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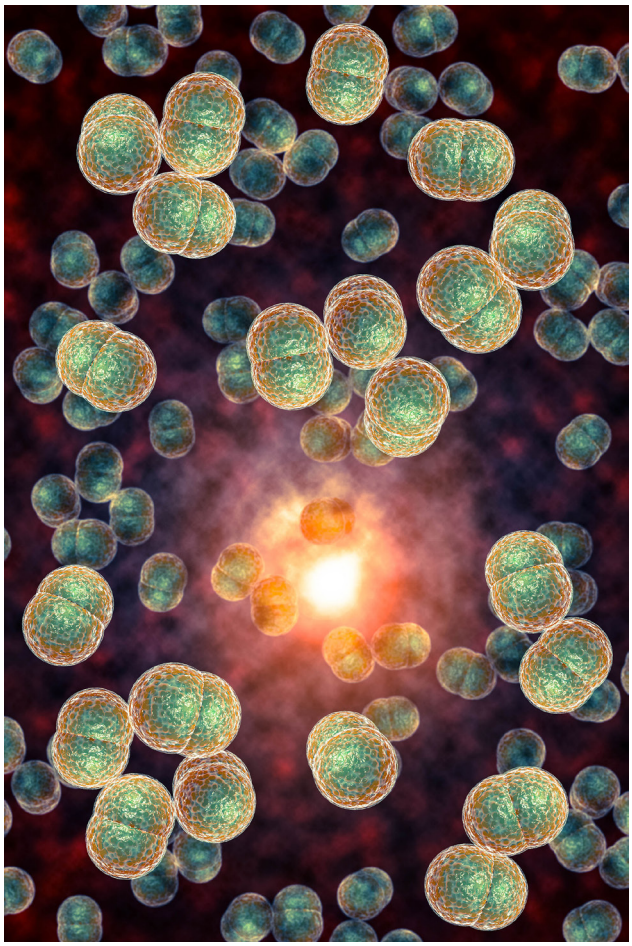

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The *Canada Communicable Disease Report* (CCDR) is a bilingual, peer-reviewed, open-access, online scientific journal published by the Public Health Agency of Canada (PHAC). It provides timely, authoritative and practical information on infectious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

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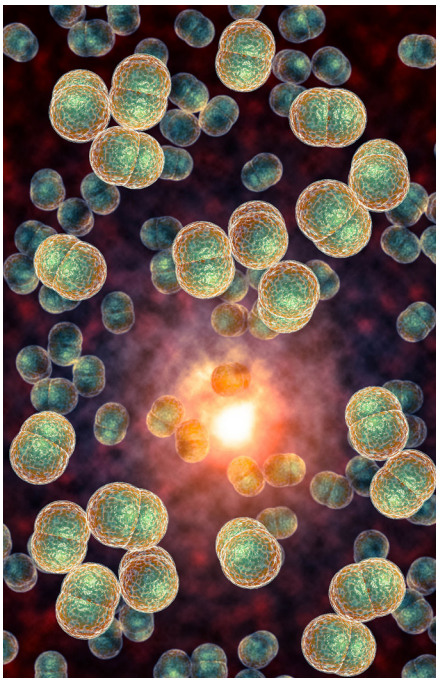

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Increase in *Neisseria meningitidis* serogroup W invasive disease in Canada: 2009–2016

RSW Tsang[1*], L Hoang[2], GJ Tyrrell[3], G Horsman[4], P Van Caeseele[5], F Jamieson[6,7], B Lefebvre[8], D Haldane[9,10], RR Gad[11], GJ German[12], G Zahariadis[13,14]

Abstract

Background: Since 2010, there has been an increase in serogroup W *Neisseria meningitidis* (MenW) disease in many countries due to an emerging sequence type-11 clonal complex (ST-11 CC). In 2016, a small increase in MenW disease due to the ST-11 CC was documented in Ontario, Canada.

Objective: To examine the trends in MenW disease in Canada and to assess whether there have been changes in the type of ST clonal complex causing MenW disease between 2009-2016.

Methods: Invasive *N. meningitidis* isolates routinely submitted from across the country to the National Microbiology Laboratory were analyzed. The proportional distribution of MenW compared with other serogroups was calculated. The MenW isolates were then further characterized by serotype, serosubtype and ST clonal complex. The geographic distribution of the emerging ST-11 CC was documented and the age of patients with ST-11 CC was compared with the traditional ST-22 CC.

Results: Of the 888 invasive isolates examined, 63 were MenW giving an average annual rate of 7.1%. However, the percentage of MenW varied from 2.7% in 2012 to 18.8% in 2016. From 2009 to 2013, 91% of the MenW were typed as the traditional ST-22 CC while from 2014 to 2016, 75% were typed to be the emerging ST-11 CC. ST-11 MenW CC was documented in five provinces across Canada (British Columbia, Alberta, Manitoba, Ontario and Quebec). The median age of patients infected with the emerging ST-11 MenW CC was 53.5 years, while for patients with the traditional ST-22 CC it was 23.5 years.

Conclusion: MenW meningococcal disease is growing in prevalence in Canada and is associated with an increase in the emerging ST-11 CC. This emerging clonal complex has now been identified in five provinces in Canada. It appears to be more common in older patients than the traditional ST-22 CC, which occurs more often in younger patients.

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Introduction

Invasive meningococcal disease (IMD) has been a notifiable disease in Canada since 1924 (1). It is caused by *Neisseria meningitidis*, which normally resides in the upper respiratory tract of healthy carriers. For reasons not completely understood, *N. meningitidis* may invade the blood stream and cause serious systemic infection leading to meningitis, septicemia, septic arthritis, bacteremic pneumonia and pericarditis (2). Initial clinical presentation of IMD can be nonspecific but it may progress rapidly, leading to septic shock. The disease has an average case-fatality rate of 10% (3).

N. meningitidis is classified into 12 serogroups based on antigenic specificities of their polysaccharide capsules. Most invasive diseases are caused by six serogroups: A (MenA), B (MenB), C (MenC), W (MenW), X (MenX) and Y (MenY).

These invasive strains belong to a handful of genetic lineages known as hypervirulent clones, such as sequence type (ST)-32 [electrophoretic type (ET)-5], ST-41/44 (lineage 3), ST-11 (ET-37), ST-8 (cluster A4), ST-5 (subgroup III) and ST-269 clonal complexes (CCs) (4,5).

The strains causing IMD have been described as "shifting sands", with unique strains emerging with the potential to spread regionally and internationally. For example, MenA of subgroup III caused epidemics in China in the 1960s and subsequently spread to Russia and then globally (6). ET-5 MenB caused an intercontinental outbreak with a wide geographic spread that lasted for over a decade (7). The ET-15 MenC clone first emerged in Canada in the mid-1980s and led to worldwide dissemination, which ultimately led to the introduction of MenC conjugate vaccine programs in many countries. Other notable MenB clones that have caused epidemics include cluster A4 and lineage 3 (5).

The first report of MenW causing a major outbreak or epidemic occurred in 2000; this outbreak started in Saudi Arabia during the Hajj and involved more than 400 cases. The strain was characterized as ST-11 clonal complex (8). With pilgrims returning to their countries in Africa, Asia, Europe, North America and South America, this strain was disseminated globally. The gradual increase in MenW disease in recent years was first reported in sub-Saharan Africa (9) and South America (10,11). Since 2010, other countries have reported an increase in IMD caused by ST-11 MenW (12-15).

In December 2016, Tsang et al. (16) reported an increase in invasive MenW strains in Ontario, Canada. This increase started in 2014 and was associated with a replacement of the traditional ST-22 clonal complex with the ST-11 clonal complex (16). There was also a small increase in the number of MenW IMD cases in that province. To determine if clonal replacement had occurred in MenW disease nationally, this study examines the trends in MenW disease and changes in clonal complex in Canada between 2009 and 2016.

Methods

Provincial public health laboratories receive case isolates from hospitals and clinical diagnostic laboratories for identification and serogroup typing. As part of the enhanced surveillance program on IMD, all provinces and territories in Canada routinely submit all their invasive *N. meningitidis* isolates from culture-confirmed cases to the National Microbiology Laboratory (NML) for serogroup confirmation and additional strain characterization (17). This study included all *N. meningitidis* isolates obtained from culture-confirmed IMD cases submitted to the NML between 2009 and 2016.

Typing of meningococci

At the NML, serogrouping is done by slide agglutination using rabbit anti-grouping antisera produced in-house and/or polymerase chain reaction (PCR) (18). Serotyping and serosubtyping is done by whole-cell enzyme-linked immunosorbent assay (ELISA) using monoclonal antibodies (19). PorA genotyping and multilocus sequence typing were conducted according to previously described standard methods (20,21).

Geographic distribution, source and patient characteristics

Based on the requisition information provided by the provincial public health laboratories, the NML collects and analyzes information on the geographic origin of the specimens, the source (e.g. blood, cerebral spinal, pericardial or intra-articular fluid) and the age and sex of patients from whom the specimens were drawn.

Results

Trends in MenW meningococcal disease

In Canada, between 2009 and 2016, a total of 888 *N. meningitidis* isolates were recovered from individual IMD cases and sent to the NML. Of these, 63 were grouped as MenW. The percentage of MenW isolates varied by year from a low of 2.7% in 2012 to a high of 18.8% in 2016 (**Table 1**), for an average percentage of 7.1%.

