outbreaks; 30% occurred in day care settings (Figure 6). More than 20% of GI outbreaks still have no identified causative agent.settings.

Sapovirus Outbreak Settings (Apr 2008 - Mar 2009)

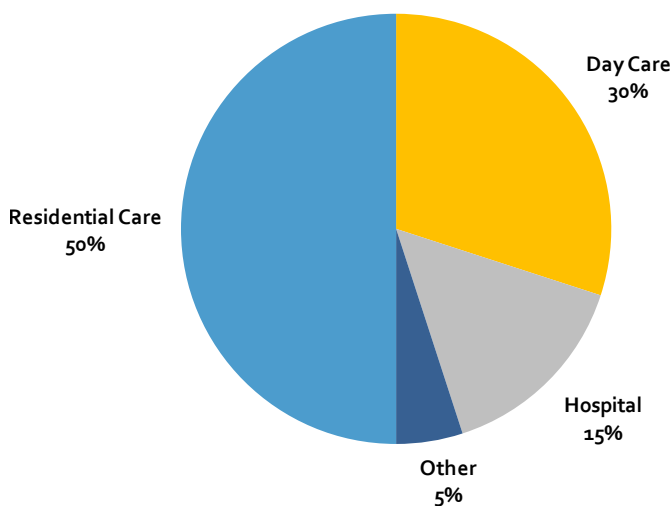


Figure 6. Sapovirus outbreak settings from Apr 2008 to Mar 2009.

VIRONET CANADA

PHMRL is a member of a CPHLN initiative, ViroNet Canada, a national bionumerics database for norovirus genomic sequence information. ViroNet Canada provides a powerful molecular approach for public health laboratories to identify, investigate, and track outbreaks. The program participated in a multicenter study comparing two sequencing region laboratory protocols; results were published in the *Journal of Clinical Microbiology*.

WATERBORNE PATHOGEN DETECTION AND GENOTYPING

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. Usefulness of *Giardia* assemblage genomics for microbial tracking was investigated.

OLYMPIC AND PARALYMPIC READINESS

The Team prepared for the 2010 Winter Games by working with Vancouver Coastal Health Authority and Metro Vancouver to provide increased water testing capacity through training of regional Drinking Water Officers. The purpose, to support the enhanced water quality surveillance required during the months leading up to and during the Games, was met through this laboratory-public health partnership.

C-ENTERNET

Led and funded by PHAC, C-Enternet is a multi-partner initiative aiming to reduce the burden of enteric disease through sentinel site surveillance; FHA became the second sentinel site in Canada. Pathogens from food and water will be evaluated. This program contributes to C-Enternet by sharing information on molecular typing of microbes and developing novel molecular methods to characterize clinical, food and water isolates. The Team partnered with the Molecular Microbiology & Genomics Program and BAM in the assessment, development and validation of *Campylobacter* and non-O157 STEC molecular assays.

HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

FOOD POISONING

Working closely with HAs and federal partners, the Team's food poisoning experts determine the source of foodborne illnesses and outbreaks. For example:

- As part of ongoing *Salmonella* Enteritidis investigations implicating eggs, a restaurant cluster affecting a number of patrons was investigated; *Salmonella* Enteritidis was detected with PFGE patterns from food isolate matching those of clinical isolates.
- An outbreak of *E. coli* O157:H7 implicating a petting zoo was investigated and environmental samples submitted. Some of these samples tested positive for *E. coli* O157:H7 with PFGE patterns matching clinical isolates.
- An outbreak of Norovirus was investigated in 2010 with seven clusters of illness linked to multiple lots of oysters harvested from BC's west coast. At least 35 people were clinically ill and norovirus Genogroup I was confirmed.

FOOD QUALITY CHECK REPORTS TO HAS

The Food Quality Check Program has been operating in BC since 1998 in a partnership between PHMRL and food safety clients in both BCCDC Environmental Health and Health Units in the five HAs. It is an educational tool related to ready-to-eat food samples from retail establishments. In 2010, a comprehensive database was developed to ease analysis of food quality data. Annual and quarterly reports are now routinely issued to the HAs.

CLOSTRIDIUM BOTULINUM TESTING

Few laboratories in Canada have the highly specialized expertise required to provide botulism testing to confirm clinical diagnoses and to investigate outbreaks. With this expertise, PHMRL carried out emergency botulism testing on more than 20 events. The Team was also first in Canada to be certified in the use of rapid molecular and ELISA assays to detect *Clostridium botulinum* and its toxins. Working with PHAC and Health Canada's team in Ottawa, EM experts have validated and implemented two new molecular assays to partner on BC food security and bioterrorism threats. Working with the Molecular Microbiology & Genomics Core Program, new developments on botulism fingerprinting methods are underway.

TEACHING ACTIVITIES

The Program provides teaching and education for public health workers (particularly BC's Environmental Health Officers), and undergraduate and post-graduate medical trainees. Co-op students assist in drinking water testing and participate in laboratory projects as part of their training.

CRITICAL TESTS

The following are considered to be critical tests with 7 day/ week services and results telephoned immediately to clients:

- Positive *E. coli* – drinking water testing results
- Botulism requests and ongoing bio-assay and molecular test results
- Outbreak testing, investigation and results



ENHANCED WATER QUALITY ASSURANCE

EWQA is a legislated province-wide peer review auditing program for certifying BC's drinking water testing laboratories. EWQA auditors ensure that drinking water testing for public health purposes meets approved laboratory standards. Public and private laboratories that test drinking water for regulatory compliance purposes are inspected on behalf of the BC PHO under the BC *Drinking Water Protection Act*. The EM Section Head, as a provincial expert, chairs the Technical Quality Assurance Working Group (QAWG) and the PHLD chairs the Steering Committee.

The EWQA Steering Committee, including a representative from the Ministry of Health, Health Protection Branch as well as private, municipal and public water testing laboratory directors, provides advice to the BC PHO, the PHLD and EWQA staff on strategic directions. The Technical QAWG consists of a voluntary group of technical and scientific experts providing best practice advice to the Steering Committee for the audit and certification process. QAWG works to ensure that EWQA processes meet or exceed international standards for public health water microbiology laboratories.

