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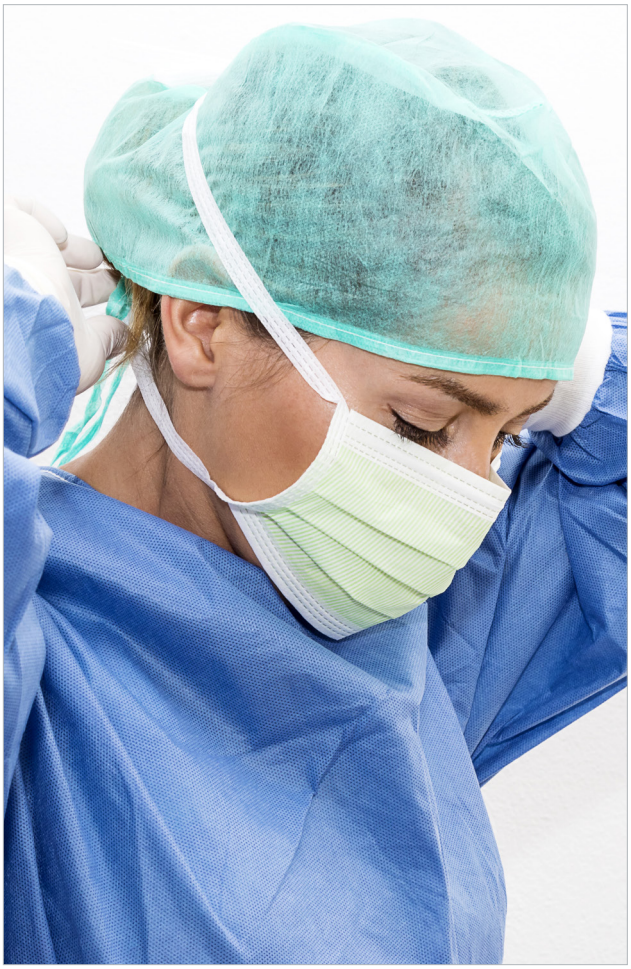
CANADA COMMUNICABLE DISEASE REPORT

HEALTHCARE-ASSOCIATED INFECTIONS AND ANTIMICROBIAL RESISTANCE



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CANADA COMMUNICABLE DISEASE REPORT

The *Canada Communicable Disease Report* (CCDR) is a bilingual, peer-reviewed, open-access, online scientific journal published by the Public Health Agency of Canada (PHAC). It provides timely, authoritative and practical information on infectious diseases to clinicians, public health professionals, and policy-makers to inform policy, program development and practice.

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This is a photo of a healthcare professional donning protective gear, highlighting that infection control procedures are as important as ever with the growing threat posed by antimicrobial resistance. Photo by Shutterstock (https://www.shutterstock.com/image-photo/surgeon-putting-mask-492074263).

Contact the Editorial Office

phac.ccdr-rmtc.aspc@canada.ca

613.301.9930

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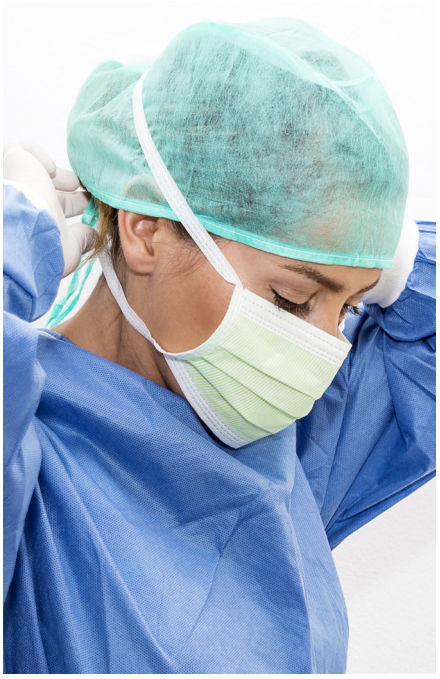

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OVERVIEW

Something wicked this way comes: What health care providers need to know about *Candida auris*

IS Schwartz[1]*, SW Smith[1], TC Dingle[2,3]

Abstract

Candida auris is a fungal pathogen that recently emerged and rapidly spread around the globe. It is now in Canada. *C. auris* can cause invasive disease with high mortality rates, is frequently resistant to one or more classes of antifungals, and can be difficult to identify in some clinical microbiology laboratories. *C. auris* can also involve prolonged colonization of patients' skin and contamination of surrounding environments, resulting in nosocomial outbreaks in hospitals and long-term care facilities.

Clinicians, infection prevention and control practitioners and public health officials should be aware of how to mitigate the threat posed by this pathogen. Index cases of *C. auris* should be suspected in patients with invasive candidiasis and recent hospitalization in global regions where *C. auris* is prevalent, as well as in patients who fail to respond to empiric antifungal therapy and from whom unidentified or unusual Candida species have been isolated. If a case of *C. auris* infection or colonization is identified or suspected, the following should take place: notification of local public health authorities and infection prevention and control practitioners; placement of colonized or infected patients in single rooms with routine contact precautions; daily and terminal environmental disinfection with a sporicidal agent; contact tracing and screening for *C. auris* transmission; and referral of suspicious or confirmed isolates to provincial laboratories. Patients with symptomatic disease should be treated with an echinocandin pending the results of antifungal susceptibility testing, preferably in consultation with an infectious disease specialist. Through the vigilance of front-line health care workers and microbiologists, robust infection prevention and control practices, and local and national surveillance efforts, *C. auris* can be detected quickly, infections managed and transmissions prevented to protect patients in our health care system.

Affiliations

[1] Division of Infectious Diseases, Department of Medicine, University of Alberta, Edmonton, AB

[2] Division of Diagnostic and Applied Microbiology, Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB

[3] Provincial Laboratory for Public Health, Edmonton, AB

***Correspondence:**
ilan@ualberta.ca

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Keywords: *Candida auris*, candidemia, fungal infections, mycology, antifungal resistance, multidrug resistance, diagnosis, nosocomial, infection prevention and control

Introduction

In July 2017, the first known case of multidrug-resistant *Candida auris* was reported in Canada in an individual who had a two-year history of recurrent ear complaints after returning from a trip to India that was marred by hospitalization for a brain abscess following oral surgery (1). This marked the arrival in Canada of a pathogen that has recently been spreading across the globe. The ability of this fungus to cause invasive disease, its frequent resistance to one or more classes of antifungal agents and its demonstrated potential for nosocomial transmission is of concern to clinicians and public health professionals alike (2,3).

The objective of this article is to summarize what we know about this fungus; outline the challenges of diagnosis, treatment and infection prevention and control, and identify what is being done to track and contain the spread of this pathogen in Canada.

Where in the world is *C. auris*?

C. auris was first described in Japan in 2009; since then, *C. auris* infections have been reported in at least 30 countries

on six continents (4). Whole-genome sequence analyses of global isolates have demonstrated that these cluster into closely related (clonal) geographic clades (5) suggesting the near-simultaneous emergence of *C. auris* on at least three continents. For example, the average genetic distances between the East Asian, South Asian, South African and South American clades were 40,000 to 140,000 single nucleotide polymorphisms (SNPs), whereas on average, fewer than 70 SNPs separated any two isolates within a given clade (3). The reasons for this phenomenon are unknown.

In some countries, *C. auris* has already led to a significant burden of hospital-acquired disease. For example, *C. auris* is the cause of candidemia in 10% of cases nationally in South Africa (6), and 38% of cases in one referral hospital in Kenya (*Okinda N et al. Candidemia at a referral hospital in sub-Saharan Africa: emergence of Candida auris as a major pathogen. Poster presented at: European Congress of Clinical Microbiology and Infectious Diseases; 2014 May 10–13; Barcelona, Spain*). In India, *C. auris* was implicated in 5% of candidemia cases in 27 intensive care units (ICUs), although some Indian centres report proportions of 17.5%–30% (7,8). As of July 31, 2018, the Centers for Disease Control and Prevention (CDC) in the United States (US) reported 361 confirmed clinical cases of *C. auris* in US health care settings; an additional 699 colonized patients were diagnosed in four states with active surveillance (4). In Europe, at least 120 cases of candidemia and 466 cases of colonization occurred from 2013 to 2017 (9).

In Canada, the first two patients reported to be infected with *C. auris* had received health care in India (1,10). In one case, genomic characterization suggested that the infection was imported from the Indian subcontinent (11). Additional imported cases are anticipated. Transmission in Canadian health care facilities is inevitable.

What are clinical features of disease caused by *C. auris*?

The clinical spectrum of *C. auris* infection ranges from asymptomatic colonization to invasive candidiasis, most commonly in the form of healthcare–associated candidemia (12). Bloodstream infections can be protracted and difficult to treat, and crude mortality rates of approximately 30%–60% have been reported (5,13,14). Metastatic complications, such as spondylodiscitis, endocarditis and ventriculitis, have been described (13). Other frequently reported clinical syndromes include otomycosis and otomastoiditis (15,16): in fact, the etymology of the fungus reflects the anatomic origin of the first identified isolate, which was collected from a patient's ear (17). Involvement of other sites, including respiratory, urogenital, abdominal, and skin and soft tissue, has also been reported (18).

Who becomes infected by *C. auris* and how?

Patients who develop candidemia caused by *C. auris* usually have risk factors in common with patients with disease caused by other Candida species (6,13,14,19). These include hospitalization and, in particular, admission to an ICU, use of central venous catheters, abdominal surgery and exposure to broad-spectrum antibiotics or antifungals (20).

There are several ways in which the pathogenesis of *C. auris* appears to differ from classically encountered Candida species (**Table 1**) (21). With the exception of *C. parapsilosis*, a skin colonizer, the majority of clinically important non-*auris Candida* species are commensals of the human gastrointestinal tract (21). The pathogenesis of candidemia caused by these species typically involves gut translocation of yeasts (21,22); although nosocomial transmission of Candida is occasionally reported, disease is most commonly caused by strains that are part of the patient's endogenous flora (23).

Table 1: Differences between *Candida auris* and classical pathogenic Candida species

Feature	*Candida auris*	Classical Candida species[a]
Habitat	Commensal of the skin	Commensals of the gastrointestinal tract[b]
Pathogenesis of infection	Exogenous	Endogenous
Healthcare–associated infections	Common	Uncommon
Environmental contamination	Common	Uncommon
Multidrug resistance	Common	Uncommon

[a] Other Candida species most commonly encountered clinically include *C. albicans*, *C. glabrata*, *C. parapsilosis*, *C. krusei* and *C. tropicalis*
[b] With exception of *C. parapsilosis*, which is a commensal of skin

C. auris is primarily carried on the skin of colonized patients, and this can lead to contamination of the patient's environment and spread to health care workers and other patients. Moreover, *C. auris* isolates implicated in healthcare–associated outbreaks have been clonally related, suggesting disease is caused by exogenous strains that are nosocomially spread (5,13,24,25).

What are the diagnostic challenges?

C. auris can be difficult to detect by routine laboratory testing. This may lead to delays in identifying and isolating colonized or infected patients. Commercial biochemical identification systems commonly used in clinical microbiology laboratories are unreliable for *C. auris* identification (26). For example, *C. auris* can be misidentified by VITEK-2 (bioMérieux, Marcy-l'Étoile,

France) (typically as *C. haemulonii*) (26) and by API20CAUX (usually as *Rhodotorula glutinis*, *C. sake* or *Saccharomyces cerevisiae*) (27). This may change as biochemical identification system databases are updated; for example, VITEK-2 YST card v. 8.01 now includes *C. auris*.

C. auris can be identified accurately using matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry instruments with databases that include *C. auris* (these include the most recent Bruker MALDI Biotyper CA and Research Use Only [RUO] databases, and the bioMérieux VITEK MS RUO database [v4.14 with *Saccharomycetales* package]) and by molecular-based sequencing methods.

What are the treatment challenges?

In general, *C. auris* isolates are less susceptible to antifungals than other Candida species, although patterns of susceptibility appear to be related to the geographic clade. Resistance to fluconazole is widespread, albeit not universal as was initially feared (2), and fluconazole resistance is now thought to be an acquired rather than a shared trait (21). Rates of fluconazole resistance have ranged from 14% among isolates from Colombia (25) to >90% among isolates belonging to the South Asian clade (14,28). Resistance to amphotericin B and the echinocandins also appear to be heterogeneous. Several studies have found amphotericin B resistance rates around 30% (5,14,25); alternatively, Chowdhary et al. reported amphotericin B resistance in 27/350 (8%) of Indian isolates (28). Significant variation in rates of amphotericin B resistance were encountered between regions in Columbia (25). Echinocandin resistance occurs in approximately 2%–5% of isolates (5,28,29). Resistance to two antifungal classes occurred in 41% of global isolates tested (5). In rare cases, isolates can be resistant to all three major classes of antifungal agents (5).

What are the challenges in infection prevention and control?

Nosocomial outbreaks are anticipated because patients can remain colonized and/or their environments can remain contaminated for weeks to months after infection (14,24,25,30). Large-scale hospital outbreaks in the United Kingdom (UK) have been associated with multi-use axillary thermometers (31); and in Spain with the use of blood-pressure cuffs (31). Moreover, *C. auris* has been recovered from a wide range of fomites from patient environments (13,14,24,25). Surface cationic-active disinfectants and quaternary ammonium disinfectants are ineffective against *C. auris* (13,33,34). *C. auris* is also relatively resistant to killing by ultraviolet light (35). Chlorhexidine gluconate, iodinated povidone, chlorine bleach and H_2O_2 vapour appear to be effective against *C. auris* (36).

The role of health care workers in spreading *C. auris* is still unknown. During investigation of the outbreak in the UK, *C. auris* was isolated from the nares of 1/258 health care workers, a nurse who was providing care for a patient who was heavily colonized (24). Moreover, an outbreak investigation in Colombia isolated *C. auris* from the hands of two health care workers and the groin of one out of six health care workers. Whole-genome sequencing established that these were genetically identical to strains isolated from a patient and his or her environment (25).

Tracking and containing *C. auris* can be particularly challenging due to interfacility transfer of infected or colonized patients in whom this status may not yet be recognized, potentiating spread of *C. auris* between facilities (14). For example, in New York, 112 patients in hospitals and long-term care facilities were affected: 61 had candidemia and 51 additional patients were found to be colonized on screening. Infected or colonized patients were transferred between a total of 24 hospitals and 24 long-term care facilities in the 90 days before their infection or colonization status was recognized (14).

Implications for clinical care

The prompt identification, management and containment of patients infected or colonized with *C. auris* require collaboration by hospitalists/intensivists, microbiologists, infectious disease experts, and infection control and prevention practitioners.

Clinicians should be aware of the yeast identification methods used by their local microbiology laboratory and consider *C. auris* when unidentified or unusual Candida species are isolated from patients who fail to respond to empiric antifungal therapy (37). Consultation with a microbiologist is recommended when *C. auris* is suspected. Isolates that are suspicious for or confirmed as *C. auris* should be referred to provincial laboratories for further testing. Given the challenges in predicting antifungal susceptibility patterns, antifungal susceptibility testing is recommended for all clinical *C. auris* isolates. Treatment of disease should be guided by antifungal susceptibility testing results, although echinocandins are appropriate for empiric therapy pending these results. Early consultation with an infectious disease expert is advised. Treatment of asymptomatic colonization is not recommended.