Table 1: Contribution of *Neisseria meningitidis* serogroup W (MenW) in culture-positive invasive meningococcal disease cases, Canada 2009–2016

Year	Number of MenW case isolates	Total number of IMD case isolates	MenW case isolates as a percentage of IMD case isolates
2009	12	168	7.1%
2010	6	118	5.1%
2011	10	133	7.5%
2012	3	112	2.7%
2013	5	103	4.9%
2014	6	86	7.0%
2015	6	88	6.8%
2016	15	80	18.8%
All years	63	888	7.1%

Abbreviations: IMD, invasive meningococcal disease; MenW, *Neisseria meningitidis* serogroup W

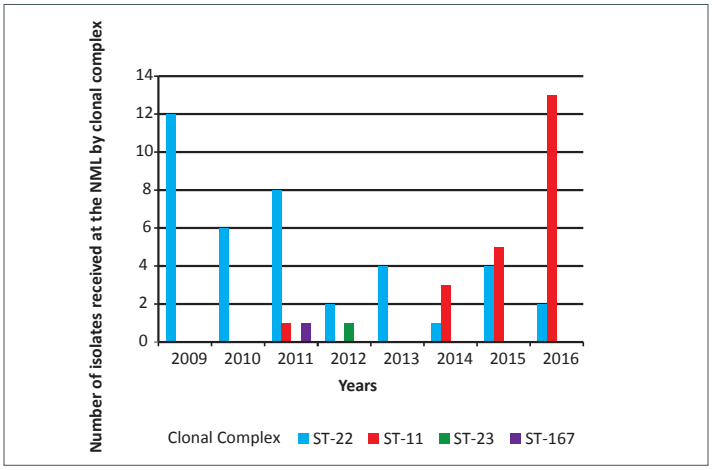
Changes in clonal complex

The increase in the number of MenW isolates from IMD cases coincided with the identification of the ST-11 (ET-37) CC (**Figure 1**). From 2009 to 2013, 91% (32 out of 35) MenW isolates were typed as the traditional ST-22 clonal complexes whereas from 2014 to 2016, only 25% (7 out of 28) MenW isolates belonged to this clonal complex. Over this same period, the emerging ST-11 clonal complex increased from 3% (1 out of 35 isolates) to 75% (21 out of 28 isolates).

Antigenic and genetic characterization

Almost 70% (27 out of 39) of the traditional ST-22 CC MenW isolates were typed as either W:NT (non-serotypeable):P1.6 (n =19) or W:NT:P1.– (non-serosubtypeable; n = 8) with the PorA genotype of P1.18-1,3,38. Five other ST-22 MenW were

Figure 1: Clonal analysis of invasive *Neisseria meningitidis* serogroup W (MenW) in Canada, 2009–2016



Abbreviations: NML, National Microbiology Laboratory; ST, sequence type

typed as W:NT:P1.– with a deletion in their PorA genes. The other seven ST-22 CC MenW were non-serotypeable with serosubtype antigens of either P1.5 (n = 1), P1.5,2 (n = 1), P1.14 (n = 2), P1.16 (n = 2) or P1.– (n = 1). Twelve different sequence types were identified among these 39 ST-22 CC MenW, with 15 isolates belonging to ST-184, 11 to ST-22, three to ST-8974 and two to ST-1617. The remaining eight isolates each belonged to a different sequence type (ST-1221, ST-1224, ST-1476, ST-2625, ST-3137, ST-3849, ST-8230 and ST-10188).

In contrast, 100% (all 22) of the ST-11 CC MenW isolates were typed as C:2a:P1.5,2 (n = 21) or C:2a:P1.2 (n = 1), with the PorA genotype of P1.5,2,36-2. Twenty-one belonged to ST-11 and one to ST-10826. There was also one MenW isolate that typed as ST-23 (ST-23 CC) and one isolate typed as ST-3705 (ST-167 CC). The former had the antigenic formula of W:19:P1.– with PorA genotype of P1.5-2,10-1,36-2 while the later was W:19:P1.5 with PorA genotype of P1.5-1,10-4,36-2.

Geographic, demographic and source data

MenW isolates of the ST-11 CC were found in British Columbia (n = 5), Alberta (n = 3), Manitoba (n = 2), Ontario (n = 8) and Quebec (n = 4). The sex and age distribution of cases due to ST-22 and ST-11 CCs are shown in **Table 2**. For the traditional ST-22 CC MenW cases, the mean and median ages were 31.7 years and 23.5 years, respectively. The mean and median ages of patients with emerging ST-11 CC MenW were 47.9 years and 53.5 years, respectively. Eight patients under 2 years old were identified with ST-22 CC MenW; no one in this age group was diagnosed with ST-11 CC MenW. Of the ST-22 CC MenW isolates, 33 were from blood cultures, three from cerebral spinal fluid cultures, two from articular fluids and one from the pericardial fluid. Of the 22 isolates of ST-11 CC MenW from across Canada, 21 were from blood cultures and only one from cerebral spinal fluid culture.

Table 2: Demographic characteristics and specimen source for invasive *Neisseria meningitidis* serogroup W (MenW) cases according to clonal complex in Canada, 2009–2016

Demographics and specimen source	ST-22 clonal complex isolates n (%)	ST-11 clonal complex isolates n (%)
Sex		
Male	20 (51%)	13 (59%)
Female	19 (49%)	9 (41%)
Age		
< 12 months	4 (10%)	0
12–23 months	4 (10%)	0
2–5 years	6 (15%)	2 (10%)
6–10 years	1 (3%)	0
11–20 years	5 (13%)	4 (18%)
21–40 years	5 (13%)	2 (10%)
41–60 years	5 (13%)	7 (31%)
> 60 years	8 (21%)	7 (31%)
Unknown	1 (3%)	0
Specimen source		
Blood	33 (84.6%)	21(95%)
Cerebral spinal fluid	3 (7.7%)	1 (5%)
Others[1]	3 (7.7%)	0
Total number. of samples	39 (100%)	22 (100%)

Abbreviations: n, number; ST, sequence type
[1] Shoulder, pericardial or articular fluid

Discussion

From 2009 to 2016, while the overall number of IMD cases in Canada decreased, the percentage of cases due to MenW increased from 2.7% in 2012 to 18.8% in 2016. This increase in MenW disease was associated with a clonal shift in the MenW strain from ST-22 CC to ST-11 CC. This emerging ST-11 CC MenW clone has now been documented in five provinces. It tends to occur in middle-aged and older adults.

ST-11 CC is a long-established hypervirulent clonal complex that was first identified in 1917 in a serogroup B strain (5). In the 1960s and 1970s, ST-11 CC was associated with MenB in North America and Europe (5). In the mid-1980s, a genetic variant of ST-11 CC that caused IMD in teenagers in Ontario appeared in a MenC clone designated as ET-15 (22). Like others in the ST-11 clonal complex, this ET-15 clone spread rapidly in North America and eventually globally (23). The MenC conjugate vaccine was first included in the publically funded childhood immunization program in the United Kingdom, in 1999 (24). In Canada, the MenC conjugate vaccine was licensed in April 2001. Beginning in 2002, some provinces started routine MenC conjugate vaccine immunisation programs and by 2007 all provinces and territories have implemented such programs (25).

The first major ST-11 CC MenW outbreak occurred during the Hajj pilgrimage in 2000. The pilgrims returning to their countries initiated the global dissemination of this clone (26). In England and Wales, the increase in the ST-11 MenW clone first became apparent in 2009/2010 (27) and its prevalence increased yearly until 2015 when a targeted vaccination program was introduced (28). A similar increase in MenW disease as a result of the same clone has been seen in Australia since 2013 (29), also leading to the introduction of a targeted vaccination program (30). The ST-11 CC MenW has now been documented in a number of other countries around the world (9-15).

The Canadian ST-11 CC MenW isolates have serotype antigen 2a and serosubtype antigen P1.5,2, typical of isolates of this clonal complex (31). They also differ antigenically from meningococci of the ST-22 CC. Currently there is no evidence to suggest that these ST-11 MenW arose by capsule switching from MenC ST-11 strain. Investigations into the MenB ST-11 that arose from MenC ST-11 by capsule switching suggest that these capsule-switched strains may not be stable for endemic spread (32). Rather, the increase in MenW ST-11 isolates in Canada and elsewhere is likely due to clonal expansion of an endemic strain (25,26).

This study has two limitations. First, it included only bacteriologic culture-confirmed cases and not those confirmed using PCR. However, only about 10% of the IMD cases confirmed in Canada between 2006 and 2011 were diagnosed by PCR (17) and there is no evidence to suggest that PCR-diagnosed cases differ from culture-confirmed cases. Second, this study does not include data on the meningococcal vaccination history of patients with MenW. The quadrivalent meningococcal A, C, W and Y conjugate vaccine has protective immunity against MenW, but determining if any of the patients had been vaccinated prior to their illness was not possible.

Some provinces in Canada have quadrivalent meningococcal A, C, W and Y conjugate vaccine programs targeting primary or high school students (33). The protective immunity offered by this quadrivalent vaccine in the student population may have moderated the effect of the expansion of the ST-11 MenW clone in Canada. Of note, fewer MenW cases have been identified in Canada than in the United Kingdom or Australia, where a vaccine program was more recently introduced (28,30).