PROVINCIAL COORDINATOR

Shelley Tiffin, 2008-2009
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STEERING COMMITTEE MEMBERS

Dr. Judy Isaac-Renton (Chair)
Barry Boettger
Tim Crowther
Joe Fung
Dr. Mike Noble
Judy Smith

HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

AUDITOR WORKSHOPS

Annual workshops for auditors have been well received. In 2009, an expert from the Canadian Standards Association (CSA) facilitated the workshop for the auditors from private, municipal and public laboratories province-wide, identifying potential improvements to the auditing process and comparing the EWQA model with the International Organization for Standardization (ISO) 19011 model.

INSPECTIONS

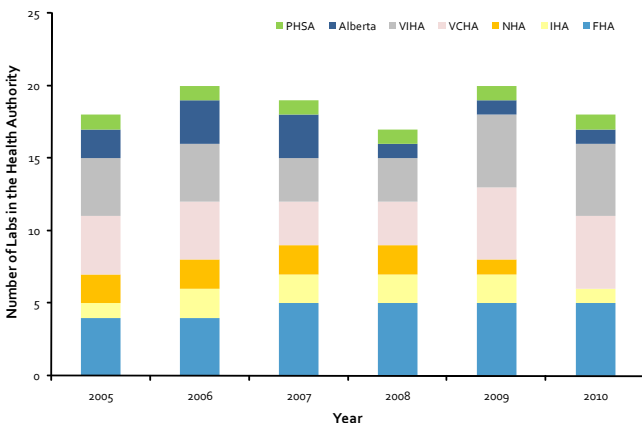
Over the 3 years, on-site inspections of 20 environmental laboratories (private, municipal and public) were carried out to meet legislated requirements (Table 2). Recommendations regarding certification were made to the PHO with necessary follow up detailed. EWQA staff review all External Quality Assurance PT.

Table 2. Inspections performed over 2008 to 2010. The inspection schedule for certification occurs over 3 years. The number of certified labs has remained between 15 and 17 while the number of auditors has increased to 15.

Year	No. Inspections	No. Auditors	No. Labs
2008	4	8	16
2009	13	15	17
2010	3	15	15

PHO APPROVED LABORATORIES

There are PHO-approved laboratories in all of BC's HAs (Figures 7 and 8). Each laboratory must successfully provide evidence to EWQA through ongoing review of PT sample testing results. External QA PT is regularly reviewed by the EWQA Technical Quality Team with reporting to the EWQA Coordinator.



CERTIFICATION UPDATE

Development of a new mid-cycle assessment has extended the period of EWQA approval certification from 2 to 3 years. A new mid-cycle questionnaire and process were developed and continue to be refined. Other improvements are underway to improve EWQA process TATs and to create efficiencies.

DISTANCE EDUCATION AND COMMUNICATIONS

A Drinking Water Distance Education module is being discussed by the Steering Committee and academic partners. Lectures explaining the microbiological bases for water quality monitoring have been developed. Ongoing, regular drinking water testing communications are carried out by EWQA including quarterly bulletins and newsletters to educate and inform the community of practice. An Annual Report is submitted to the PHO.

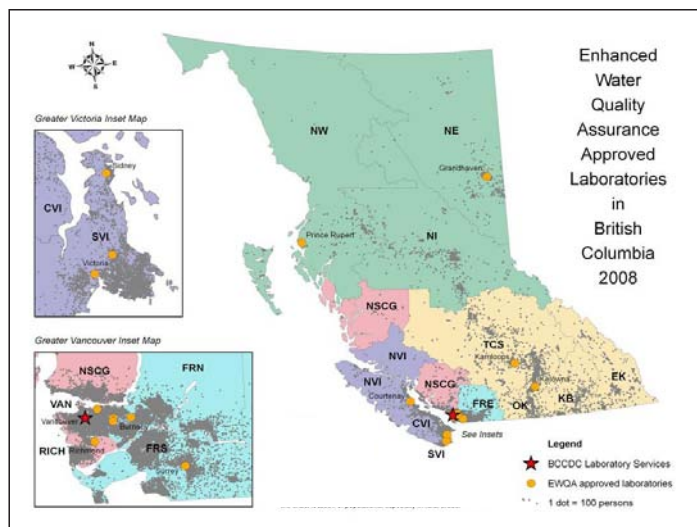


Figure 8. EWQA approved laboratories in BC, 2008.

Figure 7. EWQA approved labs by Health Authority from 2005-2010. PHTSA=Provincial Health Services Authority, VIHA=Vancouver Island Health Authority, VCHA=Vancouver Coastal Health Authority, NHA=Northern Health Authority, IHA=Interior Health Authority, FHA=Fraser Health Authority.



HIGH-VOLUME SEROLOGY

In addition to a pre-analytical receiving and triaging as the PHMRL's "front end", the CPR Program also partners with staff in the High-Volume Viral Serology Program to provide more efficient testing in a "pull" system of "one-piece flow" (an imPROVE or Lean term for directional operations with no waste). The Program continues to provide high-volume viral serology for clients province-wide including testing for HIV, hepatitis, rubella, and other viruses as well as prenatal microbiological screening. Other tests include state-of-the-art serological testing for measles, mumps, Epstein-Barr virus, parvovirus, cytomegalovirus and varicella. High volumes (more than 2000 samples per day) mean operational efficiencies are essential. This area continues to apply Lean principles through several PHSA imPROVE events to enhance quality and TATs while maintaining accuracy and safety.

For visitors to this area, it is unlike all other Programs with its intense focus on automation. Staff members manage to test thousands of different blood samples each day by directing robotics and machines so they can focus their expertise on specialized reference samples and quality-related activities.

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HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

IMPROVE (LEAN) PROJECTS

The Team participated in three *kaizen* (rapid improvement) events within this Value Stream. The projects were:

- Improvement of specimen flow through the pre-analytical gross sort area (May 2009)
- Quality control set-up for Centaurs (October 2009)
- One-piece flow for confirmatory samples and (hepatitis) HBe tests (June 2010)

These events were highly successful with improvements such as: marked decrease in TATs, more automation, application of a continuous sample volume flow using the First In First Out (FIFO) concept, implementing instrument maintenance at off-peak times, and greater non-technical staff utilization.