The identification of patients in whom infection or colonization with *C. auris* is suspected or confirmed should prompt consultation with local infection prevention and control practitioners. Infected or colonized patients should be isolated in private rooms; routine practices and contact precautions should be taken; and rooms should be cleaned daily with sporicidal disinfectants. Whether and when to discontinue isolation precautions is still being debated. The CDC currently recommends that infected or colonized patients be tested periodically with composite groin and axillary swabs for fungal culture to test for persistent colonization, with the proviso that

patients can be de-isolated after two consecutive negative screening swabs (38). In practice, few reported patients have met such criteria (14). Alternatively, Public Health England recommends that isolation precautions be continued for the duration of a patient's admission to hospital (39). This recommendation is in part because patients can become re-colonized after testing negative (*Silke Schelenz, "Management of Candida auris outbreaks at a national level". 20th Congress of the International Society for Human and Animal Mycology, Amsterdam, The Netherlands July 2018).*

Table 2 shows a summary of how to detect, assess and manage *C. auris*. Further infection prevention and control guidelines are available from the CDC (39).

Table 2: What to do to detect and manage *Candida auris*

What to do	How
Keep a high index of suspicion	Consider *C. auris* in patients who: • received health care in countries (or US states) where *C. auris* is prevalent, as tracked by the CDC (4) • have a clinical syndrome consistent with candidiasis and fail to respond to empiric antifungal therapy and from whom an atypical or unidentified yeast is isolated
Assess for *C. auris* specifically	Consult with a microbiologist and/or infectious disease specialist Refer suspicious or confirmed isolates to relevant provincial laboratory for further testing or for referral to the National Microbiology Laboratory
Manage *C. auris* with a robust clinical infection control and public health response	Notify the institutional infection prevention and control team Notify local public health officials, who will notify their provincial/territorial counterparts (who will notify the Public Health Agency of Canada) Place patient in single room with contact precautions in addition to routine practices In case of symptomatic disease, begin treatment, preferably with guidance from an infectious disease specialist (treatment of asymptomatic colonization is not recommended) Order daily and terminal cleaning of the patient's environment with sporicidal disinfectant Enable local public health officials to initiate contact tracing and screening to assess for *C. auris* transmission Order composite swab of axilla and groin when indicated for patient screening

Abbreviations: *C. auris, Candida auris*; CDC, Centers for Disease Control and Prevention; US, United States

Gaps and next steps

Many questions remain unanswered about how to best detect *C. auris* and limit its spread within and between Canadian health care facilities. Knowledge gaps regarding the optimal laboratory detection and identification of *C. auris* should be addressed by bolstering existing biochemical and MALDI-TOF identification databases and by developing simple, rapid and sensitive laboratory screening protocols. Uncertainties that affect infection prevention and control practices for *C. auris* include the duration that patients remain colonized (and thus how long patients should be isolated after first detection) and optimal screening strategies. For example, should screening be reserved for patients with documented contact with a known case or used for all patients who have travelled to or received health care in areas where *C. auris* is prevalent? Because the geographic distribution of *C. auris* will change over time, and in light of incomplete surveillance data from many regions, identifying patients at high risk for colonization can be challenging for front-line health care workers.

To better understand the epidemiology of *C. auris* in Canada, the Canadian Nosocomial Infection Surveillance Program is conducting national surveillance for infections in representative hospitals across the country. (*Garcia Jeldes F, Mitchell R, Bharat A, McGeer A for the CNISP C. auris Interest Group. Preparedness for Candida auris in Canadian Nosocomial Infection Surveillance Program [CNISP] Hospitals, 2018. IDWeek 2018. October 3–7, 2018. San Francisco, California*). In addition, a point prevalence study is planned to identify the prevalence of both colonization and infection in Canadian tertiary care hospitals (*Dr. Allison McGeer, September 2018, personal communication*). The surveillance and point prevalence data will provide evidence needed to guide the development of infection prevention and control policies surrounding this emerging pathogen.

Conflict of Interest

None.

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Canada Communicable Disease Report
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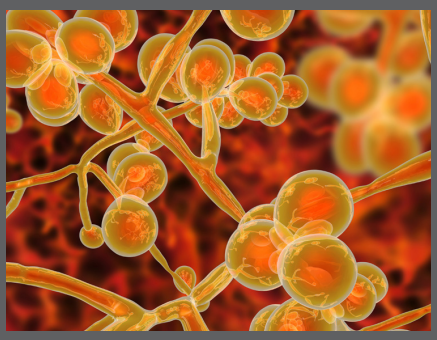
VISUAL ABSTRACT

CANDIDA AURIS WHAT HEALTH CARE PROVIDERS NEED TO KNOW

C. auris is an emerging multidrug resistant fungus

It is now in Canada

- can cause invasive disease
- is difficult to detect
- can spread easily in health care environments



Who is at risk?

Those who don't respond to antifungal therapy and have a history of:

- travel-associated healthcare
- a lab result with unidentified/ unusual candida species
- a central venous line
- abdominal surgery
- exposure to broad-spectrum antibiotics or antifungals

Best Practices

Transfer the patient to a private room and consult:

- infectious disease specialist
- infection prevention and control
- public health

Reference: Schwartz IS, Smith SW, Dingle TC. Something wicked this way comes: What health care providers need to know about *Candida auris*. Can Commun Dis Rep 2018;44(11):271-6. https://doi.org/10.14745/ccdr.v44i11a01

OVERVIEW

Bringing home unwelcome souvenirs: Travel and drug-resistant bacteria

BJ Langford[1,2], KL Schwartz[1,2,3]*

Abstract

Antimicrobial resistance poses a significant threat to public health globally and in Canada. Wide regional variability in antimicrobial resistance and ongoing increases in global travel present an important risk for the acquisition and transmission of drug-resistant organisms. Travel from high-income to low- and middle-income countries, particularly the Indian subcontinent, present the greatest risks for acquiring a drug-resistant Enterobacteriaceae. Risk factors for returning from travel with drug-resistant organisms include seeking medical care while abroad, travellers' diarrhea and antibiotic use. Health care professionals can play an important role in preventing harm for travellers by counselling patients on the risks of acquiring drug-resistant organisms, appropriate antibiotic prescribing for travellers' diarrhea and tailored empiric therapy for patients presenting with infection after travel.

Affiliations

[1] Public Health Ontario, Toronto, ON

[2] St. Joseph's Health Centre, Toronto, ON

[3] Dalla Lana School of Public Health, Toronto, ON

***Correspondence:**
kevin.schwartz@oahpp.ca

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Keywords: antimicrobial resistance, travel, antimicrobial stewardship, infection prevention and control, medical tourism

Introduction

Antimicrobial resistance (AMR) is a growing problem globally. It is identified as one of the most significant public health threats of our time. In the absence of meaningful intervention, it is estimated that deaths from drug-resistant infections will increase from 700,000 to 10 million annually by 2050, surpassing current cancer rates as the number one cause of death (1). Moreover, the prevalence of drug-resistant organisms across the globe varies widely. For example, resistance of *Escherichia coli* to third-generation cephalosporins is much more common in India, at 78%, than in Canada, at 9% (2).

In this global society, AMR knows no borders. In 2017, the number of passengers using air travel exceeded four billion for the first time; this number is forecast to double by 2036 (3).

One of the big challenges of AMR with respect to travel is infections from drug-resistant Enterobacteriaceae. Enterobacteriaceae are a large family of gram-negative bacilli that can cause a wide range of infections including those affecting the urinary, respiratory and gastrointestinal tracts. Organisms in this family include *E. coli*, Klebsiella species, Enterobacter species and Salmonella species. A key mechanism of Enterobacteriaceae antibiotic resistance is the development of beta-lactamase and carbapenemase enzymes, which hydrolyze beta-lactam antibiotics, rendering them ineffective. Genes for these enzymes are commonly encoded by plasmids, which can transfer between bacterial organisms. Key groups of Enterobacteriaceae resistance are extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-PE), and carbapenem-resistant Enterobacteriaceae (CRE). Of growing importance is the plasmid-mediated colistin-resistance gene *mcr-1*. The ability of bacteria to transfer antimicrobial resistant genes to one another via plasmids poses significant infection control challenges. A rise in Enterobacteriaceae resistance translates to more infection-related mortalities, longer hospital stays and increased costs to the health care system (4,5).

The objective of this article is to describe the clinically relevant risk of drug-resistant organisms associated with travel, with a focus on Enterobacteriaceae. For the purposes of this review, travel is defined as movement of people travelling to low- and middle-income countries in Asia, Africa and the Americas, and returning to high-income countries such as Australia, Canada, New Zealand, United States (US) and those in Europe.

What is the risk of bringing home drug-resistant bacteria after travel?

The studies on the risk of travellers acquiring either ESBL-PE or CRE are sobering and have important considerations to the management of patients in Canada.

Extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-PE)

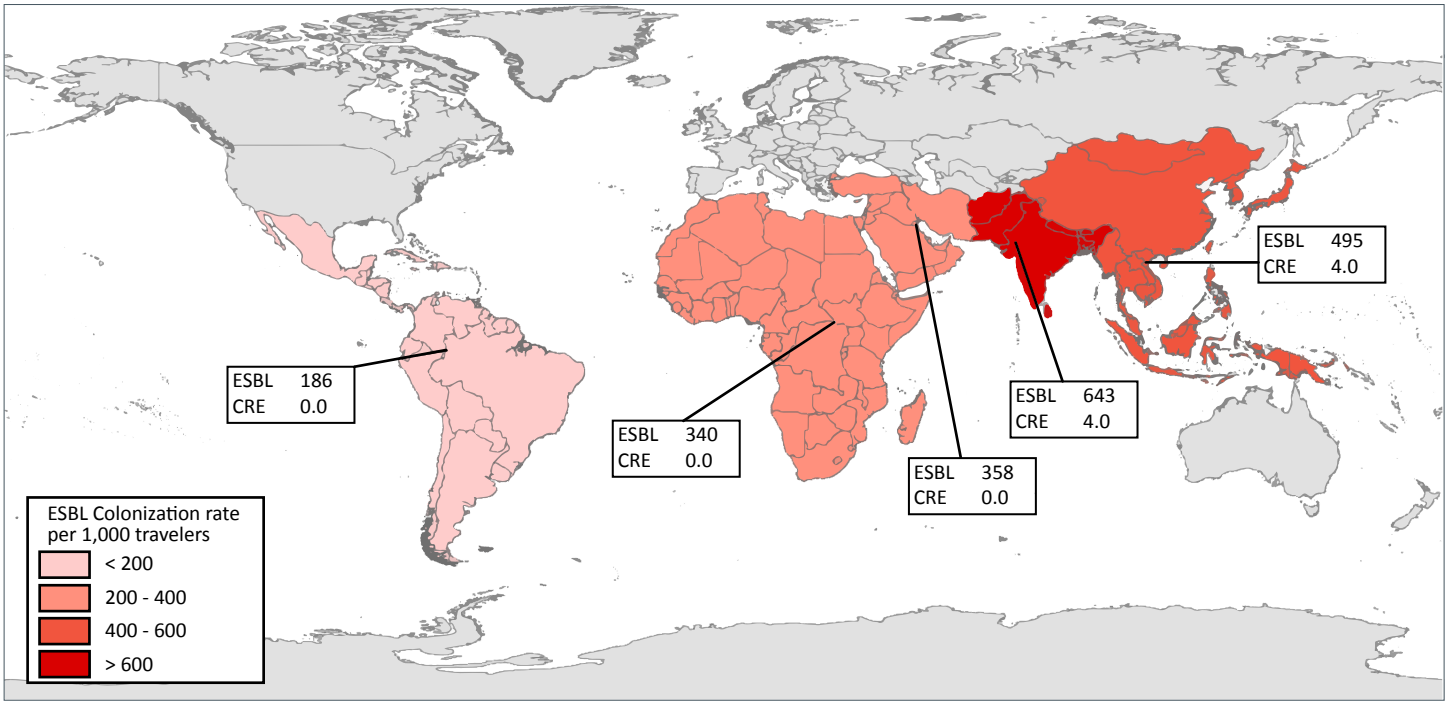
One of the largest studies to evaluate the risk of acquiring a drug-resistant organism during travel focused on the importation of ESBL-PE to the Netherlands. Through a longitudinal cohort study of 2001 travellers, the authors determined the likelihood of ESBL-PE colonization before and after the travel period. Of those individuals who did not have an ESBL-PE prior to travel, 34% acquired an ESBL-PE while abroad (6). There was marked variability in the risk of ESBL-PE colonization associated with the region visited. Travel to southern Asia presented the highest risk, at 75% incidence of colonization, followed by central and eastern Asia (49%), western Asia (43%), southeastern Asia (37%), the Caribbean and Central America (28%), middle and eastern Africa (28%), western Africa (19%), South America (18%) and southern Africa (6%). The median duration of colonization after travel was 30 days (95% confidence interval [CI]: 29–33 days). However, 11.3% remained colonized after 12 months, highlighting the importance of identifying an individual's travel history within the previous year. Multiple other smaller studies have also evaluated the risk of ESBL-PE acquisition while travelling (7). The average risk of ESBL-PE colonization after travel is 643 per 1,000 travellers from the Indian subcontinent, 340 per 1,000 travellers from Africa and 186 per 1,000 travellers from Central and South America (**Figure 1**). Although the majority of studies focus on the risk of colonization with drug-resistant organisms, recent travel has been associated with an increased risk of ESBL-PE urinary tract infections (8–11) and bacteremia with ESBL-PE post-transrectal prostate biopsy (12).

Carbapenem-resistant Enterobacteriacae (CRE)

CRE infections, which have also been increasing around the world, are of particular concern due to the limited treatment options and the high infection-related mortality rates of 40% to 70% (13,14). The three main classes of carbapenemase-producing Enterobacteriaceae that confer carbapenem resistance have distinct regional epidemiology (15):

- *Klebsiella pneumoniae* carbapenemase (KPC) is the most common carbapenemase-producing Enterobacteriaceae in North America
- OXA-48-like carbapenemases are typical in Turkey and surrounding regions
- New Delhi Metallo-beta-lactamase-1 (NDM-1) was initially associated with those who had received medical care in the Indian subcontinent, but has since been reported in every continent (16)

Figure 1: The number of extended spectrum beta-lactamase (ESBL) producing and carbapenem-resistant Enterobacteriaceae (CRE) per 1,000 travellers by region visited



Abbreviations: CRE, carbapenem-resistant Enterobacteriaceae; ESBL, extended-spectrum beta-lactamase; <, inferior to; >, superior to
Note: Data for the figure derived from weighted average of published studies. Figure modified with permission from Schwartz & Morris (7)

The Canadian Nosocomial Infection Surveillance Program (CNISP) recently characterized carbapenemase-producing Enterobacteriaceae reported in hospitals across Canada from 2010 to 2014. The incidence was 0.07 cases per 1,000 admissions, with KPC and NDM-1 being the most common. Many of those affected had a history of international travel. India was the most common travel destination with 31% of cases reporting travel to that country within the previous 12 months (17). However, the risk of acquiring a CRE while travelling is considerably lower than the risk of acquiring an ESBL-PE (Figure 1).

Colistin-resistance gene, *mcr-1*

Of further concern is the recently described plasmid-mediated colistin resistance gene *mcr-1* which can be co-located with other gram-negative resistance mechanisms. Colistin is one of few antibiotic options for managing CRE; however, it carries significant risk of nephrotoxicity and neurotoxicity. Initially discovered in animal and human clinical isolates in China, *mcr-1* has now been reported in clinical isolates globally (18). A recent Dutch study found that 5% of long-distance travellers had *mcr-1* in fecal samples. These travellers had primarily visited southeast Asia or southern Africa (19).

Travel is also playing a role in the spread of other drug-resistant bacterial organisms such as *Salmonella*, *Shigella* and *Campylobacter* species, which has been reviewed elsewhere (7).

What are the risk factors for acquiring drug-resistant organisms while travelling?