It is important to note that IMD due to MenW ST-11 CC may have an atypical clinical presentation. In England, for example, a review of MenW cases in teenagers (aged 15 to 19 years) found that 7 out of 15 patients initially presented with acute gastrointestinal symptoms of nausea, vomiting and diarrhea; four were sent home from hospital, delaying the diagnosis (34). In another study of 129 MenW cases in England and Wales from 2010 to 2013, half of which were diagnosed in patients aged 45 years or above, 23% were with atypical clinical presentations of pneumonia (12%), septic arthritis (7%) and epiglottitis or supraglottitis (4%) (26). The unusual initial clinical symptoms may have implications in the early diagnosis of the disease. Timely diagnosis of IMD is important for patient treatment, contact tracing and public health control of the disease. Ongoing surveillance of these trends is indicated.

Conclusion

In summary, the traditional endemic MenW ST-22 CC has been replaced by an abrupt emergence of MenW ST-11 CC in five provinces in Canada. Although the overall number of MenW cases in Canada remains small, MenW is responsible for 19% of all IMD cases. Of note for clinicians and public health professionals, this ST-11 MenW clone has the potential to cause outbreaks, has occurred in an older age group in Canada and may have an atypical clinical presentation. The NML will continue its surveillance program on this disease including laboratory characterization of strains.

Authors' statement

All authors (RSWT, LH, GJT, GH, PVC, FJ, BL, DH, RRG, GJG, and GZ) are involved in the surveillance of invasive meningococcal disease in Canada. RSWT prepared the first draft and all authors contributed to the final version with comments and suggestions.

Conflict of interest

None.

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RAPID COMMUNICATION

First reported case of multidrug-resistant *Candida auris* in Canada

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Abstract

Candida auris is a fungal pathogen that has recently emerged as a global threat to public health. It was first described in Japan in 2009 and has since been reported in 17 countries on five continents. This case report describes the first reported case of multidrug-resistant *C. auris* in Canada.

In May 2017, a 64 year-old individual was evaluated for chronic otitis externa. Past medical history included a recent hospitalization in India for elective oral surgery that was complicated by an odontogenic brain abscess. Upon return to Canada, the individual was admitted to a hospital for neurosurgical drainage of the brain abscess and parenteral antibiotics. Early during hospitalization, the patient was identified as a carrier of carbapenem-resistant *Enterobacteriaceae* and was placed on contact precautions. Also early during this hospitalization, a chronic otitis media was managed with placement of a typanostomy tube with drainage of clear fluid from the ear, which continued through the admission and after discharge to a post-neurosurgical rehabilitation facility. During outpatient follow-up, swabs of the ear discharge cultured *C. auris* that was resistant to fluconazole and amphotericin B. There was no clinical response to ototopical antifungal therapy. Surgical evaluation for management of the otomastoiditis is pending.

There is a potential for *C. auris* to cause infection in health care settings. It can persist in hospital environments, has the potential for transmission and can cause invasive disease. It is difficult to identify and often resistant to antifungal medications. The application of infection prevention and control recommendations can help prevent nosocomial transmission. It is now prudent to consider the risk of *C. auris*, in addition to the known risk of other antimicrobial resistant organisms, in any traveller who has been hospitalized while outside the country. When identified, contacting local public health can assist in the tracking and management of this emerging disease.

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Case

In May 2017, a 64-year-old individual was evaluated for chronic otitis externa. The patient had a two-year history of recurrent ear complaints. Nine months prior to presentation, a general practitioner clinically diagnosed otomycosis based on bilateral ear pain and drainage of serous "cheesy" fluid from one ear. Topical flumethasone pivalate 0.02%-clioquinol 1% was prescribed for eight weeks with resolution of the drainage. Two months later, the patient complained of bilateral ear pain without drainage and was prescribed oral amoxicillin by the same clinician for presumed acute otitis media.

Past medical history included oral surgery conducted in India three months prior to presentation, complicated by an odontogenic brain abscess that resulted in a 24-day hospitalization in India. While hospitalized, a high-resolution computed tomography (CT) scan of the temporal bone demonstrated chronic otitis media with mastoiditis, and osteomyelitis of the mastoid, petrous wall and anterior wall of the middle ear cavity on one side and a mild mastoiditis on the other side. The patient was treated with empiric antibacterial and anti-tuberculosis therapy and, after initial clinical improvement, returned to Canada and presented to a community hospital for further care. A CT of the brain demonstrated a persistent left frontal abscess and the patient was transferred to a tertiary care hospital for further investigations and management. Early in the tertiary hospital admission, screening rectal swabs identified carbapenem-resistant *Enterobacteriaceae*, so the patient was placed on contact precautions. An aspirate of the brain abscess was obtained for diagnosis; although bacterial, mycobacterial and fungal stains and cultures were negative for organisms, amplification and sequencing of 16S RNA identified *Streptococcus mitis*. The patient was treated with parenteral antibiotics for two months as an inpatient and another month at home, with good clinical and radiographic response. The patient also had a history of emphysema, borderline diabetes mellitus and asymptomatic, early cirrhosis of undetermined etiology.

Shortly after admission to the tertiary hospital in Canada for management of the brain abscess, the patient was also treated by an otolaryngyologist for chronic otitis media with a tympanostomy tube, leading to drainage of clear fluid. The drainage continued throughout the remaining three weeks

of admission to the tertiary care hospital and a one-month admission for post-neurosurgical rehabilitation in a third hospital for complications arising from the brain abscess.

During outpatient follow-up, a swab of the ongoing ear drainage was sent for bacterial and fungal culture. A yeast grew, identified as *Candida auris* by matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry (Bruker MALDI Biotyper System, RUO MBT Compass 4.1.70). Using the CLSI microbroth dilution method, and based on the tentative MIC break-points suggested by the United States (US) Centers for Diseases Control and Prevention (CDC) (1), testing found the *C. auris* sample was resistant to fluconazole and amphotericin B, likely resistant to voriconazaole and susceptible to micafungin. (**Table 1**). The fungus also grew on four repeat swabs of the discharge from the same ear, over a six-week period. Identification of the five isolates as *C. auris* by MALDI-TOF was done by the hospital laboratory. An isolate was sent to a mycology laboratory where drug resistance testing was performed. Whole genome sequence analysis performed by the National Microbiology Laboratory (NML) was consistent with *C. auris*. Further analyses to compare the isolate with global strains are pending.

Table 1: Summary of susceptibility testing of *Candida auris* isolate from the first reported case in Canada

Class	Drug	Tentative MIC Breakpoints[1]	Results from *C. auris* isolate	Interpretation
Triazoles	Fluconazole	≥ 32µg/mL	128 µg/mL	Resistant
	Voriconazole	N/A[2]	N/A[2]	Likely resistant[2]
Polyenes	Amphotericin B	≥ 2µg/mL	2 µg/mL	Resistant
Echinocandins	Micafungin	≥ 4µg/mL	0.5 µg/mL	Susceptible

Abbreviations: MIC, minimum inhibitory concentration, N/A, Not available
[1] Tentative (MIC) breakpoints for *C. auris* from the United States Centers for Disease Control and Prevention (CDC) (1)
[2] Until MIC breakpoint is available, CDC suggests considering using fluconazole susceptibility as a surrogate for second generation triazole susceptibility assessment, noting however that isolates that are resistant to fluconazole may respond to other triazoles occasionally

Upon outpatient reassessment by an otolaryngologist, there was evidence of myringitis and otitis externa. The ear canal contained moist white debris, which was removed. A tympanostomy tube was *in situ*, draining a clear discharge; this tube was left in place. The patient was retreated topically with flumethasone pivalate 0.02%-clioquinol 1% drops, but without improvement after two weeks. The patient has been referred to a neurotologist for surgical assessment. Case resolution of the otitis externa and the chronic mastoiditis was pending at the time of the report.

Discussion

This is the first reported case of multidrug-resistant *C. auris* in Canada. *C. auris* was first described in Japan in 2009 (3), and has since been reported in 17 countries on five continents (2,4). Only four *C. auris* isolates from prior to 2009 were identified retrospectively among 15,271 isolates in a global candidemia registry (5), suggesting rapid global dispersal. *C. auris* has already established a firm foot-hold in some healthcare settings. In developing countries, the risk of *C. auris* transmission is compounded by limitations in capacity for fungal identification, antifungal susceptibility testing and infection prevention and control (IPC). In India, for instance, *C. auris* already accounts for 5% of the isolates implicated in candidemia in intensive care units nationwide (6) and as many as 30% in some centres (7).

Several features of *C. auris* make infection challenging to manage and heighten concern for nosocomial transmission: it can persist on patients and in hospital environments; it is difficult to identify; it can cause invasive disease; and treatment options are limited (1,4,7). Indeed, recalcitrant healthcare-associated outbreaks have been reported from the United Kingdom and the United States (9,10), and genetic studies have implicated closely related (clonal) strains, suggesting effective horizontal transmission (5,7,9,10).