OUTBREAK INVESTIGATION AND IMPROVEMENTS

Using IgM / IgG serology, the Team investigated specimens for the 2008 mumps virus, 2010 measles virus and 2010 rubella virus outbreaks. To improve testing during the 2008 mumps outbreak, an interdisciplinary team of epidemiologists, virologists, occupational health workers and public health workers was organized and chaired by PICNet. This team focused on health care worker protection including evaluating immunization records. The success of this project led to expansion to include measles and rubella. Results of this review included a revision of provincial guidelines for managing health care workers during mumps and measles outbreaks (found at www.picnetbc.ca). Serological screening of health care workers with incomplete or non-existent vaccination records also required much coordination and increased testing demand for the Program.

ACUTE HIV PROJECT

Current HIV (antibody) screening tests are unable to identify newly infected individuals because HIV antibodies do not appear until several weeks into the infection. In a study funded by the Canadian Institutes of Health Research (CIHR), CPR is investigating the application of enhanced screening technologies and protocols to better assess acute HIV infection, including use of molecular assays on pooled samples. Specimens that test negative by the standard 3rd generation HIV antibody screening test are pooled in groups of 24 and an HIV nucleic acid test is performed. Evaluation of the 4th Generation Antigen/Antibody HIV assay is also ongoing using the highly automated robotics and assaying employed by this Team.

CRITICAL TESTS

Emergency tests provided by this program include:

- HAV IgM for outbreaks and acute cases
- HIV screening as well as confirmatory testing for suspect acute HIV cases
- Measles, mumps and rubella IgM testing
- Varicella IgG (pregnancy) testing
- STAT needlestick testing
- STAT organ transplant testing

Positive results are reported by telephone to the physician and MHO.



PARASITOLOGY

Detection and identification of a wide spectrum of helminths and protozoans still requires highly trained specialists using diverse tests such as microscopy, immunology, and culture. Recent work on molecular methods has improved the diagnosis of malaria and *Acanthamoeba* infections. The laboratory performs reference level characterization of blood and tissue parasites, highly pathogenic intestinal parasites, and medically important ectoparasites. The Team leads the province's West Nile virus (WNV) surveillance, identifying vectors for subsequent WNV PCR identification.

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HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

WNV VECTORS

The first mosquito pools in BC carrying WNV were identified by the Parasitology Team in August 2009. This work requires a high degree of processing efficiency combined with entomological expertise as thousands of pools of insect vectors pour in from all across BC. Ticks as vectors of such infections as Lyme disease are also identified by experts in this Program.

NEW AMOEBIASIS ASSAY

Amoebiasis is a rare but potentially serious infection; routine ova and parasite examination cannot distinguish between pathogenic and non-pathogenic species. A new stool antigen assay, the TechLab® E. HISTOLYTICA test, was validated and implemented as a useful supplemental test for differentiating between pathogenic *Entamoeba histolytica* (amoebiasis) and non-pathogenic *Entamoeba dispar*.

MALARIA SPECIATION

The Program supports province-wide malaria reference level best practices standardization. In 2008, 32 cases of malaria were identified; fewer cases were seen in 2009 (23) while 2010 saw an increase to 29 cases (Table 3). Working with the Molecular Microbiology & Genomics Team, a molecular (PCR) QA assay was implemented for speciation. This molecular test is also now used when infective agents have been difficult to speciate (significant patient treatment cases). A new PCR assay for the identification of *Plasmodium knowlesi*, a rare, bird-source parasite, was also developed and implemented as a QA tool for malaria testing.

Table 3. Incidence of *Acanthamoeba*, *Leishmania* and malaria, 2008- 2010.

Year	Positive cases (Total samples tested)		
	<i>Acanthamoeba</i>	<i>Leishmania</i>	<i>Plasmodium</i> spp.
2008	0 (13)	2 (4)	32 (222)
2009	2 (23)	2 (6)	23 (179)
2010	5 (22)	1 (15)	29 (162)

ACANTHAMOEBA MOLECULAR ASSAY

The Team worked with ophthalmologists, epidemiologists, and parasitologists to investigate cases of *Acanthamoeba* ocular infections. In 2005 and 2006 the laboratory isolated an increased number of *Acanthamoeba* (Figure 9). Further parasite strain characterization by sequencing/genotyping of *Acanthamoeba* isolates from culture is underway to understand if this is due to a single clone.

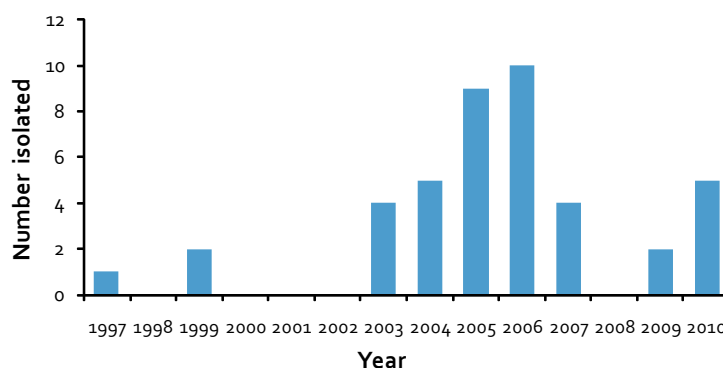


Figure 9. *Acanthamoeba* isolations, 1997-2010.

TOXOPLASMA GONDII PCR

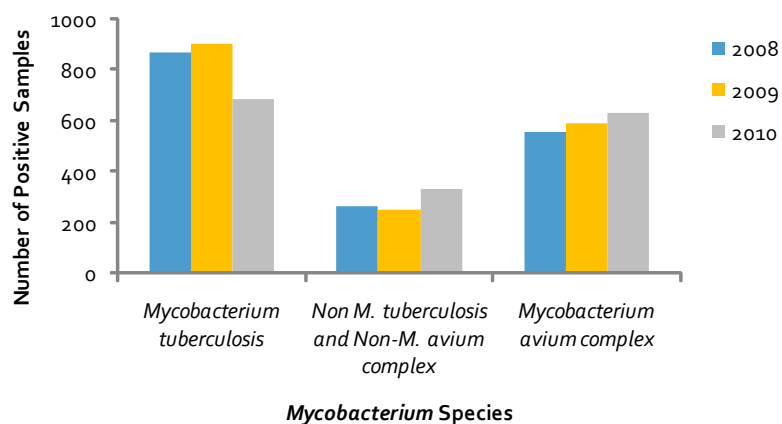
Toxoplasmosis is a systemic parasite disease that can be life threatening or the cause of serious congenital disease. A PCR method for detecting *Toxoplasma gondii* was developed with ongoing validation underway for use in medically approved cases.