Health care exposure

Recent health care exposure abroad has been noted as a risk factor for acquiring a drug-resistant organism. In the CNISP evaluation of Canadian patients with CRE, of those with a travel history available, 86% had sought medical care abroad (17). The association between health care exposure while travelling and drug-resistant organisms has also been observed in a number of European studies (20–27). Among those returning home after being hospitalized abroad, colonization with any multidrug-resistant organism (MDRO) ranged from 7% (21) to 29% (23). In these studies, MDROs were defined as ESBL-PE, CRE, other multidrug-resistant gram-negative organisms, methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus*. The greatest risk was for patients who were transferred directly or repatriated from hospitals abroad compared to those not directly repatriated (odds ratio [OR]=7.4; 95% CI: 2.1–25.2) (27). Other risk factors include a longer hospital stay abroad (20,21); history of a surgical procedure abroad (22); admission to a high-risk unit (i.e. intensive care unit) (21); tropical or subtropical country visited (particularly South Asia) (21,24); and receipt of antibiotics while hospitalized (21–23).

Although these studies included travellers with either an elective or emergent reason for hospitalization, this risk is likely applicable to medical tourists, that is, those who travel abroad for the specific purpose of accessing medical care (28). Global estimates indicate that there are about four million medical tourists annually (29); a Canadian survey indicates that over 63,000 patients sought medical care abroad in 2016 (30). Most Canadian medical tourists seek care in the US, followed by low- and middle-income countries in the Americas and Asia (31), which includes regions with elevated rates of drug-resistance. Given the risk of acquiring drug-resistant organisms while travelling, particularly for individuals who access health care systems abroad, this poses an important and often underestimated risk for those who are considering medical tourism.

Travellers' diarrhea

Travellers' diarrhea is caused by ingesting contaminated food or beverages containing bacterial enteropathogens (32). Depending on the travel location and host factors, the incidence of diarrhea during travel can range from 10% to 40%. In several studies of travellers acquiring drug-resistant organisms abroad, travellers' diarrhea was noted as a significant risk factor, particularly for acquiring an ESBL-PE. Travellers' diarrhea is associated with an approximate 2- to 3-fold increased risk of acquiring an ESBL-PE abroad (6,33,34). In a study of Finnish travellers, this risk of acquiring an ESBL-PE was 11% in those without travellers' diarrhea, 21% in those with travellers' diarrhea who did not take antibiotics and 37% in those with travellers' diarrhea who were treated with antibiotics (33).

Antibiotic exposure

Antibiotics apply selective pressure to the native organisms colonizing the gut, increasing the risk that drug-resistant organisms contracted abroad are incorporated into the microbiome. Treatment with antibiotics has been repeatedly demonstrated to present a risk to travellers. In the previously mentioned Dutch study of travellers who acquired ESBL-PEs abroad, antibiotic use was associated with a greater than 2-fold risk of acquiring these drug-resistant organisms (OR=2.7; 95% CI: 1.8–4.0) (6). In a Finnish study, 21% of those who received no treatment, 20% of those treated with the anti-diarrheal medication loperamide alone, 40% of those treated with antibiotics alone and 71% of those treated with both loperamide and antibiotics became colonized with ESBL-PE (35).

Among travellers hospitalized abroad, the risk associated with antibiotic treatment was also pronounced, with an 11-fold higher risk of being colonized with an MDRO (OR=10.7; 95% CI: 4.2–27.3) compared to those who did not travel abroad; however, being hospitalized abroad and not receiving an antibiotic was not a risk factor for MDRO colonization in this study (26). The importance of antibiotic exposure during a travel-associated hospitalization is echoed in a large study in Finland, where risk of colonization with an MDRO was significantly increased in those receiving antibiotics (OR=3.2;

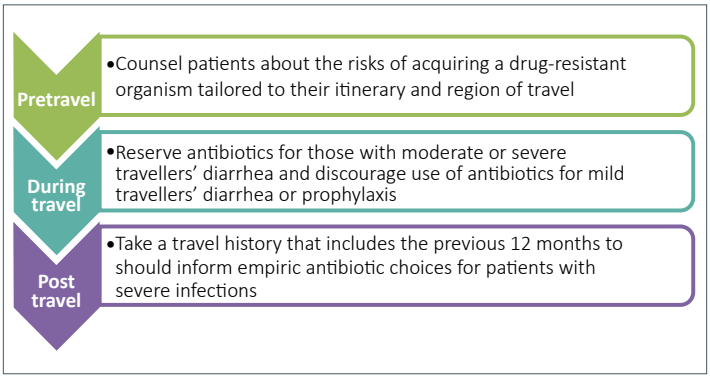
95% CI: 2.3–4.5) (23). Similarly, a study in the Netherlands found a 2.5- to 3.4-fold increased risk of gram-positive MDRO colonization in those who had been treated with antibiotics while hospitalized abroad (20).

What can clinicians do to minimize harm in Canadian travellers?

By understanding the risk of AMR associated with travel, health care professionals will be better able to implement approaches to improve management and reduce transmission of drug-resistant organisms as well as educate the public to make informed decisions (**Figure 2**). Opportunities for clinicians include:

- Counselling patients, pretravel, on the risk of acquiring a drug-resistant organism, tailored to the patient's itinerary and specific region of travel (Figure 1)
- Counselling patients on the risks of unplanned health care exposure abroad; minimizing the risk through pretravel immunizations and counselling on how to prevent travellers' diarrhea and avoid high risk activities
- Counselling patients on the risks of medical tourism, tailored to the patient's itinerary and specific region of travel (Figure 1)
- When considering a prescription for anticipatory travellers' diarrhea prior to travel, given the risk of acquiring an ESBL-PE, understanding that recent guidelines encourage supportive care only for mild travellers' diarrhea and that antibiotic prophylaxis for travellers' diarrhea is indicated only in select patients at high risk for complications (36); and
- Considering recent travel (within the past 12 months) when selecting empirical antimicrobial therapy for patients who have a severe infection (patients who have travelled to Asia, particularly the Indian subcontinent, should be considered at very high risk for drug-resistant Enterobacteriaceae)

Figure 2: Opportunities to manage risk of acquiring drug-resistant organisms from travelling



Conclusion

Travelling abroad carries a significant risk for acquiring a drug-resistant organism. Asia and the Indian subcontinent in particular present the greatest risks for acquiring an ESBL-PE or CRE. Medical care, travellers' diarrhea and antibiotic use abroad further increase the risks for travellers. Health care professionals can play an important role in reducing the risk for travellers through counselling, appropriate antibiotic prescribing and tailored empirical therapy for patients presenting with severe infections who have travelled recently.

Conflict of interest

None.

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Canada Communicable Disease Report
CCDR
VISUAL ABSTRACT

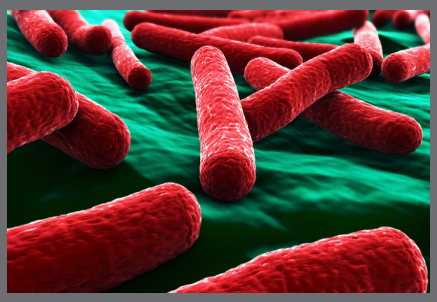
GLOBAL TRAVEL INCREASES RISK OF EXPOSURE TO DRUG-RESISTANT BACTERIA

WHAT is the risk?

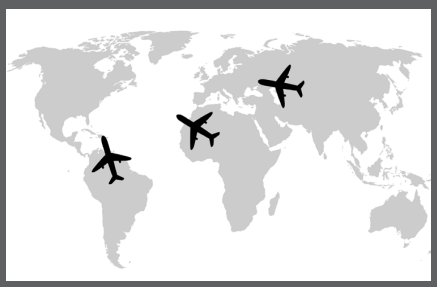
The most common is resistant Enterobacteriacea that can cause:

- travellers' diarrhea
- bronchitis/pneumonia
- urinary tract infections

Travellers may also become a carrier and pass it on to others



WHERE is the risk?



Highest Risk:

- Asia, especially the south

Also in:

- Africa and the Middle East
- The Caribbean and Central America
- South America

Best practices

Ask about travel in the past year

- especially in those with an infection unresponsive to antibiotics

Educate patients regarding:

- risk areas, hand hygiene and safe food practices
- symptomatic treatment of mild diarrhea
- minimal use of healthcare services

Reference: Langford BJ, Schwartz KL. Bringing home unwelcome souvenirs: Travel and drug-resistant bacteria. Can Commun Dis Rep 2018;44(11):277–82. https://doi.org/10.14745/ccdr.v44i11a02

The National Advisory Committee on Infection Prevention and Control (NAC-IPC)

T Ogunremi[1]*, K Dunn[1], L Johnston[2], J Embree[3], on behalf of the National Advisory Committee on Infection Prevention and Control (NAC-IPC)

Abstract

This paper describes the work of the National Advisory Committee on Infection Prevention and Control (NAC-IPC), previously Infection Prevention and Control Expert Working Group, a longstanding external advisory body that provides subject matter expertise and advice to the Public Health Agency of Canada (PHAC) on the prevention and control of infectious diseases in Canadian health care settings. Originally established by Health Canada as the Infection Control Guidelines Steering Committee in 1992, this advisory board has been providing expert advice on infection prevention and control (IPC) guideline development for over 25 years.

The NAC-IPC provides advice to inform the development of comprehensive or concise guidelines, quick reference guides and interim guidelines (usually for emerging pathogens), working closely with PHAC's national Healthcare-Associated Infections (HAIs) surveillance programs for Canadian health care facilities. PHAC's HAI-IPC professionals conduct the necessary literature research, data extraction, evidence synthesis, evidence grading (where applicable) and scientific writing for the guidelines. Due to the paucity of clinical trials and high quality observational studies to inform recommendations for emerging pathogens, expert opinion is critical for interpreting available evidence.

Affiliations

[1] Centre for Communicable Diseases and Infection Control, Public Health Agency of Canada, Ottawa, ON

[2] Dalhousie University, Halifax, NS

[3] University of Manitoba, Winnipeg, MB

Note: Committee members are noted at the end of the paper

***Correspondence:** phac.ipc.secretariat-pci.aspc@canada.ca

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Keywords: Infection prevention and control, advisory committee, evidence-based guidelines, healthcare-associated infections, infectious disease

Introduction

Global infectious disease threats call for international knowledge exchange and a national coordinated response. Since its inception in 2004, the Public Health Agency of Canada (PHAC) has provided national leadership in response to public health threats using an evidence-based approach that employs scientific excellence and relevant expert advice from external advisory bodies. These external advisory bodies provide PHAC with the means to involve individuals outside of government, who have valuable knowledge and expertise in the Agency's national guideline development process.

External advisory bodies are established to assist PHAC in developing guidance on specific medical, scientific, technical, policy or program matters within the scope of the Agency's mandate (1). Well-known external advisory bodies to PHAC include the National Advisory Committee on Immunization (NACI) and the Committee to Advise on Tropical Medicine (CATMAT) (2,3). This article describes the work of the National Advisory Committee on Infection Prevention and Control (NAC-IPC).

Background

Health Canada established the original Infection Control Guidelines Steering Committee in 1992. This committee played a key role during the SARS outbreak in 2003, and began reporting to PHAC following the creation of the Agency in 2004. Its name was changed to the Infection Prevention and Control Expert Working Group in 2011. Earlier in 2018, the decision was made to transition this expert working group to an external advisory body. This transition resulted in the name change to NAC-IPC and a change in the reporting structure. Previously reporting to PHAC through the Program Director, the NAC-IPC now reports to the Vice President of the Infectious Disease Prevention and Control Branch. The Committee's mandate and function remain the same.

The transition of NAC-IPC from an expert working group to an external advisory body complies with PHAC's policy and directive for such committees (1). The resulting change in the committee reporting structure will strengthen NAC-IPC's links with provincial and territorial partners through the Council of Chief Medical Officers of Health. Such links are particularly valuable during an emergency event, where the timely uptake of newly released Healthcare-Associated Infection-Infection Prevention and Control (HAI-IPC) guidelines and statements is critical. Examples of such work in the past include the provision of timely public health, scientific and clinical advice to PHAC during the 2009 H1N1 influenza pandemic and the 2013–2016 Ebola virus international public health emergency.

The objective of this article is to describe the mandate and membership of NAC-IPC; identify how NAC-IPC coordinates with other PHAC programs; give an overview of the guideline development process; and provide a list of current PHAC guidelines developed with expert advice from NAC-IPC.

Mandate and membership

The mandate of NAC-IPC is to support PHAC in promoting public health; preventing and controlling infectious diseases; preparing for and responding to public health emergencies; serving as a central point for sharing Canada's expertise; applying international research and development to national public health programs; strengthening intergovernmental collaboration on public health; and facilitating national approaches to public health policy and planning—all as it relates to healthcare-associated infections.

To guide these activities, NAC-IPC provides expert advice to PHAC's Healthcare-Associated Infection–Infection Prevention and Control (HAI-IPC) program for:

- developing national evidence-based IPC guidelines for health care settings (4)
- providing technical and scientific advice to PHAC in response to emerging and re-emerging pathogens and infectious disease public health threats
- developing strategies to prevent and control HAIs, antimicrobial resistance (AMR) and other related public health events in settings where health care services are delivered in Canada; and
- identifying priorities for HAI and IPC research

NAC-IPC consists of up to 15 members who are recruited through a transparent targeted nomination process. Their number may be adjusted to ensure the appropriate range of expertise, experience and geographic representation. The Committee also includes non-voting liaison members who act as representatives of provinces and territories, associations and industries and express opinions on behalf of their organization. Liaison members support NAC-IPC by providing additional knowledge and expertise; sharing relevant updates from their respective organizations; and reviewing and providing feedback on NAC-IPC statements and guidance documents.

A call for interested applicants or nominations for NAC-IPC membership is sent to relevant professional associations for circulation to their community of practice. Selection of committee members involves a range of criteria including leadership, geographical representation, advanced knowledge and certification in identified fields of practice, with specialized expertise suited to guideline development and response to emerging HAI issues.

The Committee is currently composed of members with expertise in infectious diseases, medical microbiology, infection prevention and control, public health, health care epidemiology and occupational health and/or hygiene. Task groups, led by a member of NAC-IPC and consisting of both NAC-IPC and non–NAC-IPC members with relevant subject matter expertise, are appointed to lead the development of each guideline or product. The task groups report to NAC-IPC during the product development phase and the approval process prior to release.

Interconnectedness with other PHAC programs and products

The HAI-IPC program works closely with other PHAC programs that have related interests or mandates. This includes the Canadian Nosocomial Infection Surveillance Program (CNISP), which is responsible for national surveillance (rates and trends) of HAIs, including emerging pathogens in Canadian health care facilities; and the Canadian Antimicrobial Resistance Surveillance System (CARSS), which is responsible for the national surveillance of AMR and antimicrobial use (5,6). The work of these and other inter-related programs inform the work undertaken by the HAI-IPC program (e.g. revisions to an existing guidance document on carbapenem–resistant gram-negative bacilli in health care settings and other AMR-IPC products). These AMR–related products will contribute to PHAC's national leadership on this issue while ensuring consistency and congruency of published PHAC products on HAIs and AMR.

Guideline development process

Guideline development is a resource-intensive, long term effort that necessitates ongoing prioritization and collaboration to maximize available resources. Prioritization is based on the urgency of a proposed guideline topic or issue; the scope of the issue; a public health threat or impact (especially for novel, emerging or re-emerging pathogens); PHAC and Government of Canada priorities; provincial/territorial requests or identified needs for a national perspective to facilitate a coordinated approach; and identified gaps and availability of suitable international guidance. As a group, NAC-IPC members and liaison members offer their assessment of relevant published guidelines, provide information on relevant documents under

development by other organizations and identify opportunities for collaborations.