C. auris can persist in hospital environments

The tenacity of *C. auris* has been demonstrated during outbreak investigations in which the organism could be isolated from patients' skin (up to three months following infection) and patient environments (9,14). The capacity of *C. auris* to adhere to polymeric surfaces and form biofilms may contribute to difficulty in eradicating this organism from the environment (15).

C. auris is difficult to identify

Correct identification of *C. auris* can be difficult for clinical microbiology laboratories and this may delay implementation of appropriate IPC procedures. *C. auris* can be misidentified by commercial identification systems such as Vitek-2 (as *C. haemulonii* or *C. famata*) and API-20C (as *Rhodotorula glutinis*, *C. sake* or *Saccharomyces cerevisiae*) (16). *C. auris* can be correctly identified by MALDI-TOF using "research-use only" databases and by sequencing of the internal transcribed spacer and D1-D2 domains (16). Limitations also exist for some antifungal susceptibility testing methods (16); for instance, Vitek-2 may give falsely elevated MICs for amphotericin B and the broth microdilution method may give falsely elevated MICs for caspofungin (16).

C. auris can cause invasive disease

Although the first reported cases of *C. auris* were patients with chronic otomycosis (3,11), most subsequent cases have been healthcare-associated and involved candidemia or other invasive infections (2). Persistent candidemia (lasting up to three weeks after antifungal initiation) and high mortality rates have been observed (7). A murine model of candidemia suggested that *C. auris* was nearly as virulent as *C. albicans*, the predominant cause of invasive candidiasis worldwide (12); precise virulence factors are still being investigated, although some appear to be strain-dependant (13).

Treatment options are limited

Decreased antifungal susceptibility among isolates is a universal feature of *C. auris*. Fluconazole resistance exceeds 90% (5) and reduced susceptibility to voriconazole may approach 50% (2). Tentative breakpoints for the newer triazoles, posaconazole and isavuconazole, are not available, but low MICs suggest that they may have activity against *C. auris* (2). Resistance to amphotericin B occurs in up to 35% of isolates (5) and echinocandin resistance has been reported in 2-8% of isolates (2,5). Resistance to all three major classes of antifungals was reported in 4% of isolates (5).

The optimal management of *C. auris* disease is currently unknown (2). Where invasive disease is involved, systemic antifungal therapy should be guided by results of susceptibility testing. Management of otomycosis and otomastoiditis caused by *C. auris* is even less clear. Evaluations of the efficacy of ototopical agents against *C. auris* have not been published and the options for multidrug-resistant isolates, as in this case, are limited.

Infection prevention and control can limit spread

Infection prevention and control measures can be effective in limiting the spread of *C.auris*. Interim IPC recommendations from the CDC include single rooms and contact precautions for colonized or infected patients, periodic reassessments for ongoing colonization as well as daily and terminal cleaning of surfaces with a disinfectant effective against *Clostridium difficile* spores (See **text box**) (10).

Summary of *Candida auris* Interim Recommendations for Healthcare Facilities from the United States Centers for Disease Control and Prevention (10)

Use standard and contact precautions

Patients in acute care hospitals and nursing homes should be placed in single rooms on Standard and Contact Precautions. Continue Contact Precautions as long as the person is colonized with *C.auris*.

Use a disinfectant effective against *Clostridium difficile* spores

Healthcare facilities that have patients with *C. auris* infection or colonization should ensure thorough daily and terminal cleaning and disinfection of these patients' rooms with hospital-grade disinfectant effective against *Clostridium difficile* spores

Conduct periodic reassessments

Periodic reassessments for presence of *C. auris* colonization (every 1–3 months) can help inform duration of infection control measures. Assessments of colonization should involve testing of, at a minimum, swabs of the axilla and groin and also may include sites yielding *C. auris* on previous cultures.

Provide notification upon transfer

When patients are transferred to other healthcare facilities, receiving facilities should receive notification of *C. auris* infection or colonization and the level of precautions recommended.

Document two negative tests for *C. auris* before stopping infection control procedures

Two or more assessments performed at least one week apart with negative results are needed before discontinuing infection control precautions. The patient or resident should not be on antifungal medications active against *C. auris* at the time of these assessments (wait one week).

Conclusion

This patient is currently clinically stable and awaiting surgical assessment. Best practices for IPC are being carried out in the three hospitals where this patient was cared for, local public health has been informed and regional IPC follow up is underway. Fortunately, as part of the treatment of the brain abscess associated with hospitalization outside the country, routine screening for antimicrobial resistant organisms found carbapenem-resistant *Enterobacteriaceae* and the patient had been placed on contact precautions.

The source of *C. auris* is not yet known, but one source could have been related to the hospitalization in India where *C. auris* is known to be endemic (6,17). Due to the chronicity of ear symptoms and the prior (unconfirmed) clinical diagnosis of otomycosis, the infection may have preceded the patient's most recent travel; however, the patient had been in India prior to the onset of the ear symptoms as well. Genotyping to identify the most likely source of the infection is pending.

As with other antimicrobial-resistant organisms (18), travel-associated infection or colonization from *C. auris* is likely to be increasingly encountered by clinicians. In the United States, two cases of *C. auris* infection were observed in returning travellers who had been hospitalized abroad (10,14). In addition, in a multi-state hospital-associated outbreak in the US, *C. auris* isolates from New York and New Jersey were highly related to one another and were similar to South Asian isolates (10); this suggests the introduction of *C. auris* acquired abroad to healthcare facilities in these states. Anyone who has been hospitalized while outside of the country may be at increased risk for antimicrobial-resistant organisms, including *C. auris*; contact precautions and testing may be indicated. This approach may help contain *C. auris* from nosocomial transmission within and between Canadian healthcare facilities. Alerting local public health can also assist in efforts to track and manage this emerging disease.

Authors' statement

ISS – Conceptualization, Data Collection, Writing - Original Draft, Review and Editing

GWH – Conceptualization, Investigation, Data Collection, Writing - Review and Editing, and Supervision

Conflict of Interest

None.

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BRIEF COMMUNICATION

An outbreak of Shiga toxin–producing *Escherichia coli* O121 infections associated with flour—Canada, 2016–2017†

V Morton[1], JM Cheng[1]*, D Sharma[2], A Kearney[3]

Abstract

As of May 23, 2017, 29 cases of a new *Escherichia coli* O121 infection have been identified in six provinces (Alberta, British Columbia, Newfoundland and Labrador, Ontario, Quebec and Saskatchewan) linked with the consumption of uncooked flour. One additional case was identified in a U.S. resident who traveled to Canada during the exposure period. Patients' ages ranged from 2–79 years (median = 23.5 years) and 50% were female.

Eight patients were hospitalized, and one developed hemolytic uremic syndrome. Because of the recent emergence of *E. coli* outbreaks linked to flour, public health professionals should consider flour as a possible source in *E. coli* outbreaks and communicate the risk associated with flour and raw batter/dough exposure in public health messaging.

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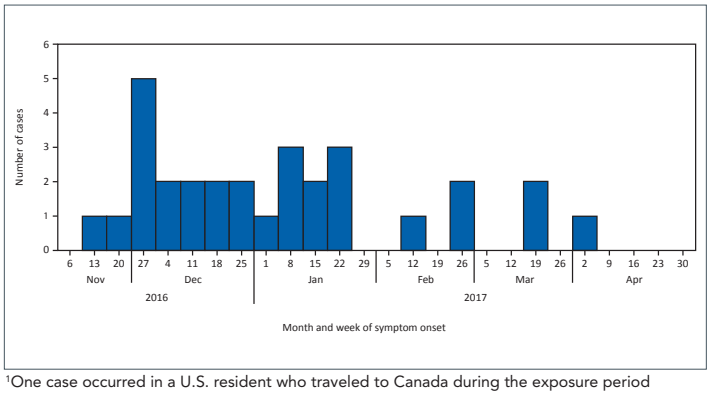
The Outbreak

On December 29, 2016, PulseNet Canada identified a cluster of six *Escherichia coli* non-O157 isolates with a matching pulsed-field gel electrophoresis (PFGE) pattern combination that was new to the PulseNet Canada database. The patients resided in three geographically distinct provinces. In January 2017, the Public Health Agency of Canada (PHAC) initiated an investigation with local, provincial, and federal partners to investigate the source of the outbreak.

A case was defined as isolation of *E. coli* non-O157 with the outbreak PFGE pattern or closely related by whole genome sequencing (WGS) in a Canadian resident or visitor with onset of symptoms of gastroenteritis on or after November 1, 2016. Patients' illness onset dates ranged from November 2016 to April 2017 (**Figure**). As of May 23, 2017, a total of 29 cases were identified in six provinces (Alberta, British Columbia, Newfoundland and Labrador, Ontario, Quebec, and Saskatchewan). One additional case was identified in a U.S. resident who traveled to Canada during the exposure period. Patients' ages ranged from 2–79 years (median = 23.5 years) and 50% were female. Eight patients were hospitalized, and one developed hemolytic uremic syndrome. Clinical isolates were typed as *E. coli* O121:H19 (one case was typed as *E. coli* O121:H undetermined) with Shiga toxin 2–producing genes by in silico toxin testing and had closely related PFGE patterns and WGS.