TEACHING ACTIVITIES

The Program provides teaching and education for staff in other BC laboratories, as well as public health workers and undergraduate and post-graduate medical trainees. Co-op students are trained in WNV surveillance.

CRITICAL TESTS

- Positive parasite cultures of *Leishmania*, *Trypanosoma*, *Naegleria* and *Acanthamoeba*
- Possible cases of *Strongyloides* and other invasive helminthes
- Response for *Acanthamoeba* ocular invasion using parasite culture and molecular genotyping
- Province-wide STAT on-call support for possible cases of malaria.



TB/MYCOBACTERIOLOGY

The TB/Mycobacteriology Team provides diagnostic services including decontamination (to improve recovery of the slow-growing bacteria) followed by smear preparation, staining and examining acid-fast smears; molecular species identification of smear positive samples; mycobacterial cultures; identification of isolated mycobacterial organisms by nucleic acid (molecular) methods; isolate genotyping; and performance of antimicrobial susceptibility tests. This laboratory also provides mycobacteriology reference services and consultations for the province, participating in surveillance and outbreak/cluster identification using molecular fingerprinting methods. Team members provide leadership through national TB networks and are committed to public health research and training for mycobacteriology.

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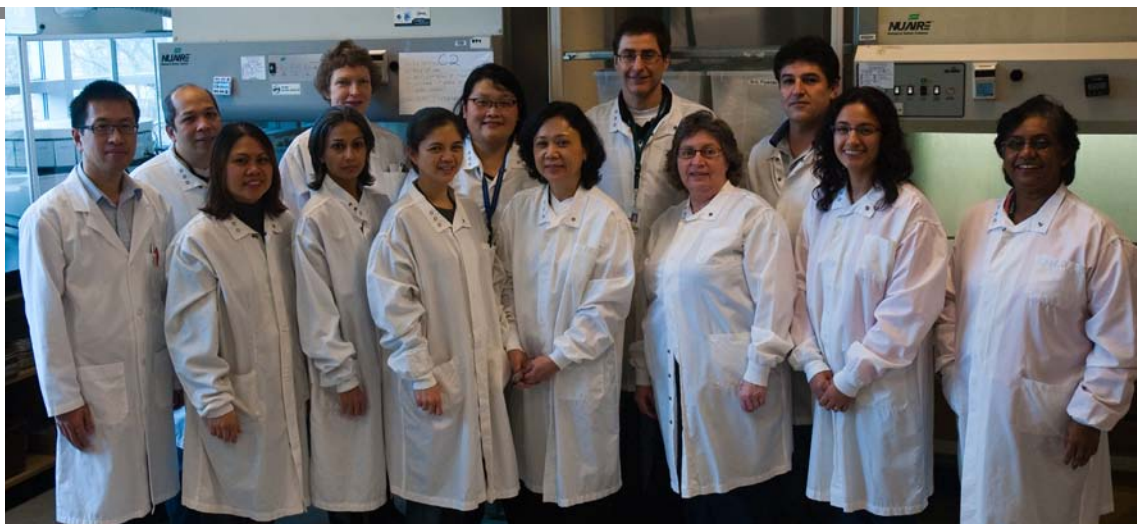
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HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

MOLECULAR ASSAYS

Working with the Core Functions Molecular Microbiology & Genomics Program, a faster and cheaper molecular assay for the identification of *Mycobacterium tuberculosis* was developed, validated and implemented in 2009. This PCR-based test was also exported to the PHC microbiology laboratory. Increased frequency of testing for all new positive *M. tuberculosis* isolates was implemented in 2010. Molecular fingerprinting on site is under development.

LEAN IMPROVEMENT EVENTS

Two PHSA imPROVE (Lean) initiatives were carried out in 2010 with workshops that focused on optimizing pre-analytical processes and improving work flow for molecular testing capacity. A new TB qPCR test is now performed daily (versus twice weekly), reducing TATs as measured from sample receipt to result reporting (Figure 10).

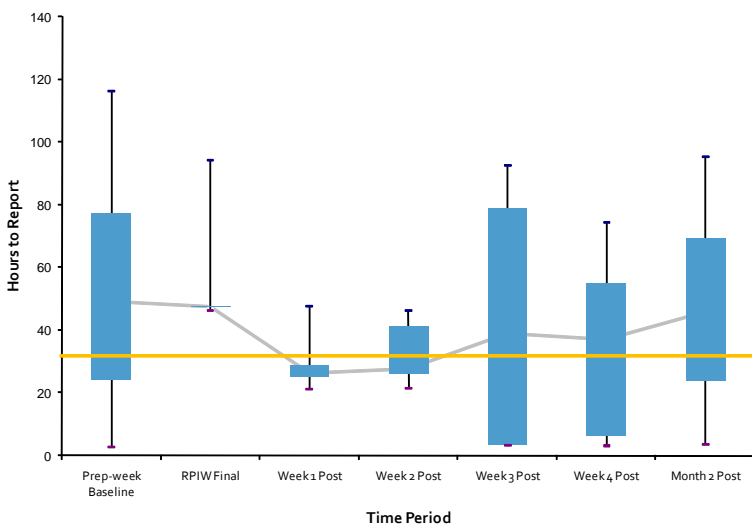


Figure 10. Molecular testing reporting time audits as the result of the 2009 imPROVE project. The red line indicates the target of 33.6hrs for the reporting of molecular results.

NEW PCR TEST

The Molecular Microbiology & Genomics Program has worked with the TB Team to introduce a new quantitative PCR (qPCR) assay that replaces the more labour intensive Amplified *Mycobacterium tuberculosis* Detection (AMTD) Kit by GenProbe. The new qPCR test is now performed Monday to Friday and improves TAT for molecular detection of smear-positive sputum samples, i.e., those with acid-fast bacilli (AFB) present.

TB NETWORK NEWS

The TB Laboratory has ongoing collaborations with the Canadian Tuberculosis Laboratory Technical Network Group and the CPHLN. The group is updating the TB section of PHAC's Laboratory Biosafety Guidelines. Another key project is the impact on TB testing of the federal HPTA.