HAI-IPC program staff function as project leads responsible for guideline development activities. These include conducting the literature research, data extraction, evidence synthesis, critical appraisal of the evidence, drafting the evidence-based guidelines and related documents, and providing secretariat support to NAC-IPC. The guidelines developed generally fall into one of four categories with varying complexity and scope: comprehensive guidelines, concise guidelines, quick reference guides and interim guidelines (usually for emerging pathogens). The development of the more comprehensive guidelines is generally done by researching peer-reviewed and grey scientific literature using a systematic review process (see **Figure 1**). Other documents developed may be informed by a narrative literature review or environmental scan with targeted literature search. Each guideline or document includes a description of the methods and/or approach used for its development. Following public release of the guidelines, the HAI-IPC program works with NAC-IPC to review relevant new evidence and update the guidelines when indicated.

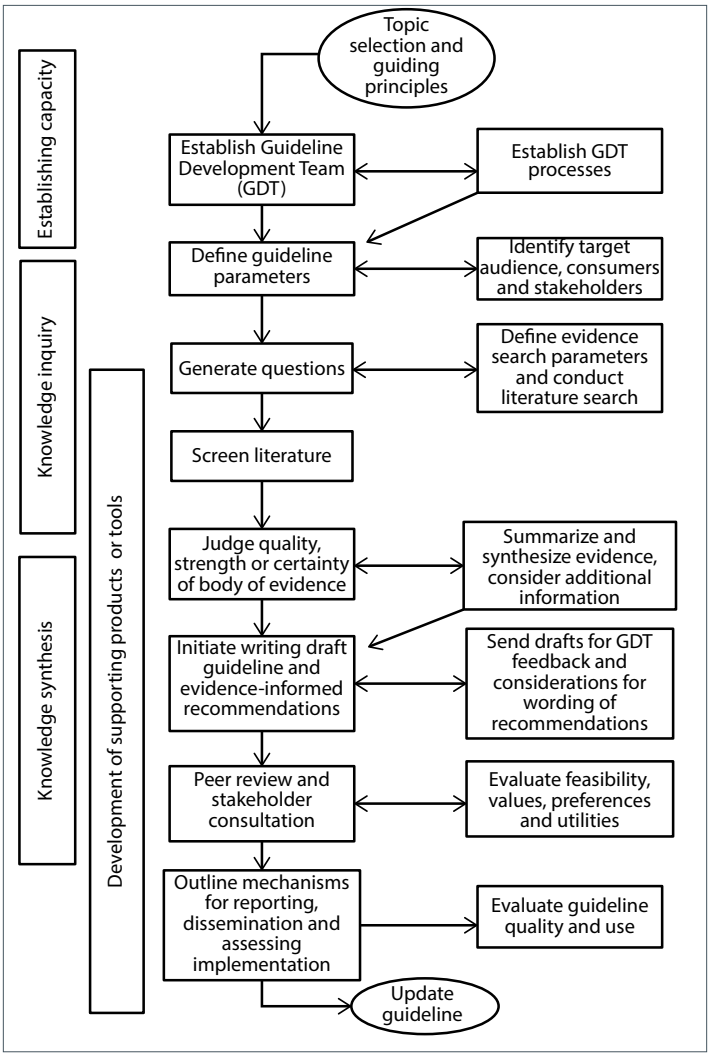
Grading of evidence

The development of guidelines involves extracting relevant data from the literature review, synthesizing the literature, interpreting the evidence and grading available evidence (where relevant). Some guidelines are mostly descriptive and informed by expert opinion due to the absence of published evidence. The criteria used for grading evidence that informs the national evidence-based IPC guideline series are outlined in **Table 1**.

Developing recommendations and providing expert opinion

Where possible, recommendations are informed by evidence from summary tables developed as part of the systematic or narrative literature review. For ethical and feasibility reasons, clinical trials for common infection prevention and control issues are almost non-existent, observational studies are limited and descriptive studies do not provide evidence on causal association. As a result, expert opinion is a necessary part of the HAI-IPC guideline development process. Expert opinion is also essential during the early phases of an epidemic brought on by a newly emerging pathogen, as peer-reviewed publications are often limited under these circumstances.
Recommendations for public health practice are also informed by health care epidemiology, monitoring and analysis of IPC issues and trends, as well as feedback from stakeholder and provincial/territorial partners. Advice provided by NAC-IPC complements provincial/territorial efforts and considers all relevant federal, provincial, territorial and local legislation, regulations and policies. **Table 2** lists the guidelines and other published documents developed by the HAI-IPC program with advice from or involvement of NAC-IPC member(s) (1).

Figure 1: Guideline development process for PHAC's national HAI-IPC guidelines



Abbreviations: GDT, Guideline Development Team; HAI-IPC Healthcare-Associated Infection-Infection Prevention and Control; PHAC, Public Health Agency of Canada

Table 1: Criteria for rating evidence for infection prevention and control guidelines for healthcare-associated infections[a]

Strength of evidence	Grades	Criteria
Strong	AI	Direct evidence from meta-analysis or multiple strong design studies of high quality, with consistency of results
	AII	Direct evidence from multiple strong design studies of medium quality with consistency of results OR At least one strong design study with support from multiple moderate design studies of high quality, with consistency of results OR At least one strong design study of medium quality with support from extrapolation from multiple strong design studies of high quality, with consistency of results
Moderate	BI	Direct evidence from multiple moderate design studies of high quality, with consistency of results OR Extrapolation from multiple strong design studies of high quality, with consistency of results
	BII	Direct evidence from any combination of strong or moderate design studies of high/medium quality, with a clear trend but some inconsistency of results OR Extrapolation from multiple strong design studies of medium quality or moderate design studies of high/medium quality, with consistency of results OR One strong design study with support from multiple weak design studies of high/medium quality, with consistency of results
Weak	CI	Direct evidence from multiple weak design studies of high/medium quality, with consistency of results OR Extrapolation from any combination of strong/moderate design studies of high/medium quality, with inconsistency of results
	CII	Studies of low quality regardless of study design OR Contradictory results regardless of study design OR Case series/case reports OR Expert opinion

[a] Source: Moralejo et al. (7)

Table 2: HAI-IPC guidelines and other related published documents

Subject	Title (year completed)	Date posted/revised
Comprehensive documents		
Routine practices	Routine Practices and Additional Precautions for Preventing the Transmission of Infection in Healthcare Settings 2013 (8)	September 5, 2014
	Routine Practices and Additional Precautions Assessment and Educational Tools 2013 (9)	September 5, 2014
	Poster: Help reduce the spread of antimicrobial resistance - Follow recommendations for routine practices in settings where health care is provided 2016 (10)	May 26, 2016
	Hand Hygiene Practices in Healthcare Settings 2012 (11)	September 5, 2014
Occupational infections	Prevention and Control of Occupational Infections in Health Care 2002 (12)	March 2002 (under revision)
Blood-borne infections	Proceedings of the Consensus Conference on Infected Health Care Workers: Risk for Transmission of Bloodborne Pathogens (13)	July 1998 (under revision)[a]
Pneumonia	Infection Control Guideline for the Prevention of Healthcare-Associated Pneumonia 2010 (14)	2010
Endoscopy	Infection Prevention and Control Guideline for Flexible Gastrointestinal Endoscopy and Flexible Bronchoscopy 2011 (15)	February 10, 2011
	NOTICE: Recommended Practices for the Prevention of Endoscopy-related Infections 2016 (16)	May 24, 2016
Targeted documents		
Carbapenem-resistant gram-negative bacilli	Guidance: Infection Prevention and Control Measures for Healthcare Workers in All Healthcare Settings: Carbapenem-resistant Gram-negative Bacilli 2010 (17)	April 3, 2012 (under revision)
Clostridium difficile	*Clostridium Difficile* Infection: Infection Prevention and Control Guidance for Management in Acute Care Settings 2013 (18)	January 11, 2013
	Clostridium Difficile Infection - Infection Prevention and Control Guidance for Management in Long-term Care Facilities 2013 (19)	July 12, 2013

Table 2 (*continued*)**: HAI-IPC guidelines and other related published documents**

Subject	Title (year completed)	Date posted/revised
Creutzfeldt–Jakob disease	Classic Creutzfeldt-Jakob Disease in Canada: Quick Reference Guide 2007 (20)	November 1, 2007
	Classic Creutzfeldt-Jakob Disease in Canada 2002 (21)	November 2002
Mycobacterium tuberculosis and other species	Canadian Tuberculosis Standards 7th Edition; Chapter 15 - Prevention and Control of Tuberculosis Transmission in Health Care and Other Settings 2014 (22)	February 17, 2014
	Mycobacterium chimaera Infections in Post–operative Patients Exposed to Heater–Cooler Devices: An Overview (23)	May 4, 2017
Seasonal influenza	Seasonal Influenza - Infection Prevention and Control Guidance for Management in Home Care Settings 2012 (24)	December 5, 2012
Seasonal influenza (*continued*)	Guidance: Infection Prevention and Control Measures for Healthcare Workers in Acute Care and Long-term Care Settings – Seasonal Influenza 2010 (25)	December 20, 2012
Emerging infections		
Ebola virus disease	Infection Prevention and Control Measures for Prehospital Care and Ground Transport of Patients with Suspected or Confirmed Ebola Virus Disease (26)	June 25, 2018
	Infection Prevention and Control Expert Working Group: Advice on Infection Prevention and Control Measures for Ebola Virus Disease in Healthcare Settings (27)	June 25, 2015
	Infection Prevention and Control Expert Working Group: Advice on the Management of Ebola Virus Disease-associated Waste in Canadian Healthcare Settings 2015 (28)	May 6, 2015
MERS-CoV	Infection Prevention and Control Guidance for Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in Acute Care Settings 2016 (29)	May 17, 2016
Other documents		
Critical appraisal	Infection Prevention and Control Guidelines: Critical Appraisal Tool Kit 2014 (30)	March 11, 2015
	Critical Appraisal Toolkit (CAT) for Assessing Multiple Types of Evidence (7)	September 7, 2017

Abbreviation: HAI-IPC, Healthcare-Associated Infection-Infection Prevention and Control;
MERS-CoV: Middle East Respiratory Syndrome Coronavirus
[a] An evidence-based document is currently under development to replace this consensus document

Conclusion

The NAC-IPC is an external advisory body that continues the work done under previous names for the past 25 years, providing expert advice on the development of national HAI-IPC guidelines. The rigour and methodology used to develop these guidelines continues to improve, as do the opportunities for international collaboration and knowledge exchange and mobilization.

The NAC-IPC is committed to strengthening linkages with other PHAC programs and external partners, and informing the wider federal-provincial-territorial public health network on HAI-IPC issues. This is important not only for current matters, but also for emerging public health threats that can potentially impact Canadian health care settings. In such a case, NAC-IPC will be able to provide expert interpretation of available evidence on emerging pathogens and, as needed, the rapid development of relevant evidence-based IPC guidelines.

Authors' statement

TO – Conceptualization, methodology, writing of original draft, review and editing
KD – Conceptualization, supervision, writing, review and editing
LJ – Conceptualization, writing, review and editing
JE – Conceptualization, writing, review and editing

Conflict of interest

None.

Contributors

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Tuberculosis drug resistance in Canada: 2017

M LaFreniere[1], H Hussain[1,2], J Vachon[1]

Affiliations

[1] Centre for Communicable Disease and Infection Control, Public Health Agency of Canada, Ottawa, ON

[2] Dalla Lana School of Public Health, University of Toronto, Toronto, ON

Correspondence: phac.tb.surveillance.aspc@canada.ca

Abstract

Background: Drug-resistant tuberculosis (TB) is a global public health issue. To monitor this in Canada, surveillance systems have been in place for the last 20 years.

Objective: To describe drug resistance patterns among TB isolates in Canada in 2017 by type of resistance as well as geographic location, demographic data and origin and to compare current data to those of the previous 10 years.

Methods: Data were derived and analyzed from two sources. The Canadian Tuberculosis Laboratory Surveillance System (CTBLSS) is an isolate-based laboratory surveillance system and was used to obtain information on the results of drug susceptibility testing (DST) as well as province or territory, sex and age of the individual from which the sample originated. The Canadian Tuberculosis Reporting System (CTBRS) is a case-based surveillance system with information on active and retreatment TB cases in Canada and was used to derive origin data, which is defined as either foreign-born, Canadian-born Indigenous or Canadian-born non-Indigenous. Analysis was descriptive and compared with data from these two sources for 2007–2016.

Results: In 2017, 1,515 TB isolates were tested for resistance to anti-TB drugs, with 123 (8.1%) demonstrating resistance to any first-line anti-TB drug. Of these, 103 were monoresistant, six were polyresistant and 14 were multidrug-resistant tuberculosis (MDR-TB). No extensively drug-resistant tuberculosis (XDR-TB) isolates were reported. Drug resistance was reported in seven provinces/territories (British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Quebec and New Brunswick). There were 63 isolates from females with drug resistance (9.5%) and 60 isolates from males with drug resistance (7.0%). Drug resistance was found in a greater percentage of isolates among those aged 25–34 (n=29, 23.6%). By origin, 1,072 (11%) foreign-born TB cases reported between 2005 and 2015 were drug-resistant. Among the Canadian-born non-Indigenous and Canadian-born Indigenous TB cases, 143 (9%) and 54 (2%) were drug-resistant, respectively. Compared with previous years, the number of isolates tested increased slightly (from 1,267 to 1,515); however, there was a decrease in the percentage of isolates with reported drug resistance (from 10.5% in 2007 to 8.1% in 2017).

Conclusion: In 2017, TB drug resistance rates remained low in Canada.

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Keywords: tuberculosis, resistance, multidrug-resistant tuberculosis, extensively drug-resistant tuberculosis, isolates, surveillance, isoniazid, rifampin, ethambutol, pyrazinamide

Introduction

Tuberculosis (TB) is an infectious airborne illness, primarily of the lungs, caused by the bacterium *Mycobacterium tuberculosis*. It is one of the most frequently reported infectious diseases globally (1). In 2016, the World Health Organization (WHO) estimated that 10.4 million people became ill with active TB (1).

Although TB is curable, resistance of *M. tuberculosis* to anti-TB treatment may develop. In 2016, WHO estimated that 4.1% of new cases and 19% of previously treated cases globally had multidrug-resistant tuberculosis (MDR-TB) or rifampin-resistant TB (1).

In Canada, incidence of TB in the general population remains low at 4.8 cases per 100,000; however, certain subpopulations are disproportionally affected. Of those TB cases reported to the Public Health Agency of Canada (PHAC) in 2016, 70% were among individuals born outside Canada. As well, the rate among all Indigenous people was 23.5 cases per 100,000 and among Inuit, 170.1 per 100,000 (2).

Surveillance of drug-resistant TB has been conducted in Canada for the last 20 years because of the international importance of the disease in terms of public health and the potential for drug-resistant TB to spread to Canada. Among the reported cases of TB, drug resistance in Canada remains uncommon. Over the past decade, drug resistance trends have remained stable and low, with resistance to any of the first-line anti-TB drugs ranging from 8.2% to 10.5%. During the same period, MDR-TB also continued to be uncommon, with the percentage of positive isolates ranging from 0.6% to 1.6% (3).

The objective of this surveillance report is to describe the drug resistance patterns of TB isolates in Canada in 2017 by type of resistance, geographic location, demographic data and origin, and to compare current data to those of the previous 10 years.

Methods

Definitions

The Canadian Tuberculosis Standards categorizes TB drug resistance patterns as follows (4):

- **Monoresistance:** Resistance to one first-line anti-TB drug only (isoniazid, rifampin, ethambutol or pyrazinamide)
- **Polyresistance:** Resistance to more than one first-line anti-TB drug, not including the combination of isoniazid and rifampin
- **Multidrug-resistant tuberculosis (MDR-TB):** Resistance to isoniazid AND rifampin with or without resistance to other anti-TB drugs; and
- **Extensively drug-resistant tuberculosis (XDR-TB):** Resistance to isoniazid AND rifampin AND any fluoroquinolone AND at least one of the three injectable second-line drugs (amikacin, capreomycin or kanamycin)

Data sources

Data were derived and analyzed from two surveillance systems, the Canadian Tuberculosis Laboratory Surveillance System (CTBLSS) and the Canadian Tuberculosis Reporting System (CTBRS).