Figure: Number of confirmed cases of *Escherichia coli* O121 (n = 30)[1]**, by week of symptom onset —Canada, November 2016–April 2017**



[1]One case occurred in a U.S. resident who traveled to Canada during the exposure period

Initial investigation into the source of the outbreak did not identify any clear hypotheses; common exposures were ground beef, sausage style deli-meats, pizza, and pork, but the data did not converge on any specific products. Patients were reinterviewed by PHAC using an open-ended approach. Knowledge of a recent *E. coli* O121 flour-associated outbreak prompted interviewers to ask about baking and exposure to raw

flour or dough (1). Patients were also asked if any food items of interest, including flour, were available for testing.

In March 2017, *E. coli* O121 with the outbreak PFGE pattern was isolated from an open flour sample from a patient's home and a closed sample collected at a retail store, both of the same brand and production date. The clinical and flour isolates grouped together, with only 0–6 whole genome multilocus sequence typing allele differences. As a result of these findings, a product recall was issued. Based on possible connections to the recalled lot of flour, market sampling of flour within certain periods was initiated. The investigation led to additional recalls of flour and many secondary products (2).

As of May 23, 2017, 22 patients had been asked about flour exposure in the seven days before illness onset; 16 (73%) reported that the implicated brand of flour was used or probably used in the home during the exposure period. Comparison data on the expected proportion with exposure to this brand of flour were not available. Eleven of these sixteen patients reported they ate or probably ate raw dough during their exposure period.

This is the first national outbreak of non-O157 Shiga toxin–producing *E. coli* infections identified in Canada and the first Canadian outbreak linked to flour. An open-ended interview approach and flour sampling were used to implicate flour as the source. Because of the recent emergence of *E. coli* outbreaks linked to flour, public health professionals should consider flour as a possible source in *E. coli* outbreaks and communicate the risk associated with exposure to flour, raw batter, and dough in public health messaging.

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Conflict of interest

None.

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Public health surveillance for the Toronto 2015 Pan/Parapan American Games

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Abstract

Background: Public health surveillance for previous Olympic and Paralympic Games have been described in the literature, but surveillance for regional, multisport events on a smaller scale have rarely been explored.

Objective: To describe the public health surveillance planning, implementation, results, and lessons learned from the 2015 Pan/Parapan American Games in Toronto, Ontario, Canada.

Intervention: Public health surveillance planning for the Games began two years in advance and involved local, provincial and federal partners, primarily focusing on infectious disease. From June to August, 2015, enhanced public health surveillance was conducted to support situational awareness and to facilitate the detection of infectious diseases and outbreaks, environmental health hazards and impacts and other major health events.

Outcomes: No major public health incidents occurred that were associated with or a result of hosting the Games. There were two cases of reportable infectious diseases associated with the Games, and 18 public health investigations involving Games-accredited individuals (six related to vaccine-preventable diseases and 12 related to gastrointestinal illnesses or food/water safety violations). Enhanced communication mechanisms, rather than routine and syndromic surveillance systems, were the primary sources of initial notification to surveillance partners on investigations.

Conclusion: Working with its partners, Ontario created a robust public health surveillance system for the 2015 Pan/Parapan American Games. Lessons learned, as well as the relationships and capacity developed through this experience, will be applied towards public health surveillance planning for future events.

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Introduction

In July and August 2015, Toronto and 15 neighbouring municipalities in Ontario, Canada hosted the Toronto 2015 Pan/Parapan American Games (referred to collectively as "the Games"), a regional multisport event involving approximately 10,000 athletes and officials representing 41 countries from the Americas. The combined event involved more athletes and competitions than any multisport event ever held in Canada, including the Vancouver 2010 Olympics and Paralympics. During the 2015 Games, which ran from July 10 to 26 for the Pan American Games and August 7 to 15 for the Parapan American Games, about 250,000 spectators and 20,000 volunteers participated in the sporting and associated cultural events (1,2).

Like other international multisport events, the Games are a type of planned mass gathering (3). The goals of the health-related planning for the Games were to mitigate their impact on the Ontario health care system and to protect the health of residents, event participants and visitors. This was a complex effort given the expansive geographic footprint of the Games across southern Ontario. One aspect of this process was public health surveillance planning, which required close collaboration between 15 surveillance partner organizations including the Toronto 2015 Pan/Parapan American Games Organizing Committee (TO2015), the Public Health Agency of Canada, provincial government agencies and ministries, a local public health informatics team, 10 local public health units and public health laboratories.

Many previous international multisport events have also involved significant advanced health planning. Potential public health–specific hazards that have been previously identified include trauma, injury and substance misuse; extreme weather events; chemical, radiological, biological and nuclear threats; and infectious diseases such as food- and waterborne disease, sexually transmitted infections and respiratory infections (4-6).

Despite a lack of clear evidence that international multisport events increase the risk of transmission of infectious diseases (4,7), these events may increase opportunities for disease transmission because:

- infectious diseases can be imported from visitors' countries of origin;
- susceptible visitors may be exposed to infectious diseases endemic to the host country;
- living arrangements are communal and events can be crowded;
- new, mobile or temporary food vendors and sanitation facilities are brought in; and
- the strain on the health care system may cause delayed responses (5,7-9).

During international multisport events, public health surveillance is intended to identify and quantify—or to reassure in the absence of—public health threats to allow for timely action, if necessary (5,8,10). Enhanced public health surveillance planning and response is not required for all mass gatherings; its usefulness depends on a number of factors: the type of event, geographic area, duration and number of international visitors. The need for enhanced surveillance is also influenced by the nature and comprehensiveness of the existing routine public health surveillance system (10).

Enhanced public health surveillance systems have been described for several previous Olympic Games (11-14); however, smaller-scale, regional, multisport events such as the Pan/Parapan American Games have rarely been explored.

This article describes the Toronto 2015 Pan/Parapan American Games public health surveillance planning, implementation, results, and lessons learned in order to help inform future planning for similar mass gathering events.

Intervention

The primary purpose of public health surveillance for the Pan/Parapan American Games was to support ongoing situational awareness leading up to, during, and immediately following the Games, facilitating the ability to quickly detect sporadic infectious disease activity, outbreak activity, environmental health hazards and impacts, and major health events.

Advance planning

From November 2013 to December 2014, an advance planning group of public health surveillance experts from multiple jurisdictions developed public health surveillance recommendations in Ontario using a consensus approach. The planning group was primarily focused on infectious disease; a separate group was responsible for ensuring food and water safety related to the Games. The group's work involved determining surveillance objectives for each phase (i.e., before/during/after the Games), identifying potential public health threats based on a review of literature and results from a Hazard Identification and Risk Assessment process; reviewing available sources of data and information; and identifying gaps in available sources. Sources were recommended based on an assessment of the threats to be monitored, population covered, timeliness, availability, status (i.e. whether established or needing development) and usage (pre, during or post event). Overarching themes considered in making the recommendations included how the information would meet surveillance objectives and inform public health action. The completed recommendations included strengthening reporting and analysis of established sources; adopting and using additional sources at local levels where available; and acquiring or developing new sources (**Table 1**).

Operational planning

A separate working group composed mainly of local and provincial epidemiologists implemented the recommendations. From December 2014 to June 2015, members collaborated to develop processes, schedules, templates and other reference documents for use when conducting surveillance for the Games. Concurrently, each surveillance partner also developed complementary surveillance plans and analyses for their

Table 1: Overview of data and information sources used to monitor public health threats at the provincial level[1] for the Toronto 2015 Pan/Parapan American Games (June 17–August 27, 2015)

Surveillance type	Data or information source (surveillance partners responsible)	Games-specific/ Enhanced/Routine surveillance activities
Event surveillance	**Public health coordinator** (provincial/Games): A public health professional who was embedded in the polyclinic in the athletes' village	**Games-specific:** The coordinator worked with the TO2015 medical team to gather and share information and provide support for public health–related issues
	Surveillance teleconferences (all partners): Held on those days that public health surveillance reports for P/PAG were produced	**Games-specific:** Calls were used to share and assess situations of potential public health concern, and to help decide which situations would be listed as report highlights
Reportable infectious diseases	**iPHIS** (provincial): Ontario's infectious disease surveillance and reporting system	**Routine:** Ran daily aberration-detection algorithms on select diseases **Enhanced:** Automated production of case counts of reportable diseases by week compared to historical averages; search for P/PAG-related exposures reported in a standardized format in accordance with a Games-specific enhanced surveillance directive
Laboratory	**PHOL** (provincial): Repository of all submissions to Public Health Ontario for laboratory testing and confirmation (excludes testing by hospitals and community laboratories)	**Enhanced:** Summarized notifications and submissions of Games-related specimens to PHOL for testing
Syndromic	**Gold Medal System** (provincial/Games): System included records of medical encounters with accredited individuals (including athletes, coaches, and officials) when they accessed medical services provided by TO2015	**Games-specific:** TO2015 provided aggregate counts for provincial analysis of illness- and infection-related (determined by clinical assessment) medical encounters by day and overall, reporting on increases beyond two standard deviations above a three-day moving average
	Telehealth Ontario (provincial): A free, confidential telephone service for Ontario's general public to seek health advice or information	**Games-specific:** Categorized calls across the province into five syndromes[2] during the Games and completed statistical analyses on these syndromes for potential geographic clusters that were greater than the expected number of calls for the time period and geographic area in question, using a three-year historical