TB OUTBREAKS

A team of communicable disease nurses, MHOs, members of BCCDC TB Control and TB laboratory experts worked together in 2010 to integrate clinical and laboratory data for the investigation of two large TB outbreaks in BC. The laboratory investigated using whole genome sequencing methods, targeted nucleic acid assays, and genotyping. In one outbreak, a novel pattern of transmission was uncovered using new microbiology laboratory genomic tools, allowing public health officials to better understand the root cause of the outbreak. The second outbreak is still under investigation and has the potential to yield new insights into the development and transmission of antibiotic resistant TB, again through use of novel microbial genomic tools.

HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

PROVINCIAL TB POLICY

This Program actively participates in the development of provincial policies related to TB such as the creation of BC's Strategic Plan for the Prevention of Tuberculosis. Recently both the TB and Zoonotic Diseases and Emerging Pathogens (ZEP) Programs (Interferon-Gamma Release Assay testing) participated in strategic planning with public health workers from BC's HAs.

NEW LIQUID CULTURE SYSTEM

In 2008, the TB Laboratory switched its liquid culture system from BioMerieux MB BacT/Alert to the Becton-Dickinson BACTEC Mycobacterium Growth Indicator Tube (MGIT) system. The laboratory now participates in USA Food and Drug Administration (FDA)-approved second line antibiotic susceptibility testing along with other public health reference laboratories in Canada.

TB SUSCEPTIBILITY TESTING

The TB/Mycobacteriology Laboratory is responsible for all susceptibility testing for *M. tuberculosis* in BC. Results show that susceptibility rates to anti-TB drugs have been relatively stable over the past 10 years (Figure 11). Reports on anti-tuberculosis therapeutic agents such as isoniazid are compiled and provided to BCCDC TB Control as a part of ongoing, national surveillance.

TEACHING ACTIVITIES

The Program provides teaching and education for staff in other BC laboratories, as well as public health workers and undergraduate and post-graduate medical trainees.

CRITICAL TESTS

The following results are considered critical and are reported immediately to physicians, TB Control and other clients.

- AFB-positive smears on new patients
- Positive cultures pending identification where the smear result was not positive
- Positive Mycobacteria cultures on new patients
- ANY Mycobacterial positive culture from cerebral spinal fluid (CSF) or blood samples

TB Drug Resistance in British Columbia, 2000-2010

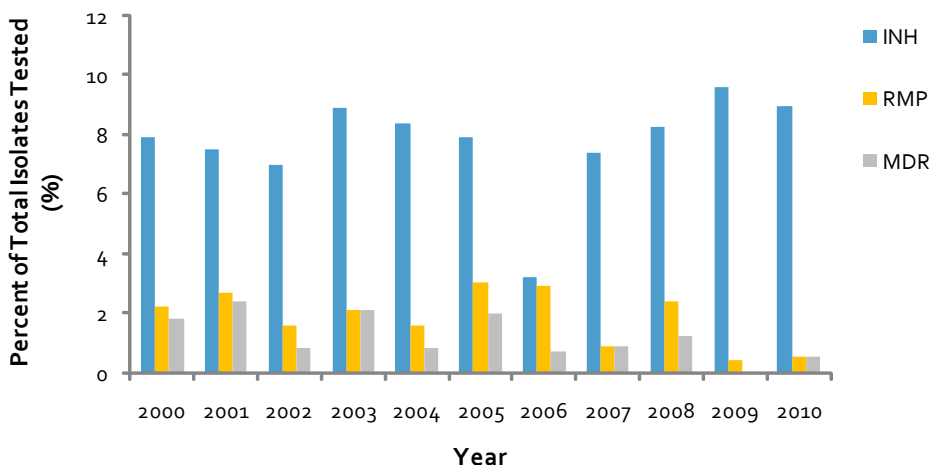


Figure 11. Susceptibility of *M. tuberculosis* isolates to anti-TB drugs, 2000-2010. INH=isoniazid, RMP=rifampin, MDR=multi-drug resistance.



VIROLOGY

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

Additional roles in outbreak detection and management include enterovirus and vaccine-preventable diseases such as measles, mumps and rubella. Molecular tests for hepatitis, herpes virus group, pox viruses, severe acute respiratory syndrome (SARS), varicella zoster, and WNV are also performed. The Program provides province-wide leadership, with national and international linkages including expertise in development of the national framework for pandemic influenza testing through the Pandemic Influenza Laboratory Preparedness Network (PILPN) of CPHLN.

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HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

PANDEMIC H1N1 INFLUENZA

The 2009 pandemic influenza H1N1 outbreak illustrated a rapid, integrated, highly complementary team approach to the emergence of the novel respiratory virus involving the Molecular Microbiology & Genomics Team, the Surveillance & Outbreaks Team, the BBBC Team and the PHMRL Leadership Team. New molecular approaches were created in record time (over a weekend) using data shared by CDC. Concentrated support and effort of the entire PHMRL responded to unprecedented volumes of respiratory samples (Figure 12). The emergence of the novel virus in BC prompted the use of high-throughput equipment and a new duplex detection and subtyping RT-PCR assay. The Virology Team, supported by the whole PHMRL staff, was formally recognized by the BC PHO for its outstanding work in the response to this event. shared by CDC.

IMPROVED MEASLES AND MUMPS TESTING

Molecular testing was developed, validated, and implemented for these important public health events. RT-PCR assays for mumps and measles viruses on buccal swabs or in urine specimens allow faster, more accurate investigation, enhancing outbreak management for the 2008 and 2010 mumps outbreak and 2010 measles outbreaks. Partnership with the NML included genotyping services.