Canadian Tuberculosis Laboratory Surveillance System

The CTBLSS is an isolate-based laboratory surveillance system. Isolates from culture-positive TB cases undergo drug susceptibility testing (DST), and the results are reported to PHAC on a voluntary basis by the testing laboratory.

This current article includes the DST results for first-line drugs, and others if required, as well as sex, age and province/territory of the individual from whom the sample originated. To the extent possible, only one set of DST results per case was included in the analysis; we identified potential duplicates using sex, date of birth or age and the province/territory and clarified these with the submitting laboratory. Isolate counts were verified by the submitting laboratories to ensure report completion and to clarify any data inconsistencies.

Canadian Tuberculosis Reporting System

Whereas the CTBLSS collects data on *M. tuberculosis* isolates, the CTBRS is a case-based surveillance system with information on active and retreatment TB cases in Canada. The CTBRS collects some drug resistance data on TB cases when provincial and territorial health authorities report these cases to PHAC.

In the current article, we used information from CTBRS to obtain data on origin, which is defined here as either foreign-born, Canadian-born Indigenous or Canadian-born non-Indigenous. Further information on the CTBRS system can be found in *Tuberculosis in Canada, 2012* (5). The most recent data available for this analysis were for 2015.

Data analysis

Data were cleaned and analyzed using SAS Enterprise Guide 5.1 (Cary, North Carolina, United States [US]) and Microsoft Excel 2010 (Redmond, Washington, US). Any TB isolates that were demonstrated as positive for *Mycobacterium tuberculosis* complex on culture, specifically *M. tuberculosis*, *M. africanum*, *M. canetti*, *M. caprae*, *M. microti*, *M. pinnipedii* or *M. bovis*, were included in the analyses. TB isolates that were positive for *M. bovis* Bacille Calmette Guérin (BCG) were excluded from the analyses.

Descriptive analyses of the resistance data, geographic and demographic data for 2017 and data on origin from 2015 were completed. These analyses were then compared with the trends from the previous 10 years.

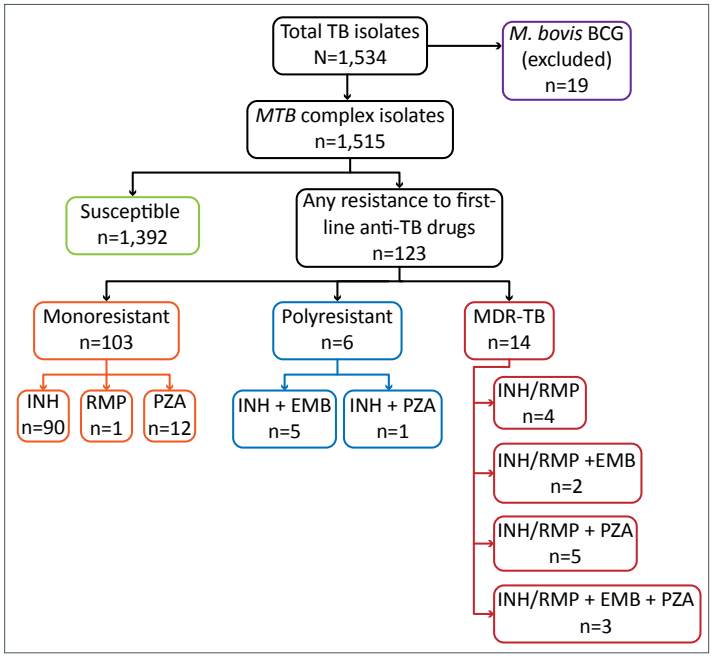
Results

Anti-TB drug resistance patterns

In 2017, DST results from 1,534 isolates were reported to PHAC. Of these, 19 were *M. bovis* BCG and were not included in the analysis (**Figure 1**). Of all 1,515 isolates included, 123 (8.1%) showed resistance to any of the first-line anti-TB drugs and 1,392 (91.9%) were sensitive to all first-line anti-TB drugs.

While the number of culture-positive TB isolates receiving DST has risen slightly overall since 2007 (from 1,267 isolates), the number of reported isolates with drug resistance to any anti-TB drug has fluctuated from year to year, resulting in an overall

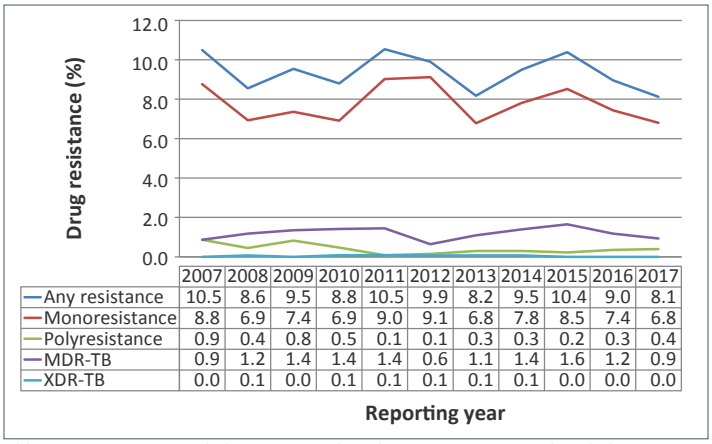
Figure 1: Number of tuberculosis isolates tested for anti-TB drug susceptibility and results, Canada, 2017



Abbreviations: BCG, Bacille Calmette Guérin; EMB, ethambutol; INH, isoniazid; MDR-TB, multidrug-resistant tuberculosis; *MTB*, *Mycobacterium tuberculosis*; *M. bovis*, *Mycobacterium bovis*; PZA, pyrazinamide; RMP, rifampin; TB, tuberculosis

small decrease in the percentage of isolates with reported drug resistance (from 10.5% in 2007 to 8.1% in 2017) (**Figure 2**).

Figure 2: Proportion of tuberculosis isolates with reported drug resistance by drug resistance pattern, Canada, 2007–2017



	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Any resistance	10.5	8.6	9.5	8.8	10.5	9.9	8.2	9.5	10.4	9.0	8.1
Monoresistance	8.8	6.9	7.4	6.9	9.0	9.1	6.8	7.8	8.5	7.4	6.8
Polyresistance	0.9	0.4	0.8	0.5	0.1	0.1	0.3	0.3	0.2	0.3	0.4
MDR-TB	0.9	1.2	1.4	1.4	1.4	0.6	1.1	1.4	1.6	1.2	0.9
XDR-TB	0.0	0.1	0.0	0.1	0.1	0.1	0.1	0.1	0.0	0.0	0.0

Abbreviations: MDR-TB, multidrug-resistant tuberculosis; XDR-TB, extensively multidrug-resistant tuberculosis

Monoresistance

Monoresistance was the most commonly reported resistance pattern. Of the isolates that were resistant to any first-line anti-TB drug in 2017, 103 (83.7%) were monoresistant. Of those, 90 were resistant to only isoniazid, 12 to only pyrazinamide and one to only rifampin. No isolates were monoresistant to ethambutol (Figure 1). This is consistent with previous data; since 2015, there has been a slight downward trend between 2007 and 2017 (Figure 2).

Polyresistance

In 2017, six isolates (0.4%) were polyresistant: five were resistant to the combination of isoniazid and ethambutol, and one was resistant to isoniazid and pyrazinamide (Figure 1). Compared with previous years, the percentage of isolates that were polyresistant has remained low (Figure 2).

MDR-TB and XDR-TB

In 2017, 14 (0.9%) isolates were identified as resistant to both isoniazid and rifampin (with or without resistance to other anti-TB drugs) and therefore considered to be MDR-TB. Of these, four were resistant to the combination of isoniazid and rifampin; five were resistant to isoniazid, rifampin and pyrazinamide; and two were resistant to isoniazid, rifampin and ethambutol. Three isolates were resistant to all four first-line drugs (Figure 1). Between 2007 and 2017, 172 (1.1%) TB isolates were reported as MDR-TB, with the percentage reported being low and the overall trend stable during this time (Figure 2).

No isolates were reported as XDR-TB in Canada in 2017. Although two isolates were resistant to isoniazid, rifampin and any fluoroquinolone, and another two were resistant to isoniazid, rifampin and at least one of the injectable anti-TB drugs, none were resistant to the combination of all four. Since 2007, only six isolates have tested positive for XDR-TB in Canada; the most recent was reported in 2014.

Distribution

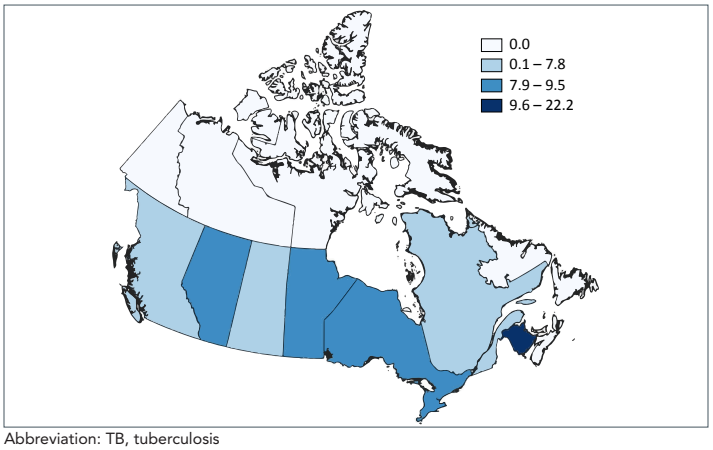
Cases were examined by geographic distribution, as well as distribution by sex, age and origin.

Geographic distribution

In 2017, Ontario reported the largest number of isolates (559 isolates; 36.9%), followed by 260 (17.2%) in British Columbia, 199 (13.1%) in Alberta, 183 (12.1%) in Quebec, 157 (10.4%) in Manitoba, 64 (4.2%) in Saskatchewan and 60 (4.0%) in Nunavut. Newfoundland and Labrador, Nova Scotia, New Brunswick, Yukon and Northwest Territories accounted for 2.2% of the total isolates tested in 2017. Compared to 2016, Nunavut submitted almost twice as many isolates for DST in 2017, likely due to increased cases of TB in that jurisdiction (6). There were no reported cases of TB in Prince Edward Island in 2017.

Of all the provinces and territories, British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Quebec and New Brunswick reported some type of drug resistance in 2017 (**Figure 3**). For British Columbia, Alberta, Saskatchewan, Manitoba, Ontario and Quebec, the proportion of isolates with any anti-TB drug resistance ranged from 6.9% to 9.5%. Of the nine isolates submitted by New Brunswick, two were reported to demonstrate anti-TB drug resistance (22.2%). No drug-resistant isolates were reported from Nunavut, Newfoundland and Labrador, Nova Scotia, Yukon and Northwest Territories in 2017.

Figure 3: Proportion (%) of isolates demonstrating any anti-TB drug resistance by province/territory, Canada, 2017



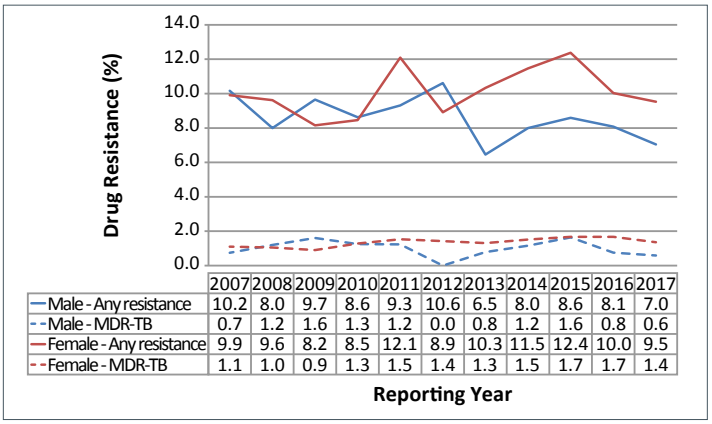
Abbreviation: TB, tuberculosis

Of the 14 total MDR-TB isolates reported in 2017, Ontario accounted for seven isolates, New Brunswick, Quebec and British Columbia each reported two, and Alberta reported one isolate.

Distribution by sex

In 2017, 60 (7.0%) of the isolates from males and 63 (9.5%) of the isolates from females had any resistance to first-line drugs (**Figure 4**). The percentage of isolates with any resistance to first-line drugs has fluctuated by sex since 2007. However, overall, the percentage has decreased among males (68 isolates; 10.2%), with a similar decrease showing among females (54 isolates; 9.5%). Between 2007 and 2012, the percentage of isolates reported with any drug resistance among males and females was similar, but since that time, a larger proportion of isolates from females had any drug resistance (Figure 4). Of the 14 MDR-TB isolates, five were from males and nine were from females. The percentage of isolates in both sexes identified as MDR-TB remained low and stable from 2007 through 2017, ranging from 0.1% to 1.6% of isolates from males and from 0.9% to 1.7% in isolates from females. For XDR-TB reported from 2007 through 2017, there were only six isolates total; five were from females.

Figure 4: Percentage of TB isolates with reported drug resistance by sex and resistance pattern, Canada, 2007–2017



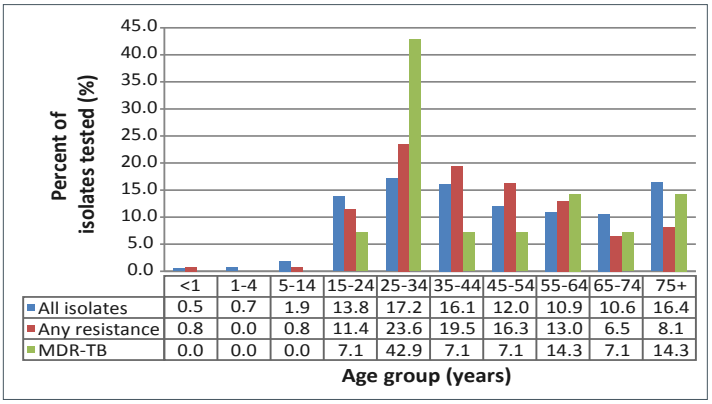
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Male - Any resistance	10.2	8.0	9.7	8.6	9.3	10.6	6.5	8.0	8.6	8.1	7.0
Male - MDR-TB	0.7	1.2	1.6	1.3	1.2	0.0	0.8	1.2	1.6	0.8	0.6
Female - Any resistance	9.9	9.6	8.2	8.5	12.1	8.9	10.3	11.5	12.4	10.0	9.5
Female - MDR-TB	1.1	1.0	0.9	1.3	1.5	1.4	1.3	1.5	1.7	1.7	1.4

Abbreviations: MDR-TB, multidrug-resistant tuberculosis; TB, tuberculosis

Distribution by age

Isolates from individuals under 15 years of age represented a very small proportion of the total tested and those with any drug resistance in 2017 (**Figure 5**). Only 46 (3%) of the isolates were from this age group with two having any drug resistance, neither of which was MDR-TB. In contrast, isolates from the 25–34 year age group represented the largest proportion tested (260 isolates; 17.2%) and the largest proportion with any drug resistance (29 isolates; 23.6%) and MDR-TB (six isolates; 42.9%).