Surveillance type	Data or information source (surveillance partners responsible)	Games-specific/ Enhanced/Routine surveillance activities
Syndromic (con't)		baseline; the number of callers with attendance at P/PAG events was available; also assessed call volume by syndrome
	ACES (local/provincial analysis by ACES team): System captures data on chief complaints from emergency department visits and all hospital admissions, covering 53 reporting hospitals across 10 local public health units in the Games geographical area (15)	**Enhanced:** Real-time analysis of 15 predefined syndromes of interest (e.g. heat-related illness, asthma and gastrointestinal issues). System-generated alerts or deviations over expected seasonal baseline levels were reported
Situational	**PHIMS** (local/provincial analysis by the ACES team): Online platform displays real-time environmental data (e.g. air quality markers, storm events and temperature stress) along with ACES, demographic, and social deprivation indices on a geographical interface (16)	**Enhanced:** PHIMS platform data streams were monitored in the event that at-risk populations might need to be informed or evacuated due to a weather-related emergency or potential terrorist threat
International	**GPHIN** (provincial/federal): Program that uses an automated web-based system to scan newspapers and other communications worldwide for potential indicators of outbreaks. These are then analyzed and rapidly assessed by a multilingual, multidisciplinary team (17)	**Enhanced:** Assessed identified events for their potential risk and impact on the Games, with the most relevant or concerning events included in provincial surveillance report following subjective expert review

Abbreviations: ACES, Acute Care Enhanced Surveillance System; GPHIN, Global Public Health Intelligence Network; iPHIS, integrated Public Health Information System; P/PAG, Pan/Parapan American Games; PHIMS, Public Health Information Management System; PHOL, Public Health Ontario Laboratory; TO2015, Toronto 2015 Pan/Parapan American Games Organizing Committee
[1] Other recommended data and information sources used by public health units for their local surveillance during the Games are not listed in this table
[2] Telehealth Ontario calls were categorized into five syndromes of interest for P/PAG surveillance: fever/influenza-like illness, gastrointestinal syndrome, heat syndrome, rash syndrome and respiratory syndrome

organization, with the opportunity for sharing ideas through the working group. In spring 2015, the group completed three practice runs of the Games surveillance cycle and applied the lessons learned to finalizing the processes and materials.

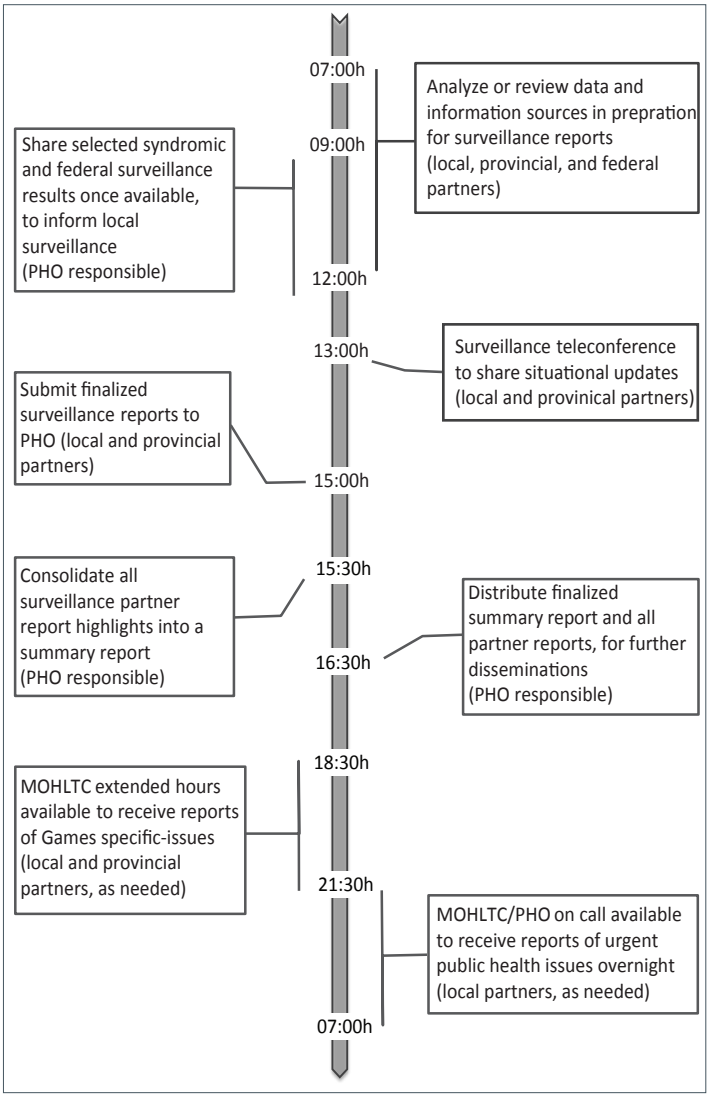
Public health coordinator

In line with the surveillance recommendations, a Public Health Coordinator acted as a key link between TO2015 and the public health system. Before the Games, the coordinator met regularly with the TO2015 medical team to establish a strong relationship and to understand the processes and infrastructure associated with the Games. During the Games, the coordinator was embedded in the TO2015 medical team working from the polyclinic (a large multidisciplinary clinic) in the main athletes' village. The coordinator developed courses and arranged training on onsite infectious disease reporting and preventive measures; coordinated disease reporting, laboratory communications and requests for scientific/technical advice; participated in outbreak investigations; and extracted TO2015 clinic data for syndromic surveillance.

Surveillance cycle

The working group set the surveillance period for the Games to run from June 17 to August 27, 2015, that is, starting from approximately two weeks before the competitions began until approximately two weeks after the last one. As part of operational planning, the working group developed a schedule of 38 reporting dates within this surveillance period for holding surveillance teleconferences and producing the surveillance report. During the competitions, reporting took place Monday through Friday; whereas reporting was less frequent in the periods before and after competition days, as well as during the break between the Pan/Parapan American Games. The process, activities, responsibilities and timelines for the Games surveillance cycle on a reporting day are outlined in **Figure 1**.

Figure 1: Daily public health surveillance cycle for the Toronto 2015 Pan/Parapan American Games (June 17–August 27, 2015)



Abbreviations: MOHLTC: Ministry of Health and Long-Term Care; PHO: Public Health Ontario

The advanced planning group identified nine data and information sources that met the criteria for Games surveillance at the provincial level (Table 1). For each of the 38 reporting days, Public Health Ontario (an arms-length agency of the Ontario government) produced or distributed reports based on analyses of these sources. Generally, any increases above baseline or clusters/aberrations detected through statistical analysis were included in surveillance reports. Depending on when events were scheduled in their jurisdiction, each of the 10 public health units in the Games footprint produced reports based on surveillance data and information sources available at the local level (e.g. complaint hotlines, food establishment closures, water safety issues, weather alerts) and participated in surveillance teleconferences for a subset of these dates. All other surveillance partners participated throughout the entire surveillance period. The surveillance teleconferences that took place at 1 p.m. (13:00 hours) provided an opportunity for partners to share and assess situations of potential public health concern. A series of questions developed during operational planning (**Text box**) were used by partners as guiding principles to help determine which situations to include as highlights for their respective surveillance reports and for further dissemination. No rating scale or additional instructions were provided in applying the questions; surveillance partners were free to use the questions in any way that would be helpful for their assessment.

Criteria considered in selecting situations to highlight in surveillance reports for the 2015 Pan/Parapan Games

- Does the issue impact the Games or have the potential to impact the Games?
- Is the issue of public health significance (regardless of whether it is Games related)?
- Does the issue have the potential to have a high public health impact (e.g., pathogen with high potential to cause an epidemic)?
- Is the issue high profile (i.e., is receiving or has the potential to receive media attention)?
- Would other surveillance partners who receive the report benefit from being informed of the issue for their situational awareness?
- Will there be public health action as a result of the issue?
- Is the event usual or unexpected?
- Is there a significant risk of international spread?

After receiving surveillance partner reports, Public Health Ontario compiled local, provincial and national highlights into a summary report. The report was emailed, along with other surveillance reports, back to surveillance partners and was also sent to the Ontario Ministry of Health and Long-Term Care's Emergency Operations Centre for further dissemination.

Outside of this regular schedule, the Ministry Emergency Operations Centre and supporting on-call structures (**Figure 1**) provided after-hours support throughout the Games surveillance period so that partners could report any immediate, urgent public health incidents.

Disseminating surveillance findings

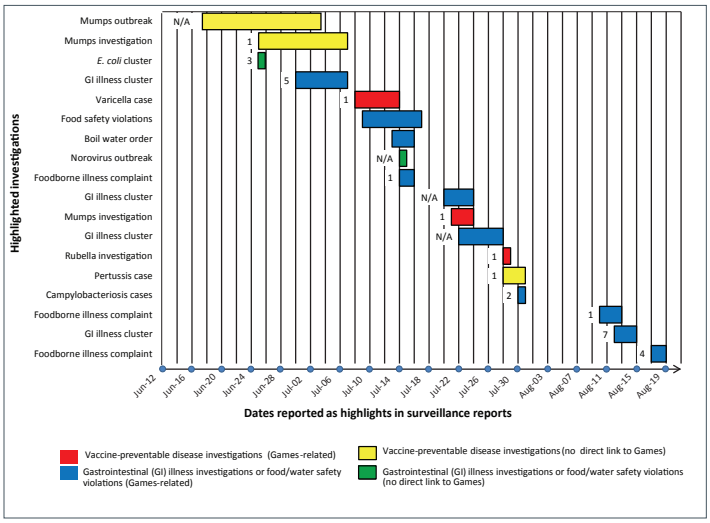
The Ministry Emergency Operations Centre was active throughout the surveillance period, coordinating situational awareness and response to the Games, including a daily health system communications cycle. This cycle included regularly scheduled calls with a variety of health system partners and culminated in daily situation reports that summarized each day's health system status, risks and actions.