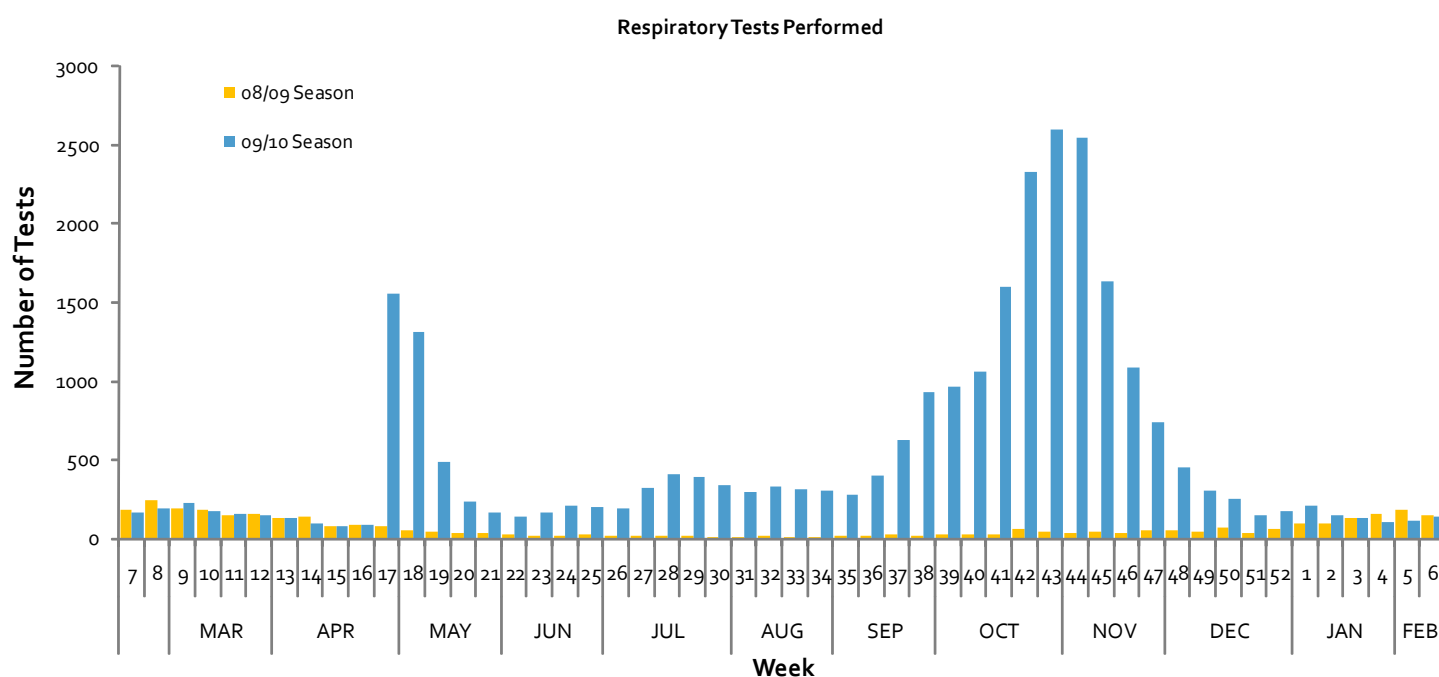


Figure 12. Numbers of respiratory tests performed for the 2009/2010 season. The H1N1 outbreak came in two waves in 2009 – late April and late October.

HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

MUMPS VIRUS DETECTION BY PCR AND CULTURE DURING AN OUTBREAK IN AN UNVACCINATED POPULATION

A multidisciplinary team carried out an investigation and analysis of mumps virus detection via PCR and culture during a 2008 outbreak. The study addressed conflicting information regarding the isolation period following mumps infection. Identified were 180 cases of mumps, with most cases confirmed by laboratory testing or strong epidemiological links. Nearly half of the cases were unvaccinated. During the outbreak, PHMRL High Volume Serology staff and Virology staff used serology and PCR or cell culture. Serology was the most common test performed, although it was found to be less sensitive than PCR. Due to less than 100% sensitivity, this assay cannot be used to rule out mumps and PCR is now recommended as part of testing. Virus detection was highest immediately after the onset of parotitis, but could be detected up to 9 days after (see Figure 13), suggesting that a 5-day isolation period may not be sufficient to control spread of the infection.

NEW HERPES AND VARICELLA-ZOSTER ASSAYS

A new, multiplex PCR assay for detecting the herpes simplex 1 and 2 and varicella zoster viruses was developed, validated, and implemented in 2010. This new assay replaces culture, increases sensitivity of viral detection, decreases TAT and improves efficiency of laboratory testing. It also uncovered previously undetected and misdiagnosed cases of herpes zoster (shingles) infections that had been considered to be genital herpes simplex.

NEW PCR ASSAYS

Human enterovirus (HEV) infections are the leading cause of aseptic meningitis. Conventionally, enteroviruses have been diagnosed by isolation in cell culture but a new RT-PCR assay (targeting the highly conserved region within the 5' non-translated region of the virus) for the detection of enteroviruses from CSF and other clinical samples has been developed, validated, and implemented for routine use in order to improve sensitivity and TAT.

CRITICAL TESTS

The following tests are considered critical for this Program:

- Outbreak test results for respiratory viruses (detection and characterization)
- Herpes viruses diagnosed in CSF
- Results from STAT organ transplant testing
- Mumps and measles diagnosed by RT-PCR

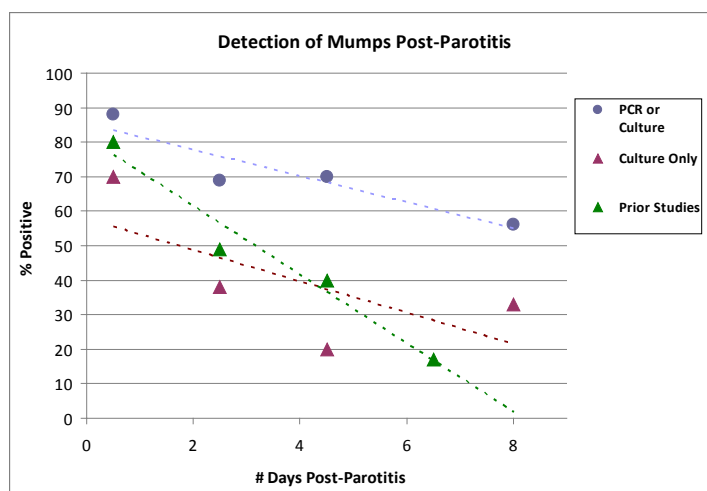


Figure 13. Proportion of positive mumps by either PCR or cell culture over time. The curve is hypothesized to be a negative log curve, but the study's data fits a linear trend.

The Prior Studies curve is from the meta-data based on cell culture that CDC Atlanta used to help create their guidelines.