Figure 5: Percentage of TB isolates with reported drug resistance, by age group and resistance pattern, Canada, 2017



	<1	1-4	5-14	15-24	25-34	35-44	45-54	55-64	65-74	75+
All isolates	0.5	0.7	1.9	13.8	17.2	16.1	12.0	10.9	10.6	16.4
Any resistance	0.8	0.0	0.8	11.4	23.6	19.5	16.3	13.0	6.5	8.1
MDR-TB	0.0	0.0	0.0	7.1	42.9	7.1	7.1	14.3	7.1	14.3

Abbreviations: MDR-TB, multidrug-resistant tuberculosis; TB, tuberculosis; <, less than; +, and over

In all other age groups, the number of total isolates ranged from 160 (10.6%) among those aged 65–74 to 248 (16.4%) among those aged 75+. The percentage of isolates with any resistance ranged from 6.5% (eight isolates) among those aged 65–74 to 19.5% (24 isolates) among those aged 35–44. The number of MDR-TB isolates ranged from one among the 15–24, 35–44, 45–54 and 65–74 age groups, respectively to two among the 55–64 and 75+ age groups, respectively.

Distribution by origin

There were 9,745 cases of the foreign-born cases with active culture-positive TB reported to the CTBRS between 2005 and 2015, 1,050 (11%) had any resistance to first-line anti-TB drugs and 151 (1.5%) were MDR-TB. There were 2,711 of Canadian-born Indigenous TB cases, 67 (2%) had any resistance and none were MDR-TB. Among the 1,588 of Canadian-born non-Indigenous TB cases, 149 (9%) had reported resistance to at least one of the first-line anti-TB drugs and seven (0.5%) were MDR-TB. Of all the TB cases reported to be MDR-TB, 96% were foreign born and 4% were Canadian-born or non-Indigenous.

See Appendix for a list supplementary tables that are available upon request.

Discussion

In Canada, the rates of drug resistance among culture-positive TB isolates remained relatively low in 2017. Of these isolates, 8.1% were resistant to any of the first-line anti-TB drugs and 0.9% were MDR-TB. No isolates of XDR-TB have been reported in Canada since 2014. The rates of TB drug resistance between 2007 and 2017 remained relatively low. While there was an increase in the number of culture-positive TB isolates reported in 2017 compared to 2007, the proportion of isolates with resistance to at least one of the first-line anti-TB drugs decreased over time.

In general, trends in TB drug resistance tend to echo the overall trends in active TB cases in Canada reported in the CTBRS. Ontario continues to have the majority of isolates and positives for drug resistance, as well as the largest reported number of active TB cases in Canada. This is not surprising as Ontario has the largest population of all the Canadian provinces/territories and receives the highest percentage of immigrants to Canada annually (39.0% of immigrants to Canada in 2016) (7).

About half the provinces/territories have not reported any MDR-TB cases between 2007 and 2017 (Yukon, Northwest Territories, Nunavut, Nova Scotia, Prince Edward Island, Newfoundland and Labrador). These provinces/territories have small populations and constitute a small number of the overall TB cases reported in Canada annually. Similar to all TB cases reported in Canada (2), drug resistance continued to be most frequently reported among isolates from persons aged 25–34 (42.9% of MDR-TB).

Foreign-born individuals comprised 71% of the total TB cases reported in Canada in 2015 (8), and also constituted a larger proportion of cases of MDR-TB (96%). This may be due to incomplete treatment from a previous episode of TB or the acquisition of a drug-resistant strain in their countries of origin (4).

This surveillance report is subject to a few limitations. In terms of data quality, there is the potential of reported errors, missing data and duplicates; however, every effort has been made to identify and remove additional isolate results per individual and to correct errors through multiple rounds of validation by submitting laboratories. As the CTBLSS is a laboratory-based surveillance system, limited demographic information is available, and the isolates reported are not able to be directly linked to case-based surveillance data from the CTBRS. Therefore, we are currently not able to describe the CTBLSS data further by ethnic origin, country of birth or treatment outcomes, as is done by other countries and organizations (1,9,10). In an effort to provide a more complete epidemiological picture of TB drug resistance in Canada, CTBRS data were used to describe TB cases with drug resistance by ethnic origin. Drug resistance information reported in CTBRS is fairly complete (98%) (11) and reasonably comparable to the CTBLSS, although some discrepancies may exist between the two which cannot be resolved.

Drug resistance remains a concern worldwide as MDR-TB continues to spread globally (1). In Canada, despite drug resistance rates remaining consistently low, monitoring emerging trends and patterns in TB drug resistance continues to be important, as the potential for importing drug-resistant TB into Canada remains a possibility. The CTBLSS will continually be updated as newer technology for detecting drug resistance (e.g. whole genome sequencing) and drugs for TB treatment (e.g. bedaquiline, delaminid) become available.

Authors' statement

ML – Conceptualization, methodology, software, validation, formal analysis, writing (original draft)
HH – Conceptualization, software, validation, formal analysis, writing (review) and editing
JV – Conceptualization, writing (review) and editing, supervision

Conflict of interest

None.

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Appendix

List of supplementary tables available upon request

Supplementary Table 1: Total number and percentage of *Mycobacterium tuberculosis* complex isolates identified with any resistance, as multidrug and extensively drug resistant, by year, 2007-2017, Canada

Supplementary Table 2: Overall pattern of reported tuberculosis drug resistance in Canada, 2007 to 2017

Supplementary Table 3: Results for routine to anti-tuberculosis drug susceptibility testing of *Mycobacterium tuberculosis* complex isolates originating from Alberta, 2007 to 2017

Supplementary Table 4: Results for routine to anti-tuberculosis drug susceptibility testing of *Mycobacterium tuberculosis* complex isolates originating from British Columbia, 2007 to 2017

Supplementary Table 5: Results for routine to anti-tuberculosis drug susceptibility testing of *Mycobacterium tuberculosis* complex isolates originating from Manitoba, 2007 to 2017

Supplementary Table 6: Results for routine to anti-tuberculosis drug susceptibility testing of *Mycobacterium tuberculosis* complex isolates originating from New Brunswick, 2007 to 2017

Supplementary Table 7: Results for routine to anti-tuberculosis drug susceptibility testing of *Mycobacterium tuberculosis* complex isolates originating from Newfoundland and Labrador, 2007 to 2017

Supplementary Table 8: Results for routine to anti-tuberculosis drug susceptibility testing of *Mycobacterium tuberculosis* complex isolates originating from Northwest Territories, 2007 to 2017

Supplementary Table 9: Results for routine to anti-tuberculosis drug susceptibility testing of *Mycobacterium tuberculosis* complex isolates originating from Nova Scotia, 2007 to 2017

Supplementary Table 10: Results for routine to anti-tuberculosis drug susceptibility testing of *Mycobacterium tuberculosis* complex isolates originating from Nunavut, 2007 to 2017

Supplementary Table 11: Results for routine to anti-tuberculosis drug susceptibility testing of *Mycobacterium tuberculosis* complex isolates originating from Ontario, 2007 to 2017

Supplementary Table 12: Results for routine to anti-tuberculosis drug susceptibility testing of *Mycobacterium tuberculosis*

complex isolates originating from Prince Edward Island, 2007 to 2017

Supplementary Table 13: Results for routine to anti-tuberculosis drug susceptibility testing of *Mycobacterium tuberculosis* complex isolates originating from Quebec, 2007 to 2017

Supplementary Table 14: Results for routine to anti-tuberculosis drug susceptibility testing of *Mycobacterium tuberculosis* complex isolates originating from Saskatchewan, 2007 to 2017

Supplementary Table 15: Results for routine to anti-tuberculosis drug susceptibility testing of *Mycobacterium tuberculosis* complex isolates originating from Yukon, 2007 to 2017

Supplementary Table 16: Multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis isolates by province/territory of origin, 2017

Supplementary Table 17: Total number of *Mycobacterium tuberculosis* complex isolates by reporting and originating province/territory, 2017

Supplementary Table 18: Provincial/territorial breakdown by any resistance, multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis in Canada, 2007 to 2017

Supplementary Table 19: Tuberculosis drug resistance by sex and age group in Canada, 2017

Surveillance of laboratory exposures to human pathogens and toxins: Canada 2017

D Pomerleau-Normandin[1], M Heisz[1], F Tanguay[1]*

Abstract

Background: Under Canada's *Human Pathogens and Toxins Act* and *Human Pathogens and Toxins Regulations*, the Public Health Agency of Canada (PHAC) is mandated with monitoring laboratory incident notifications through the Laboratory Incident Notification Canada (LINC) surveillance system. The year 2017 marks the second complete year of data.

Objective: To describe the laboratory exposure and laboratory-acquired infection incidents that occurred in Canada in 2017 by sector, human pathogens and toxins involved, number of affected persons, incident type and root causes.

Methods: The incidents included in the analysis occurred between January 1 and December 31, 2017. They were reported by laboratories with active licences to PHAC through the LINC surveillance system. Microsoft Excel 2010 was used for basic descriptive statistics.

Results: A total of 44 exposure and laboratory-acquired infection incidents were reported to the LINC in 2017. Compared by sector and their respective shares of licences, the number of incidents was highest in the academic and hospital sectors compared with government laboratories and private industry. Altogether 118 people were exposed for an average of 2.7 people per incident (range of 1–29). There were no reports of secondary exposure. Six exposure incidents (14%) led to "suspected" (n=5) or confirmed (n=1) cases of laboratory-acquired infection. Although overall, risk group (RG)2 human pathogens and toxins were involved in the majority of incidents (n=23; 52%), *Francisella tularensis* (n=4; 9%) and *Coccidioides immitis* (n=3; 7%) were the most frequently involved in reported exposure incidents. These two pathogens are both RG3 and security-sensitive biological agents (SSBAs). An average of 2.3 root causes were identified per incident (n=101). Problems with standard operating procedures (SOPs) and human error were the two most common causes.

Conclusion: The incidence of laboratory exposure incidents was relatively low in 2017. The most common route of exposure was through inhalation and the most common root causes were problems with SOPs and human error. Since this is a new surveillance system, baseline estimates are still being established.

Affiliation

[1] Centre for Biosecurity, Public Health Agency of Canada, Ottawa, ON

***Correspondence:**
florence.tanguay@canada.ca

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Keywords: laboratory exposures, laboratory incidents, laboratory-acquired infections, human pathogens, surveillance, bacteria, virus, toxins, biosafety

Introduction

Laboratories that enable the study and diagnosis of pathogens and their associated toxins pose an inherent risk of exposure to those who work in them. Yet until recently, laboratory incidents were only reported internally and, when applicable, to occupational health authorities. A few countries developed some reporting requirements for biosafety and biosecurity-related incidents at the national level (1–3). However, it was the Public Health Agency of Canada (PHAC) that established one of the

first comprehensive and standardized surveillance systems of laboratory incidents involving human pathogens and toxins at the national level. The Laboratory Incident Notification Canada (LINC) surveillance system was launched in December 2015 in response to the requirements established by the 2009 *Human Pathogens and Toxins Act* (*HPTA*) (4) and the subsequent the *Human Pathogens and Toxins Regulations* (*HPTR*) (5). The year 2017 therefore represents the second complete year of data gathered through the LINC surveillance system.

Under the *HPTA* and *HPTR*, it is mandatory for organizations performing controlled activities with human pathogens and toxins to be licenced, unless otherwise exempted. Of note, one organization may possess multiple licences, and one licence can cover multiple containment zones. The vast majority of the laboratory work performed in Canada involves risk group (RG)2 human pathogens and toxins (93.2%), which pose a moderate risk to individuals but low risk to public health, because they can cause serious disease in humans but are unlikely to do so. A minority of the laboratory work performed (6.4%) involves RG3 human pathogens, which pose a high risk to individuals but a low risk to public health, because they are likely to cause serious disease but are unlikely to spread. Work with RG4 organisms, which are of highest risk to both individuals and the community, represent only 0.2% of all regulated work. Similarly, activities involving Security-Sensitive Biological Agents (SSBAs) represent only 0.2% of all regulated work in Canada. SSBAs constitute a subset of human pathogens and toxins that pose an "increased biosecurity risk due to their potential or use as a biological weapon" (6,7). See **Appendix** for the definition of some commonly used terms.

Under the *HPTA*, it is mandatory for all licenced facilities to report incidents involving human pathogens and toxins of RG2 or higher to PHAC. Notifications include both exposures and non-exposure incidents. Exposures are defined as contact with, or close proximity to, human pathogens or toxins that may result in laboratory-acquired infections or intoxication (LAI). Non-exposure involves inadvertent possession, production and/or release of a human pathogen or toxin; a missing, lost or stolen human pathogen or toxin; or an SSBA not being received within 24 hours of expected arrival (8). The first full year of data from Canada's LINC surveillance system was in 2016 (9). This study focuses on exposure incidents that occurred in 2017.

The objective of this report is to describe the laboratory exposure incidents that occurred in Canada between January 1 and December 31, 2017, by sector, human pathogens and toxins involved, number of affected persons, incident type and root causes.

Methods

The LINC surveillance system uses a customized interface of the Microsoft Dynamics Customer Relations Management (Microsoft Corporation, Redmond, Washington, United States) program. Data is entered using standardized forms specific to the type of report submitted; most data fields in these forms are mandatory, which enables precise and accurate comparison. While incidents are self-reported, accuracy is validated throughout the investigatory process; the information can be updated until the final follow-up report is marked as complete and submitted online by the reporter. It is important to note that several follow-up reports can be submitted for a single event. In this study, we used the data of the final follow-up report. Incidents found to fall outside the scope of the *HPTA* and *HPTR* were removed from analysis.

The initial notification report provides the essential elements related to the incident such as the administrative information and brief description of the incident. The follow-up report provides information on the investigation results, the affected persons and corrective actions.

Data from reports of exposures and laboratory-acquired infections (suspected or confirmed) that occurred in 2017 were extracted from the system once it had been ensured that all expected data from that year had been entered. LAIs are often confirmed in the follow-up report based on the results of the investigation. However, some cases are never confirmed and remain "suspected". For instance, if it is impossible to rule out that the infection might have been acquired outside the containment zone (i.e., community acquired) then the LAI will remain "suspected". Ultimately, the status of the LAI is based on the local risk assessment and investigation.

Data elements used for analysis from the initial exposure reports included the licence information (number of licences, sector [academic, hospital, private industry/business, public health, veterinary/animal health, environmental, other]) and the key dates (incident dates, dates reported to internal authority, initial notification dates to PHAC). Data elements used for analysis from the follow-up report included the incident type, information on affected persons (number of primary affected, number of secondary affected, route of exposure, first aid, drug treatment and postexposure prophylaxis), the date of the submission of the follow-up report, the biological agent involved (type, risk group level), incident type(s) and the root cause(s) of the incident.

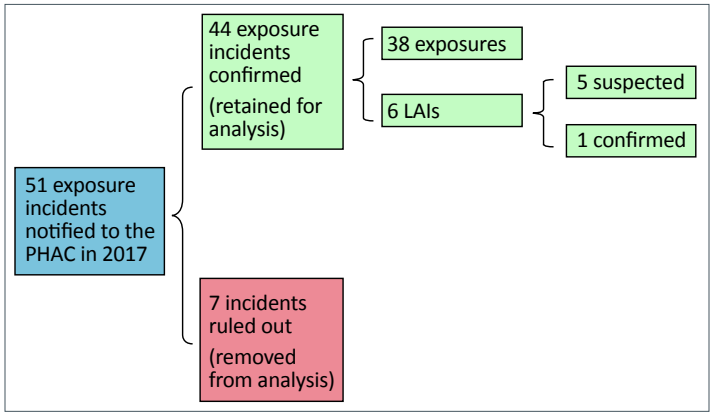
Microsoft Excel 2010 was used for basic descriptive analysis. All exposure and LAI data were reported except where it could lead to the exact identification of a licenced facility. In such cases, for security and confidentiality purposes, the information was not included in this report.