Highlights of the summary surveillance reports were included in the daily situation reports. These situation reports were then shared across the Ontario health system within the geographical areas involved with the Games, including public health units, paramedic and ambulance services, hospitals and primary care. The reports were also disseminated to TO2015 and other non–health planning partners such as the central Provincial Emergency Operations Centre, which coordinates the Ontario government's overall response.

Outcomes

There were no major public health incidents associated with or as a result of hosting the Games. Surveillance partners highlighted 18 local public health investigations. Surveillance partners were initially notified of these investigations through the Public Health Coordinator, surveillance teleconferences and/or the extended hours and on-call processes (**Figure 2**); only two investigations involved confirmed cases of reportable infectious diseases: an athlete's case of chickenpox and a spectator's case of campylobacteriosis. Twelve of the investigations involved Games-accredited individuals (i.e. athletes, coaches and officials), including six investigations related to vaccine-preventable diseases and 12 related to gastrointestinal illnesses or food/water safety violations (three of these investigations are described in **Appendix 1**).

Figure 2: Highlighted public health investigations during the Toronto 2015 Pan/Parapan American Games public health surveillance period (June 17–August 27, 2015)



Abbreviations: GI, gastrointestinal; N/A, information on number of cases under investigation was unclear and/or not included in surveillance reports
Legend: Numbers to the left of the bars represent the number of people under investigation for each situation. A blank space indicates that the investigation was related to food safety but no related cases were identified

The results of provincial-level surveillance activities by data and information source are summarized in **Table 2**. Syndromic surveillance systems did not identify any trends, clusters or other alerts that initiated or corresponded with any of the investigations reported by public health units. Although exposures and confirmed cases were reported through the reportable infectious disease information system, data entry

occurred after the information had already been shared through the Games surveillance reporting process. In general, provincial-level surveillance was largely supportive in nature and provided situational awareness.

Table 2: Results of provincial public health surveillance for the Toronto 2015 Pan/Parapan American Games (June 17–August 27, 2015)

Data/information source(s)	Surveillance results
Public health coordinator	Two individuals shared the role of providing rotating support over 44 days in the Athletes' Village Sixteen requests for public health support received
Surveillance teleconferences	A total of 38 surveillance teleconferences held with participation from up to 14 partner organizations, corresponding with each surveillance report production day
iPHIS	Four Games-related exposures reported in association with reportable disease investigations, resulting in two confirmed cases: a chickenpox case in a P/PAG athlete and a campylobacteriosis case in a spectator with foodborne exposure from an unknown food vendor
PHOL	Five notifications on incoming specimens to the P/PAG response phone number Nine Games-related specimens received for laboratory testing
Gold Medal System[1]	A total of 7,677 medical encounters were reported based on medical services provided by TO2015 to P/PAG-accredited individuals. Of these, 1,940 were illness-related (of these, 376 were infection-related) A total of 197 of infection-related medical encounters affected the respiratory system
Telehealth Ontario	A total of 75,547 calls from across Ontario during the surveillance period, with volumes highest for gastrointestinal syndrome (5,283 calls) and respiratory syndrome (4,195 calls) A total of 130 temporal-spatial clusters of public health interest detected across Ontario; the most common clusters of interest were for respiratory syndrome (46 clusters), followed by rash syndrome (34 clusters) and gastrointestinal syndrome (29 clusters) Eight callers from the detected clusters reported attending a P/PAG-related event
ACES and PHIMS	A total of 19 ACES syndromes and numerous PHIMS environmental indicators were monitored
GPHIN	A total of 237 events worldwide assessed with potential risk and impact to Games; 52 of these events further assessed as possibly having impact on the Games

Abbreviations: ACES, Acute Care Enhanced Surveillance System; GPHIN, Global Public Health Intelligence Network; iPHIS, integrated Public Health Information System; P/PAG, Pan/Parapan American Games; PHIMS, Public Health Information Management System; PHOL, Public Health Ontario Laboratory; TO2015, Toronto 2015 Pan/Parapan American Games Organizing Committee
[1] TO2015 medical clinic services were only provided on July 1–29 and August 2–18, 2015

Discussion

Public health surveillance during the 2015 Pan/Parapan American Games in Toronto identified no major public health incidents that were associated with, or as a result of, hosting the Games. The lack of major incidents was not surprising given similar experiences from previous summer Olympic and Paralympic Games (11-14), Canada's well-established public health infrastructure, results from the Hazard Identification Risk Assessment, and the profile of visitors to the Pan/Parapan Games (18).

Performance of surveillance system

Syndromic surveillance systems are intended to provide rapid yet unspecific data as a complement to traditional surveillance systems, to enable early identification and intervention for potential public health threats (19). The provincial-level syndromic surveillance data sources used during the Games did not produce the initial notifications or alerts that triggered the highlighted public health investigations; nor were these alerts corroborated by the other data and information sources used for Games surveillance. Although alerting thresholds were developed as part of the planning process for the Games, limited prior experience in using these data sources and/or applying them for syndromic surveillance meant that these criteria were largely based on subjective expert input, and their usefulness had not been previously validated. When preparing new syndromic surveillance data sources or methods for future mass gathering events, sufficient time for training, practice and gathering of baseline data and trends should be allowed.

On the other hand, surveillance partners have had extensive experience with Ontario's routinely used reportable infectious disease information system, where reported cases must meet routine provincial case definitions. However, the time required to meet these criteria meant that initial notification of infectious disease case investigations during the Games arose through other sources. From our experience, a reportable disease surveillance system serves best as a historical record for details on Games-associated reportable disease cases and to understand baseline incidence.

The enhanced communication mechanisms (including the Public Health Coordinator, surveillance teleconferences, and extended hours/on-call process) implemented for Games were the primary sources of initial notification to surveillance partners on new investigations. Developing relationships, and new or enhanced communication mechanisms during planning phases, proved to be the most effective methods for providing timely and relevant updates to inform public health action. This experience further supports the importance of having processes and people in place to rapidly communicate potential public health threats and support public health action, a point often made in mass gatherings surveillance literature (7,10,13).

Lessons learned

The local public health units across the Games footprint had various levels of involvement with the Games, which led to planning challenges in balancing flexibility and consistency. Although efforts were made to accommodate variations in local systems, some public health units requested further provincial guidance and a standard surveillance report template. Another challenge was balancing a comprehensive approach with sustainability of activities. Planning and implementing the

surveillance cycle throughout the Games had significant resource implications for all surveillance partners, with the commitment being particularly burdensome for public health units with few events.

The planning structure for the Games involved a separate planning process for food and water safety. Public health units and other health system partners were unsure of the appropriate forum for reporting food handling and water safety issues at venues, especially in the absence of any reported illness. As a result, such issues were inconsistently reported through various channels. The relationship between surveillance and other reporting structures could have benefited from more clarity and integration. During a mass gathering, an environmental health surveillance system that is integrated with the rest of the public health surveillance cycle could better facilitate timely public health interventions (20).

Over the course of the Games surveillance cycle, reaction to the disseminated public health surveillance information highlighted a knowledge gap between health partners and non–health partners (e.g. Games organizers; fire, police and intelligence services; other government ministries involved with the events such as transportation). Non–health partners who received surveillance reports often did not know what types of infectious diseases can be expected during the summer in Ontario; they occasionally needed to be reassured that the situations being reported were manageable through routine follow-up. In future, public health partners who disseminate surveillance information should be diligent in providing the necessary context and interpretation in reports and other pre-Games communications to help non–health partners understand the appropriate level of response for the reported situations.

Conclusion

Public health surveillance for the Toronto 2015 Pan/Parapan American Games provided situational awareness and reassured organizers, government partners and the media, thus fulfilling an important role. In carrying out these activities, we have learned that Ontario can provide efficient and sustainable support to future mass gathering events. Support for future events should involve continuing with Ontario's well-developed routine surveillance activities as well as ensuring that enhanced communication mechanisms are in place. Particular attention must be paid to integrating food and water safety into the communication channels and ensuring that non–health partners understand the context and implications of the updates presented. Moving forward, staff from all surveillance partner organizations can apply the relationships and capacity gained through their involvement with the Games to more efficiently support mass gathering events across the province, large and small. As technologies advance, new and evolving surveillance methods and sources such as crowd-sourced or participatory surveillance initiatives may be used for future events.