ZOONOTIC DISEASES & EMERGING PATHOGENS

The ZEP Team provides testing and consultation services for vector-borne, zoonotic and emerging and/or re-emerging diseases of public health importance. The laboratory employs a variety of techniques including antibody testing for bacterial, parasitic, fungal and viral agents. High volume testing includes syphilis (acute cases and pre-natal screening) and *Helicobacter pylori*. Also provided are tests for Lyme disease, *Toxoplasma*, *Cryptococcus*, *Bartonella*, West Nile, Dengue virus, and Group A Streptococcal infections (Antistreptolysin O). The laboratory acts as the reference centre for many infectious diseases such as Hantavirus, *Legionella*, relapsing fever and other parasitic and rickettsial pathogens. It is a recognized national leader, collaborating with NML and CDC in spirochaetal diseases such as Lyme disease and syphilis. Recently, Interferon-Gamma Release Assay (IGRA), a cell-mediated immune response serological assay for latent TB was validated then implemented. The ZEP Team leads the province-wide IGRA testing program including training and QA support for regional laboratory nodes

PROGRAM HEAD

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CONTACT

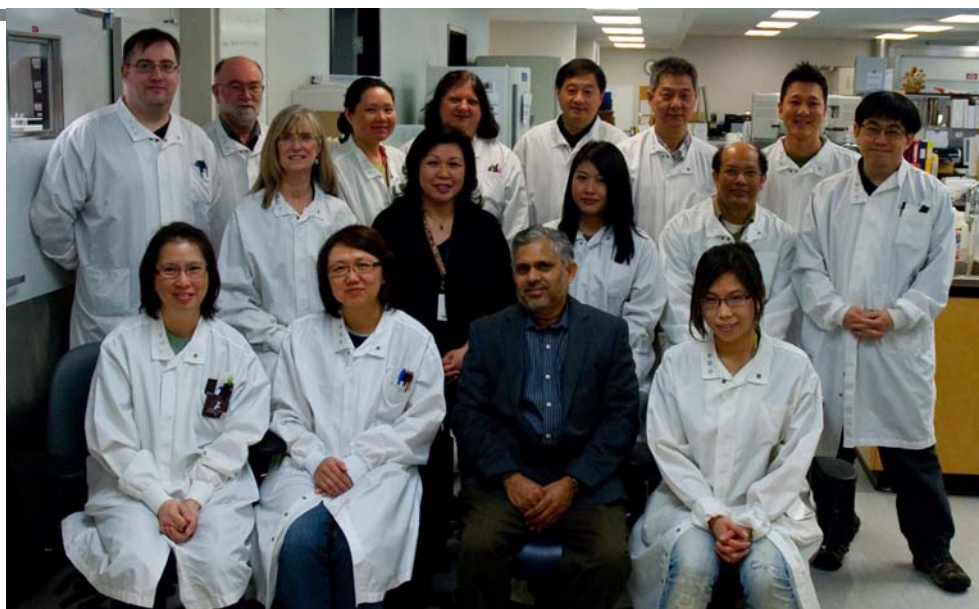
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HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

WEST NILE VIRUS

WNV was first detected in BC in August 2009. The first human case was detected by the ZEP Team using immunological methods. Positive mosquito pools from the South Okanagan area (Interior Health Authority) were also detected by the ZEP Team in collaboration with the Parasitology Program using nucleic acid amplification methods. The ZEP Program continues to partner with Parasitology at PHMRL and public health in select HAs in surveillance of WNV for the province.

INTERFERON-GAMMA RELEASE ASSAY

The tuberculin skin test (TST) has traditionally been the sole diagnostic tool for latent TB, often leading to false positive and false negative results. It also requires at least two patient visits to health care providers. In 2009, the ZEP Program implemented the IGRA, a more effective blood test for latent TB. IGRA results, while continuing to be studied as to optimal interpretation and application to various patient populations (e.g., the immunocompromised) are more specific, more sensitive, and more cost-effective than TST alone. Experts in the ZEP Program provided HA staff training to allow implementation of IGRA specimen collection and transport. IGRA is now available to defined high risk groups for several HAs, and on special request. Studies are underway with PHC (use of IGRA in immunocompromised hosts such as renal dialysis patients), with BCCDC TB Control and with public health in HAs.

CRYPTOCOCCUS GATTII

Using newly developed and validated genetic fingerprinting tools, the slow spread of *Cryptococcus gattii*, an emerging fungal agent, continues to be documented. A new molecular fingerprinting method, Multi-Locus Sequence Testing (MLST) was developed by ZEP experts and is proving to be more effective for speciation than phenotypic methods. Further work related to the genomes of these unique pathogens is ongoing.

LYME SPIROCHETE MOVING TO THE NORTH

The Team discovered *Borrelia burgdorferi* infections in *Ixodes* ticks near Hazelton, BC. Lyme disease, although not yet a significant health risk in BC, continues to be under intense surveillance. In 2008, an *Ixodes angustus* tick and serum from a dog bitten in Hazelton were submitted for analysis. BSK-II media was used to culture and isolate the *Borrelia* spirochetes from the mid-gut region of the tick with spirochetes confirmed using darkfield microscopy followed by PCR. Dog serum revealed positive serology against anti-*Borrelia burgdorferi* antibodies. The lack of travel history suggested a locally-acquired infection and in comparison to previous findings (Figure 14), this is the most northern infection identified to date. More surveillance data are needed to understand the distribution of this tick-borne disease in northern latitudes.