Results

As of December 31, 2017, Canada had issued 905 active licences permitting regulated activities involving human pathogen or toxins. From laboratories with active licences, a total of 51 exposure incidents were reported to the LINC surveillance system for incidents that occurred between January 1 and December 31, 2017. Following the investigation process, exposure was ruled out in seven cases, leaving a total of 44 exposure incidents. The sample included three incidents for which the exact dates remained unknown but the circumstances (type of incident and date internal authorities were first notified) allowed us to conclude that they occurred in the year 2017. In total, exposure and/or laboratory-acquired infection incidents occurred in 4.9% of all licenced facilities.

All confirmed exposures (n=44, 100%) occurred in containment level two laboratories. The majority were exposure-only cases (n=38; 86%). Of the six LAI cases, five remained "suspected" and only one resulted in a confirmed LAI (**Figure 1**).

Figure 1: Case selection and exposure incidents retained for analysis, Canada 2017



Abbreviations: LAI, Laboratory-acquired infection or intoxication; PHAC, Public Health Agency of Canada

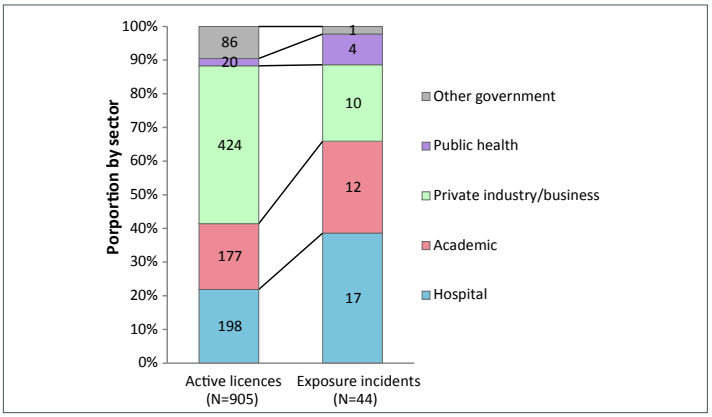
Exposure incidents by sector

Figure 2 compares the number of active licences (N=905) to the number of exposure reports (N=44) submitted to the LINC surveillance system by sector in 2017. The laboratories that reported the highest number of exposure incidents in 2017 were from the academic and hospital sectors. Yet, compared to their respective shares of licences, the incidence of exposure incidents was higher in the public health (20%) and hospital (8.6%) sectors. The lowest incidence was in the private industry/business sector and other government sectors, with exposure incidents occurring in 2.4% and 1.2% of licenced facilities respectively.

Human pathogens and toxins involved

Table 1 presents the distribution of each human pathogen security status (non SSBA, SSBA), toxin risk group (2, 3 or 4) and type (bacterium, virus, toxin, prion or unknown) cited. RG2 human pathogens or toxins were involved in the majority of

Figure 2: Active licences and reported human pathogen or toxin exposure incidents, by sector, Canada 2017



Abbreviation: N, total number
Notes: Data are from the Laboratory Incident Notification Canada (LINC) surveillance system (Canada, retrieved 23-03-2018)
"Academic" includes universities, veterinary colleges, colleges, CEGEP [publicly funded pre-university and technical colleges in the province of Quebec] and others
"Hospital" includes academic-affiliated and non-academic–affiliated hospitals
"Private industry/business" includes animal health, human health, biotechnology, pharmaceutical and the food industry, and pathogen and toxin distributors
"Public health" includes at federal, provincial, territorial and municipal governments
"Other governments" includes veterinary/animal health, environmental and other governmental laboratory at the federal, provincial, territorial and municipal level

incidents (n=23; 52%). RG3 human pathogen or toxins were involved in 14 incidents (32%). The human pathogen or toxin involved remained unknown in seven incidents (16%). Among incidents with known pathogen or toxin involved (n=37), bacteria were the most often involved (n=21; 57%), followed by viruses (n=10; 27%).

Table 1: Reported human pathogens or toxins involved in exposure incidents by risk group level and biological agent type, Canada 2017

Biological agent type by risk group	Non SSBA		SSBA		Total	
	n	%	n	%	n	%
RG2	22	88	1	8	23	52
Bacterium	11	44	0	-	11	25
Toxin	1	4	1	8	2	5
Virus	10	40	0	-	10	23
RG3	3	12	11	92	14	32
Bacterium	2	8	8	67	10	23
Fungus	0	-	3	25	3	7
Prion	1	4	0	-	1	2
Unknown	0	-	0	-	7	16
Total	25	100	12	100	44	100

Abbreviations: n, number of occurrences; SSBA, security-sensitive biological agent; RG, risk group; –, not applicable
Notes: Data are from the Laboratory Incident Notification Canada (LINC) surveillance system. Work at the RG1 level is not regulated under the HPTA. Numbers rounded to the nearest whole number

In the 44 exposure incidents, 25 different human pathogens and toxins were identified. The three most frequently involved in the reported exposure incidents were *Francisella tularensis* (n=4;

9%), *Coccidioides immitis* (n=3; 7%)—both RG3 SSBAs—and *Salmonella* species (n=3; 7%).

Number of affected persons

A total of 118 persons were exposed in the 44 exposure and/or laboratory-acquired infection incidents reported. The number of persons exposed per incident in 2017 ranged from 1 to 29. The average was 2.7 with a median of one. In the majority of exposure incidents (n=33; 75%), only one person was exposed. The incidents in which more than 10 persons were exposed (n=3) were reported from the private industry/business (n=1) and hospital (n=2) sectors. The incident in which 29 persons were exposed occurred in a diagnostic setting and was related to the slow growth of a *Brucella* species culture on standard media that was manipulated over more than one work shift. **Table 2** presents the pathogens associated with exposures and laboratory-acquired infection.

Table 2: Number of laboratory incidents and persons exposed by risk group and type of human pathogens, Canada 2017

Biological agent	Incidents (N=44)	Exposed persons (n=118)	Suspected LAI (n=5)	Confirmed LAI (n=1)
RG2	23	25	3	1
Rubella virus	2	4	–	–
Salmonella spp	3	3	2	–
Escherichia coli O157:H7	1	1	–	1
Vaccinia virus	2	1	1	–
Other RG2 organisms	15	16	–	–
RG3	14	85	1	0
Brucella suis	1	29	–	–
Francisella tularensis	4	23	–	–
Brucella abortus	1	19	–	–
Coccidioides immitis	3	4	–	–
Mycobacterium spp	2	4	1	–
Other RG3 organisms	3	6	–	–
Unknown	7	8	1	0
Total	44	118	5	1

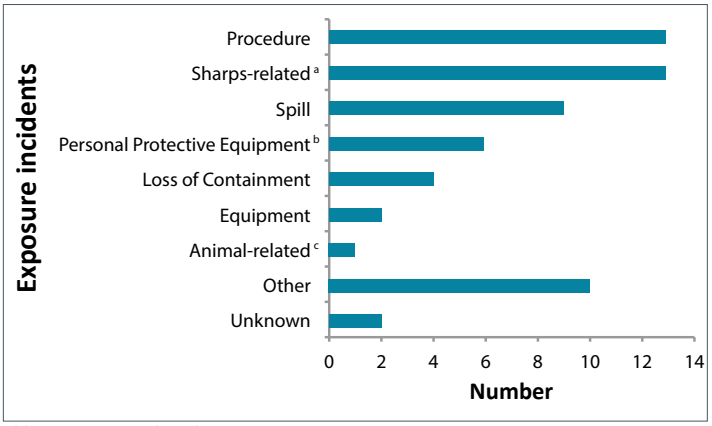
Abbreviations: LAI, laboratory-acquired infections; N, total number; n, number; RG, risk group; spp, species; –, not applicable
Notes: Data are from the Laboratory Incident Notification Canada (LINC) surveillance system. Work at the RG1 level is not regulated under the *HPTA*

Over a quarter of the affected persons (n=34; 29%) received postexposure prophylaxis within seven days of the exposure incident. In addition, 16 (14%) received first aid and seven (6%) underwent drug treatment. No secondary transmission was reported from the LAI.

Incident types

Figure 3 presents the types of exposure incidents reported in 2017 related to the specific action/event that prompted the incident. Most reports described incidents related to inadequate or breaches in procedures (n=13; 30%) and sharps (n=13; 30%). In 14 (32%) of the 44 exposure incidents, inadvertent possession of a RG3 biological agent in a containment level two laboratory also played a role in leading to exposure (data not shown). Such a scenario is more common in diagnostic settings as the specimen received may contain an unidentified human pathogen or toxin. Among the 14 cases of inadvertent possession, 11 (79%) were reported from the public health and hospital sectors. Exposures related to inadvertent possession often involved human pathogens or toxins that can be transmitted through aerosols (e.g., when handling *Brucella* species, *Burkholderia pseudomallei*, *Coccidioides immitis* and *Francisella tularensis*).

Figure 3: Reported incident types of human pathogen or toxin exposure incidents, Canada 2017 (N=60)



Abbreviation: N, total number
Notes: Data are from the Laboratory Incident Notification Canada (LINC) surveillance system (Canada)
[a] Sharps-related includes needle sticks and other sharp injuries
[b] Personal protective equipment-related includes inadequate or failure of personal protective equipment
[c] Animal-related includes bites and scratches

Route of exposure

Of the 118 persons affected in the 44 incidents, the majority were potentially exposed to infectious material through inhalation (n=72; 61%). The second most common route of exposure was through inoculation/injection via needle or sharps injury (n=11; 9%). Absorption via contact with the skin or mucous membrane, inoculation/injection via bites or a scratch, or ingestion were also routes of exposure reported in a few instances.

Root causes

A total of 101 root causes were identified for the 44 incidents reported in 2017, for an average of 2.3 root causes cited per incident. **Table 3** presents the distribution of each root cause listed in the follow-up report. Standard operating procedures (SOPs) were cited in 37 (84%) reports, followed by human interaction in 14 reports (32%). Equipment was also a root cause in a quarter (n=11; 25%) of reported incidents.

Table 3: Root causes in reported human pathogen or toxin exposure incidents, Canada 2017 (N=101)

Root cause	Areas of concern	Citations	
		n	%
Standard operating procedure (SOP)	Documents were known but not followed	37	84
	Documents were not known by user		
	Documents were not followed correctly		
	Documents were not correct for the task/activity		
	Documents were not in place but should have been in place		
Human interaction	Labelling/placement/operation/ displays of tools/equipment needed improvement	14	32
	Environmental factors within the work area needed improvement		
	Workload constraints/pressures/ demands needed improvement		
Equipment	Equipment design needed improvement	11	25
	Equipment was not properly maintained		
	Equipment failed		
	Equipment was not fit for purpose		
	Quality control was not performed/needed improvement		
Communication	There was no method or system for communication	10	23
	Communication did not occur		
	Communication was unclear, ambiguous or misunderstood		
Training	Training was not developed or implemented	8	18
	Training was inappropriate or insufficient		
	Training was available, but not completed		
	Staff were not qualified or proficient in performing the task		
Management and oversight	Supervision needed improvement	7	16
	Auditing/evaluating/enforcement of standard operating procedure needed improvement		
	Auditing/evaluation/enforcement of training needed improvement		
	Preparation needed improvement		
	Human factors needed improvement		
	Risk assessment needed improvement		
	Worker selection needed improvement		
Other		14	32

Abbreviations: N, total number; n, number
Notes: More than one root cause can be identified in an incident, percentages rounded to nearest whole number. Data are from the Laboratory Incident Notification Canada (LINC) surveillance system

Discussion

Overall, the incidence of laboratory exposures to pathogens and toxins in Canada remain relatively low in 2017, with a total of 44 incidents nation-wide representing slightly less than 5% of all licenced facilities. Most reports described were related to inadequate or breaches in procedures and sharps. Accordingly, SOPs and human error were cited most frequently as root causes of the incident.

We are unable to compare these findings to those in other countries, as there is no other comparable comprehensive national surveillance system. For example, in the United States the focus of incident reporting is limited to bloodborne pathogens.

The main strength of this study is that it is based on mandatory and standardized reporting of laboratory incidents across Canada, across all regulated toxins and pathogens. It therefore provides an overarching picture of biosafety in all licenced laboratories and allows the assessment of the true incidence of exposures and LAIs in Canada (10).

Conversely, the main limitation of this study is that the data may be incomplete. Under certain circumstances, laboratory incidents may not be reported. Incidents may not be detected or may simply not be reported due to a lack of awareness or understanding of the reporting requirements or due to reluctance to report because of the generally negative interpretation of the term "incidents" (9). This is being addressed and, as regulated parties learn more about and normalize the reporting requirements, we expect the reporting frequency will increase over the next few years.

The information provided in the follow-up reports may also be biased due to the nature of the investigative process. Trying to identify the causes of the incident working backward based on the symptoms or general outcome can foster recall bias in the results of the investigation. To mitigate these limitations, the LINC surveillance system continuously makes adjustments to improve the user-friendliness and clarity of the forms and interface. PHAC is developing guidance documents to support regulated parties in incidents reporting and investigation.

There are some interesting preliminary comparisons of the 2016 and 2017 data. Despite the expectation that reporting incidents would increase over the first few years of the system, reporting incidents declined from 46 in 2016 (11) to 44 in 2017. The frequency of exposure incidents decreased in the academic sector (from 35% in 2016 to 27% in 2017) and increased in the hospital sector (from 26% in 2016 to 39% in 2017). Although the number of reported exposure incidents decreased in 2017,

the number of people exposed increased by 18%, largely due to the one exposure incident of 29 people to *Brucella suis*. The proportions of SSBAs increased from 24% in 2016, to 27% in 2017. In both 2016 and 2017, procedures and sharps-related occurrences were the most cited incident types, which concur with the results reported in other studies (9,12,13). Inadvertent possession of an RG3 human pathogen in a containment level two laboratory was more frequently reported in 2017 (at 32%) compared to 2016 (at 22%). However, it should be noted that with only two years of complete data, it is too early to establish reliable baselines or identify trends.

The information acquired from this report is significant for several reasons. It provides an overarching snapshot of the current biosafety practices in laboratories across Canada and the biosafety risks that exist in these settings, which can serve as a comparative baseline for other reporting programs in Canada and elsewhere. PHAC has been able to develop outreach initiatives to improve awareness of commonly occurring incidents. For example, PHAC developed a newsletter with a notice related to sharps injuries due to disposable scalpel blades, and wrote a journal article describing the risk of misidentification of RG3/SSBAs by Matrix Assisted Laser Desorption/ Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS) device (14).

Conclusion

The incidence of laboratory exposure incidents was relatively low in 2017. The most common route of exposure was through inhalation and the most common root causes were problems with SOPs and human error. The LINC surveillance system will continue to identify risk factors and recurrent challenges in biosafety and biosecurity in laboratory settings and contribute to building excellence in investigation and response to laboratory incidents by sharing expertise and lessons learned among the laboratory community.

Authors' statement

DPN – Incident monitoring, data analysis, writing – original draft, writing – review and editing
MH – Incident monitoring, writing – editing, supervision
FT – Incident monitoring, data analysis, writing – editing, supervision

Conflict of interest

None.