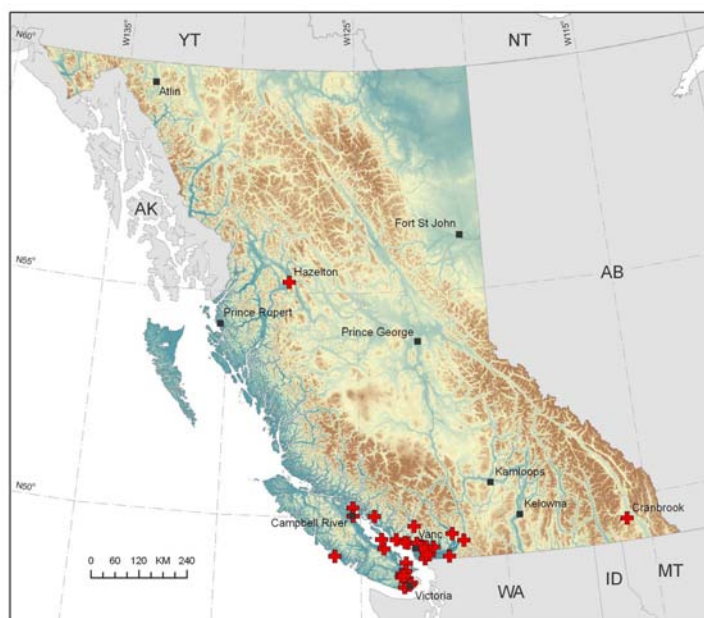


Figure 14. Distribution map for *Borrelia* spp. positive ticks and mice tested between 1993 and 2008. The positive isolate is highlighted in red. The Hazelton case is the first positive tick vector reported at the latitude of 55 degrees north in BC.

HIGHLIGHTS FOR THIS PROGRAM INCLUDE:

NEW ASSAY DEVELOPMENT

Test improvements in this program include a new serological test for *Bartonella*, MLST for *Cryptococcus*, an improved fluorescent treponemal antibody (FTA) test for syphilis, and a semi-automated platform for Antistreptolysin O testing. A syphilis point-of-care test and PCR for syphilitic lesions were evaluated with public health partners across BC for possible use in challenging and difficult-to-reach high-risk populations.

TEACHING ACTIVITIES

Education activities include training of HA technical staff in collecting, processing and transporting samples for IGRA testing, annual training of co-op students for WNV surveillance, and annual workshops for medical residents. Staff members also supervised PhD students working on Dengue virus and WNV topics and taught medical and Bachelor of Medical Laboratory Science (BMLSc) undergraduate students.

CRITICAL TESTS

The following tests are considered critical for this Program with results telephoned to clients:

- Prenatal syphilis RPR and confirmatory testing
- Syphilis dark field, DFA, RPR and confirmatory testing
- Prenatal toxoplasmosis IgG and IgM reactives
- WNV serology IgG and IgM reactives

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ABBREVIATIONS & ACRONYMS

AFB	Acid-Fast Bacilli	LIS	Laboratory Information System
AMTD	Amplified <i>Mycobacterium tuberculosis</i> Detection	LLTO	Laboratory Liaison Technical Officer
BAM	Bacteriology & Mycology	LOINC	Logical Observations Identifiers Names and Codes
BBBC	Biosafety Biosecurity Biohazard Containment	MARS	Measles and Rubella Surveillance
BC	British Columbia	MGIT	Mycobacterium Growth Indicator Tube
BCAMM	BC Association of Medical Microbiologists	MHO	Medical Health Officer
BCCDC	BC Centre for Disease Control	MLST	Multi-Locus Sequence Typing
BCPHLN	BC Public Health Laboratory Network	MOA	Memorandum of Agreement
BMLSc	Bachelor of Medical Laboratory Science	MOHS	Ministry of Health Services
CAP	College of American Pathologists	MPHRL	Microbiology for Public Health Laboratories
CDC	Centers for Disease Control and Prevention	MRSA	Methicillin-Resistant <i>Staphylococcus aureus</i>
CDI	<i>Clostridium difficile</i> Infection	NAT	Nucleic Acid Test
CGF	Comparative Genomic Fingerprinting	NESP	National Enteric Surveillance Program
CFIA	Canadian Food Inspection Agency	NDM	New Delhi Metallo-beta-lactamase
CIHR	Canadian Institutes of Health Research	NML	National Microbiology Laboratory
CL ₂	Containment Level 2	PCR	Polymerase Chain Reaction
CL ₃	Containment Level 3	PFGE	Pulsed Field Gel Electrophoresis
CLRN	Canadian Laboratory Response Network	PHAC	Public Health Agency of Canada
CNPHI	Canadian Network for Public Health Intelligence	PHC	Providence Health Care
CPHLN	Canadian Public Health Laboratory Network	PHLD	Public Health Laboratory Director
CPR	Central Processing & Receiving	PHLN	Public Health Laboratory Network
CSA	Canadian Standards Association	PHMRL	Public Health Microbiology & Reference Laboratory
CSF	Cerebrospinal Fluid	PHO	Provincial Health Officer
DAP	Diagnostic Accreditation Program	PHSA	Provincial Health Services Authority
DFA	Direct Fluorescent Antibody	PICNet	Provincial Infection Control Network
DNA	Deoxyribonucleic Acid	PILPN	Pandemic Influenza Laboratory Preparedness Network
ELISA	Enzyme-Linked Immunosorbent Assay	PLIS	Provincial Laboratory Information Solution
EM	Environmental Microbiology	PSLS	Patient Safety & Learning System
ERAP	Emergency Response Assistance Program	PT	proficiency testing
EWQA	Enhanced Water Quality Assurance	PVL	Panton-Valentine Leukocidin
FDA	Food and Drug Administration	QA	Quality Assurance
FIFO	First In First Out	QAWG	Quality Assurance Working Group
FHA	Fraser Health Authority	QMRA	Quantitative Microbial Risk Assessment
FTA	Fluorescent Treponemal Antibody	qPCR	Quantitative Polymerase Chain Reaction
GI	Gastrointestinal	RCD	Reportable Communicable Disease
HA	Health Authority	RPR	Rapid Plasma Reagin
HEV	Human Enterovirus	RT-PCR	Reverse Transcriptase Polymerase Chain Reaction
HIV	Human Immunodeficiency Virus	SARS	Severe Acute Respiratory Syndrome
HAV	Hepatitis A Virus	TB	Tuberculosis
HPTA	Human Pathogens and Toxins Act	TAT	Turn-Around Time
IQA	Internal Quality Audit	TPPA	<i>Treponema pallidum</i> Particle Agglutination Assay
IgG	Immunoglobulin G	TST	Tuberculin Skin Test
IgM	Immunoglobulin M	UBC	University of British Columbia
IGRA	Interferon-Gamma Release Assay	WNV	West Nile Virus
IM	Information Management	ZEP	Zoonotic Diseases & Emerging Pathogens
IQA	Internal Quality Audit		
ISO	International Organization for Standardization		
LIA	Line Immunoassay		



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