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Appendix

Definitions relating to the *Human Pathogens and Toxins Act*

Term	Definition
Biological safety officer (BSO)	An individual designated for overseeing the facility's biosafety and biosecurity practices.
Containment level (CL)	Minimum physical containment and operational practice requirements for handling human pathogens or toxins safely in laboratory environments. There are four containment levels, ranging from a basic to the highest level of containment (1 to 4).
Containment zone	A physical area that meets the requirements for a specified containment level. A containment zone can be a single room, a series of co-located rooms or several adjoining rooms. Dedicated support areas, including anterooms (with showers and 'clean' and 'dirty' change areas, where required), are considered to be part of the containment zone.
Exposure	Contact with, or close proximity to, human pathogens or toxins that may result in infection or intoxication, respectively. Routes of exposure include inhalation, ingestion, inoculation and absorption.
Exposure follow-up report	A tool used to report and document incident occurrence and investigation information for an exposure incident previously notified to the Public Health Agency of Canada.
Exposure notification report	A tool used to notify and document preliminary information to the Public Health Agency of Canada of an exposure incident.
Incident	An event or occurrence involving infectious material, infected animals or toxins that have the potential to result in injury, harm, infection, disease or cause damage.
Laboratory-acquired infection/ intoxication	Infection or intoxication resulting from exposure to infectious material, infected animals, or toxins being handled or stored in the containment zone.
Licence	An authorization to conduct one or more controlled activities with human pathogens or toxins issued by the Public Health Agency of Canada under Section 18 of the *Human Pathogens and Toxins Act*. One licence can cover many containment zones.
Risk group (RG)	The classification of biological material based on its inherent characteristics, including pathogenicity, virulence, risk of spread and availability of effective prophylactic or therapeutic treatments, that describes the risk to the health of individuals and the public as well as the health of animals and the animal population.
Security-sensitive biological agents (SSBAs)	The subset of human pathogens and toxins that have been determined to pose an increased biosecurity risk due to their potential for use as a biological weapon. Security-sensitive biological agents are identified as prescribed human pathogens and toxins by Section 10 of the *Human Pathogens and Toxins Regulations*. This includes all risk group 3 and 4 human pathogens that are in the *List of Human and Animal Pathogens for Export Control*, published by the Australia Group, as amended from time to time, with the exception of Duvenhage virus, Rabies virus and all other members of the Lyssavirus genus, Vesicular stomatitis virus, and Lymphocytic choriomeningitis virus. This also includes all toxins listed in Schedule 1 of the *Human Pathogens and Toxins Act* that are listed on the *List of Human and Animal Pathogens for Export Control* when in a quantity greater than that specified in Section 10(2) of the *Human Pathogens and Toxins Regulations*.
For more definitions, please see the Canadian Biosafety Standard, Second Edition (15).	

CPHLN recommendations for the laboratory detection of Shiga toxin-producing *Escherichia coli* (O157 and non-O157)

L Chui[1]*, S Christianson[2], DC Alexander[3], V Arseneau[4], S Bekal[5], B Berenger[1], Y Chen[6], R Davidson[7], DJ Farrell[8], GJ German[4], L Gilbert[9], LMN Hoang[10], RP Johnson[2], A MacKeen[11], A Maki[6], C Nadon[2], E Nickerson[12], A Peralta[6], SM Radons Arneson[11], Y Yu[6], K Ziebell[2] on behalf of Canadian Public Health Laboratory Network (CPHLN)

Abstract

Shiga toxin-producing *Escherichia coli* (STEC) are important enteric pathogens responsible for sporadic cases and outbreaks of gastroenteritis. *E.coli* O157:H7/NM (STEC O157) are the most commonly known STEC serotypes but it is now increasingly apparent that non-O157 STEC serotypes have been underreported in the past because they were not part of routine screening in many front-line laboratories. The Canadian Public Health Laboratory Network (CPHLN) has identified the need for improved detection and surveillance of non-O157 STEC and has developed the following recommendations to assist in the decision-making process for clinical and reference microbiology laboratories. These recommendations should be followed to the best of a laboratory's abilities based on the availability of technology and resources.

The CPHLN recommends that when screening for the agents of bacterial gastroenteritis from a stool sample, front-line laboratories use either a chromogenic agar culture or a culture-independent diagnostic test (CIDT). CIDT options include nucleic acid amplification tests (NAATs) to detect Shiga toxin genes or enzyme immunoassays (EIAs) to detect Shiga toxins. If either CIDT method is positive for possible STEC, laboratories must have a mechanism to culture and isolate STEC in order to support both provincial and national surveillance as well as outbreak investigations and response. These CPHLN recommendations should result in improved detection of STEC in patients presenting with diarrhea, especially when due to the non-O157 serotypes. These measures should enhance the overall quality of healthcare and food safety, and provide better protection of the public via improved surveillance and outbreak detection and response.

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Keywords: Laboratory testing recommendations, Shiga toxin-producing *Escherichia coli*, O157 STEC, non-O157 STEC, culture independent diagnostic tests, nucleic acid amplification tests (NAATs), enzyme immunoassays (EIAs), chromogenic agar culture

Affiliations

[1] Provincial Laboratory for Public Health, Alberta Public Laboratories, AB

[2] National Microbiology Laboratory, MB & ON

[3] Cadham Provincial Laboratory, MB

[4] Health Prince Edward Island, PE

[5] Laboratoire de Santé Publique du Québec, QC

[6] Public Health Ontario, ON

[7] Queen Elizabeth II Health Science Centre, NS

[8] Roy Romanow Provincial Laboratory, SK

[9] Provincial Public Health and Microbiology Laboratory, Eastern Health, NL

[10] BC Centre for Disease Control Public Health Laboratory, BC

[11] Canadian Public Health Laboratory Network, MB

[12] The New Brunswick Enteric Reference Centre, NB

***Correspondence:**
linda.chui@ahs.ca

Introduction

Escherichia coli are part of the normal flora of the gut. However, Shiga toxin-producing *Escherichia coli* (STEC) are intestinal pathogens. Although they typically cause a self-limited episode of diarrhea and abdominal pain, on rare occasions they cause severe—and potentially fatal—sequelae such as hemolytic uremic syndrome (1).

E. coli O157:H7/NM (STEC O157) are the most common STEC serotypes causing infection in humans, but many non-O157 STEC serotypes have been associated with serious illness and major outbreaks (2). In 2011 there was a European outbreak of *E. coli* O104:H4 (3). In 2016, there was an outbreak in Canada and the United States of STEC O121 infections associated with flour (4).

These recent outbreaks of non-O157 serotypes have highlighted the clinical importance of timely and reliable detection and surveillance of these organisms (5–10).

In 2016, 642 cases of STEC infections were reported to the Canadian National Enteric Surveillance Program (NESP); approximately 35% were caused by non-O157 STEC (11). Current data for Canada on non-O157 STEC infections are likely an underestimate as they are not part of routine screening in many laboratories (11,12). There are several reasons for this gap. STEC O157 is readily identified using differential and selective media such as Sorbitol-MacConkey agar and chromogenic O157 agar. Unlike O157 STEC, non-O157 STEC lack the phenotypic characteristics that readily distinguish them from generic *E. coli*, making culture-based isolation challenging.

Detection of non-O157 STEC subtypes

Improvements to laboratories' ability to identify non-O157 STEC are based on the use of chromogenic and/or selective agars and culture-independent diagnostic tests (CIDT). The two common CIDTs include nucleic acid amplification tests (NAATs) for detection of Shiga toxin genes, and enzyme immunoassays (EIAs) that detect Shiga toxins. Less common CIDTs include Shiga toxin detection by cell culture cytotoxicity assays or reverse passive latex agglutination test, and isolation of selected serogroups by O-antigen immunomagnetic bead-capture methods. However, these methods are not practical in most front-line microbiology laboratories. Not only is it important to identify the STEC subtype, it is also essential to have isolates for further characterization such as serotyping, molecular genotyping and whole genome sequencing.

Each detection method has its advantages and disadvantages. Chromogenic agar has a sensitivity of greater than 85% (13). It is less costly than other methods and can be easily substituted into a laboratory's workflow by replacing the current O157-specific plates. However, chromogenic agar can be inhibitory to some STEC serotypes (14). As for the detection of Shiga toxins by EIA, both microwell and lateral flow formats are available. The sensitivity of EIAs is lower for direct stool testing; however, overnight enrichment in MacConkey broth (15) or other suitable broth may provide sensitivity approaching that of NAATs (13,16). Both in-house and commercial NAATs have equivalent sensitivities and are the most sensitive methods available (15,17). Many NAATs can be performed directly on stool samples (18), improving the turn-around time compared to culture and EIA. Multiplex NAATs have the added advantage of detecting multiple pathogens concurrently. Both EIAs and NAATs will detect Shiga toxins and Shiga toxin genes respectively from any serotype of STEC. However, EIAs and NAATs are more expensive than agar for screening. NAATs also require laboratories to purchase additional equipment, designated space for molecular set-up and specialized training of personnel, which may be impractical for many frontline laboratories.

Public health implications

Isolation and further subtyping enables the comparison of STEC strains in order to identify outbreaks and potential sources of infection. Once the suspected source of the outbreak is identified, tracing and outbreak management activities by public health officials can prevent further transmission and promote public awareness.

The objectives of the following recommendations are to identify laboratory choices in a testing workflow for the detection, confirmation of STEC in stool specimens, and recovery of positive isolates for further characterization.

Recommendations

The Canadian Public Health Laboratory Network (CPHLN) recommends that when screening for the agents of bacterial gastroenteritis, front-line laboratories use one or more of three options for the detection of STEC: NAAT, culture on selective agar, or broth enrichment plus an EIA (**Figure 1**). Stool specimens submitted for STEC detection should follow local guidelines for submission and testing. Laboratories using chromogenic agar as their primary screening method may consider using an EIA method with broth enrichment or a NAAT in selected cases where there is a high suspicion of STEC infection and chromogenic agar results are negative.

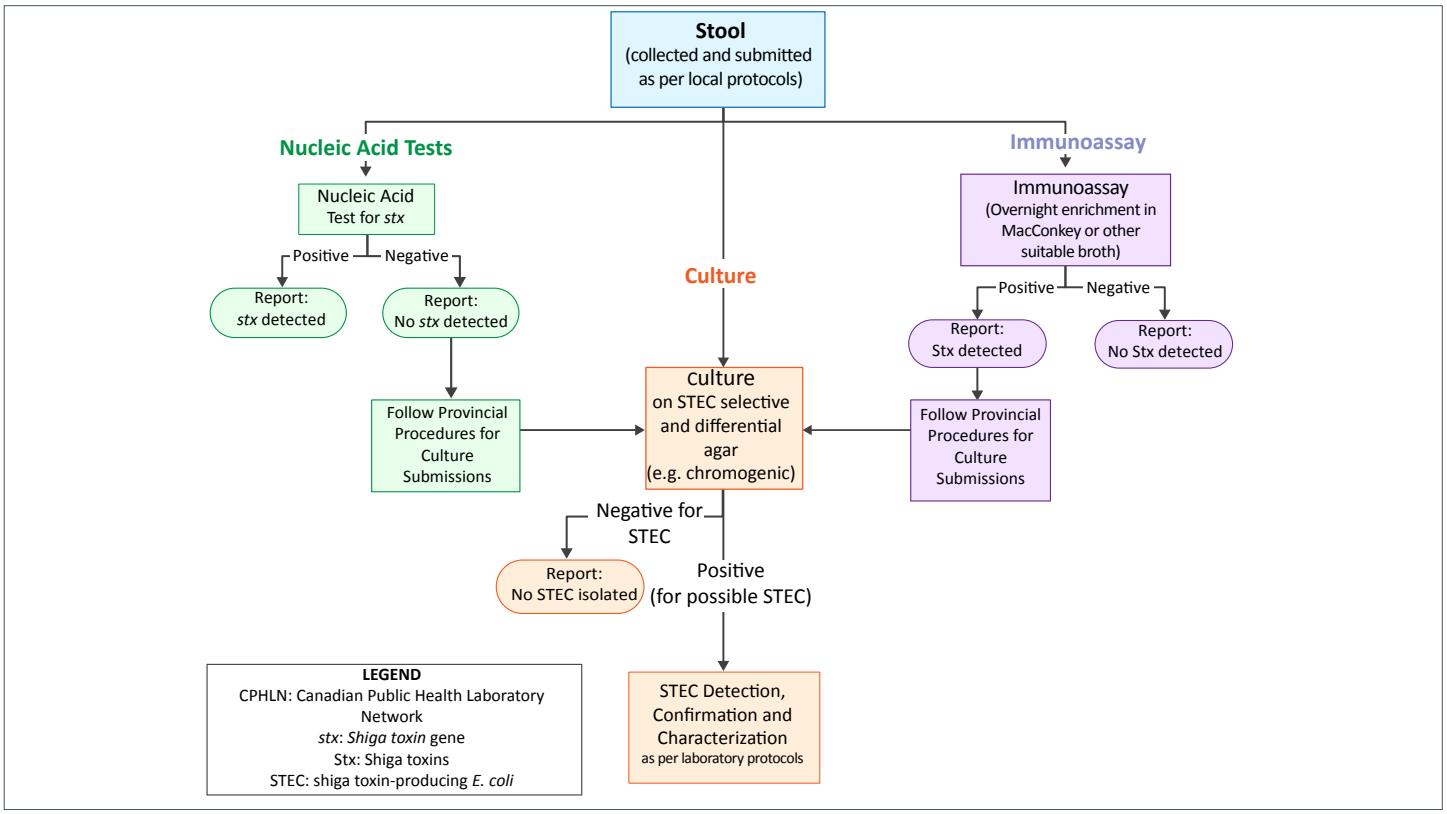
If CIDT is implemented for STEC testing, culture is still recommended for the recovery of isolates for further characterization when Shiga toxins or Shiga toxin genes are identified. CPHLN culture recommendations following CIDT can be found in Berenger et al. (19). It is imperative that front-line laboratories communicate with their referral public health laboratories to determine the required work-up for culture, isolation or characterization of isolates before submitting any samples.

Discussion

To accurately diagnose all STEC-related cases of gastroenteritis that may lead to outbreaks and have public health implications, it is important that both O157 and non-O157STEC serotypes are identified. To facilitate this, screening should be done using either culture or CIDT by a NAAT or an EIA. If the CIDT is positive for possible STEC, then culture is needed for STEC confirmation and characterization.

Laboratories should follow the CPHLN recommendations to the best of their abilities based on the availability of technology and resources. It is important to emphasize that when STEC are detected, culturing the organism is of paramount importance for further characterization (typing and subtyping), as well as

Figure 1: Recommendations for the detection of Shiga toxin-producing *Escherichia coli* in stool specimens



to facilitate the outbreak response and support surveillance programs, including PulseNet Canada and the National Enteric Surveillance Program.

The role of the provincial or federal laboratories is to support front-line laboratories by performing confirmatory testing as necessary, as well as serotyping and other reference laboratory services for STEC isolates. These laboratories are also available to assist with facilitating the implementation of these new testing algorithms for non-O157 STEC. The public health laboratory system varies among provinces; so any changes in public health laboratory protocols that may impact the capacity of front-line laboratories to follow these recommendations must be discussed with the front-line laboratories and other stakeholders prior to implementation.

Conclusion

Following these CPHLN recommendations should result in improved detection of STEC in patients presenting with diarrhea, especially the non-O157 serotypes. These measures will enhance the overall quality of health care and food safety, and provide better protection of the public via improved surveillance, and outbreak detection and response.

Authors' statement

All authors are members of the Canadian Public Health Laboratory Network (CPHLN) Shiga toxin-producing *Escherichia coli* (STEC) Working Group. This group was chaired by L Chui (Provincial Co-Chair) and S Christianson (Federal Co-Chair).

Conflict of interest

None.

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Canada Communicable Disease Report Editorial Team[1]

Affiliation

[1] CCDR Editorial Office, Infection Prevention and Control Branch, Public Health Agency of Canada Ottawa, ON

***Correspondence**: phac.ccdr-rmtc.aspc@canada.ca

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In the article "The continued rise of Lyme disease in Ontario, Canada: 2017" (1) the following correction was made on October 11, 2018 upon the request of the authors.

In the section titled "Affiliations", the following affiliation was added and identified as number eight (8), National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, MB and associated with the author K. Cronin.

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Public Health Agency of Canada
130 Colonnade Road
Address Locator 6503A
Ottawa, Ontario K1A 0K9
phac.ccdr-rmtc.aspc@canada.ca

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