Authors' statements

BL, TB, MH, JRH - advance planning group members (methodology)

EC, KH, BL, TB, MH, JRH - operational planning and implementation of public health surveillance for the Games (methodology)

Authors' statements (continued)

BL, EC - software, validation, formal analysis

EC, KH - data collection and curation, investigation

BL, EC, KH - visualization

EC, KH, BL, TB, MH, JRH - writing-original draft

All authors - conceptualization, writing-review/editing

Conflict of interest

None.

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Appendix 1: Summary of three investigations conducted during the 2015 Pan/ Parapan American Games in Toronto, Canada

On July 8, an athlete presented to a Games medical clinic with suspected varicella (chickenpox) and was advised to self-isolate. The Public Health Coordinator notified the local public health unit by phone. Local and provincial public health developed guidance on addressing varicella in a Games environment where susceptibility may be higher than normal. When the diagnosis was confirmed by the public health laboratory, return-to-play guidance was provided to the athlete and coach, and a vaccination clinic was held for susceptible teammates. Secondary cases were expected to present between 15 July and 1 August; none were reported.

On July 17, the TO2015 medical team identified a possible cluster of gastrointestinal illness among accredited individuals, following an increase in requests for antidiarrheal medications from the Games pharmacy by a specific team. As per the established after-hours process, the TO2015 medical team informed the Public Health Coordinator, who notified a public health unit and the Ministry Emergency Operations Centre by phone. During the investigation, it was difficult to identify and follow-up with the affected individuals because of initial miscommunication at the lodging site and the transient nature of the population; several individuals left the Games soon after the investigation began. No common food exposure was identified among cases and no specimens were submitted to the laboratory; symptoms resolved within 24 hours of onset.

On July 30, a public health unit notified surveillance partners about two cases of campylobacteriosis through the teleconference and report. The two individuals had consumed food purchased while attending different Games events on separate dates. Further investigation determined that one case was unrelated to the Games. The food vendor related to the second case was inspected; food samples test results were negative.

Canada's pandemic vaccine strategy

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Abstract

The Public Health Agency of Canada has a mandate to prepare and respond to public health events, including influenza pandemics. Pandemic preparedness requires a multifaceted approach with collaboration from all levels of government. The *Canadian Pandemic Influenza Preparedness: Planning Guidance for the Health Sector* (CPIP) is a guidance document that outlines key health sector preparedness activities designed to ensure Canada is ready to respond to the next influenza pandemic.

This article, the first in a series, outlines Canada's pandemic influenza vaccine strategy as described in the CPIP annex on vaccines. The strategy encompasses all elements of a vaccine program including prioritization of the initial vaccine distribution, securing a pandemic vaccine supply, regulatory approval of a pandemic vaccine, vaccine safety, distribution and storage of the vaccine, allocation and vaccine uptake.

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Introduction

Influenza pandemics are recurring but unpredictable events that arise when a novel influenza A virus spreads widely and causes a worldwide event. Planning for a prolonged and widespread health emergency with an unpredictable impact is challenging but essential. The Public Health Agency of Canada (PHAC) has a mandate to prepare for and respond to public health events through leadership, partnership and action. In an influenza or other pandemic, PHAC leads the health sector preparedness and response at the national level, collaborates with international partners and represents Canada on global health security initiatives.

Pandemic preparedness necessitates a multifaceted approach with collaboration from all levels of government (local, provincial/territorial, federal). Key components of health sector preparedness include disease surveillance, laboratory testing and research, health care service and public health guidance, communications and medical countermeasures to mitigate transmission and reduce burden of illness through the use of antivirals and vaccines.

The 2009 H1N1 pandemic (pH1N1) provided the first test of Canada's pandemic preparedness planning and led to unprecedented collaboration among all levels of government and successful stakeholder engagement. Leveraging existing laboratory networks, such as the Canadian Public Health Laboratory Network, and surveillance systems, such as the national influenza surveillance system FluWatch, proved invaluable.

Health planners learned a lot from the 2009 pH1N1 (1). Two key lessons that informed subsequent planning considerations were to ensure that:

- triggers for activation and deactivation of specific response elements are well defined; and
- pandemic plans allow for scalability and flexibility.

These reflect the fact that the impact and timing of pandemic virus activity can vary by region and that there can be unique considerations for each jurisdiction (e.g., province, territory and federal government). Finally, there is a need to clearly articulate the roles and responsibilities of federal, provincial and territorial (FPT) governments in the event of any public health emergency.

National pandemic planning for the health sector

The *Canadian Pandemic Influenza Preparedness: Planning Guidance for the Health Sector* (CPIP) is an FPT guidance document that outlines how the jurisdictions can work together to ensure a coordinated and consistent health sector approach to pandemic preparedness (2). The body of the CPIP describes the overarching principles, concepts and shared objectives that are critical to effective pandemic preparedness and response. This is followed by the annexes that provide technical operational plans on specific issues such as surveillance, public health measures and the vaccine strategy.

The CPIP is an evergreen document that is routinely reviewed and updated as new information and best practices emerge. This article marks the beginning of a series providing an update on the different sections of the CPIP by summarizing Canada's pandemic influenza vaccine strategy as outlined in the CPIP's Vaccine Annex (3).

Canada's pandemic vaccine strategy

Immunization of susceptible individuals is the most effective method of preventing disease transmission and death from influenza. A safe and effective vaccine is the cornerstone of pandemic preparedness and response. Canada's pandemic influenza vaccine strategy is built upon the strength of the seasonal influenza programs; however, there are unique differences to consider during a pandemic.

Pandemic vaccine prioritization framework

Initial supplies of a new pandemic vaccine are unlikely to be sufficient to immediately supply everyone living in Canada. To address this situation in an equitable manner, national recommendations for the prioritized use of the vaccine will be developed by the National Advisory Committee on Immunization (NACI) using the *Pandemic Vaccine Prioritization Framework* until sufficient vaccine is available for all Canadians (approximately one month after initial lots are available) (4).

NACI is an expert advisory body to the PHAC, responsible for making recommendations on all vaccines used in Canada (5). This includes the seasonal and pandemic influenza vaccines, through NACI's Influenza Working Group. The NACI guidance on the use of the pandemic vaccine will be updated as required. For example, initial recommendations may change as the specific epidemiology of a pandemic becomes clear.

At the outset of a pandemic, the prioritization framework provides a systematic way of looking at all the relevant scientific evidence while taking into account ethical, logistical and other considerations. The recommendations will categorize risk and age groups into various priority groupings, using the most effective strategies to address national pandemic goals. The framework was successfully used to develop sequencing guidelines for the rollout of the vaccine during pH1N1. The determined priority groups included people under 65 years with chronic conditions, pregnant women, children between six months and five years of age, people in remote and isolated settings, health care workers involved in the pandemic response or providing essential services, household contacts and care providers of people at high risk who could not be immunized, and other high-risk populations (6).

Vaccine supply

Domestic production of the influenza vaccine is essential to guarantee that Canada has access to an adequate supply as the availability of offshore-manufactured vaccine may be limited during a pandemic because of trade and travel embargoes, as well as increased demand. Canada was one of the first countries to implement a long-term pandemic vaccine contract with a vaccine manufacturer in 2001. The first opportunity to benefit from this came during pH1N1 in 2009 and the result was sufficient vaccine for all Canadians who wanted to be immunized. Since then, Canada has put in place another 10-year contract (which began in 2011). The contract stipulates that the manufacturer fulfill their commitment to Canada before selling the vaccine to other countries, ensuring an adequate supply for every person residing in Canada. To ensure capacity for manufacturing the vaccine, the current contract includes access to a share of Canada's seasonal influenza vaccine market.

Vaccine regulation

All vaccines intended for use in Canada are subject to the provisions of the *Food and Drugs Act* (7) and the *Food and Drug Regulations* (8). Before authorizing a new vaccine, Health Canada evaluates the scientific and clinical evidence submitted by the manufacturer. The process used to authorize approved seasonal influenza vaccines each year is a modification of the full process for a new vaccine because seasonal vaccines involve only a change in the influenza strain(s) used. Months before the flu season begins, manufacturers send updated information to regulatory authorities on the strains anticipated in the upcoming season. Health Canada then expedites a review of the data and authorizes the new seasonal vaccine.

Standard regulatory processes cannot be used in a pandemic because the production of a pandemic vaccine cannot begin until the virus strain has been identified. For a vaccine to be useful in mitigating the pandemic impact, it will be needed almost immediately after it is manufactured. So what can be done to pass regulatory review with limited time and data?

Regulatory approval of a pandemic vaccine can occur in three ways. First, similar to seasonal vaccine, a prototype pandemic vaccine can undergo prior market authorization based on surrogate immunogenicity data as this would be followed by subsequent authorization of the strain change. Second, the Extraordinary Use New Drugs (EUND) regulations, enacted in 2011 after pH1N1, may be used (9). These regulations allow Health Canada to expedite authorization of a pandemic vaccine based on animal data supplemented by any available human data as long as a complete "quality package" (information on manufacturing the vaccine) is available and a rigorous postmarket surveillance plan is in place. Finally, if the EUND regulations do not apply (because the quality package is incomplete, for example), an Interim Order, based on a state of public health emergency, may be issued by the federal Minister of Health. Such an Interim Order can suspend certain requirements of the *Food and Drugs Act* and *Food and Drug Regulations Act* allowing the issuance of a time-limited authorization with additional sponsor obligations, such as timely submission of missing quality and clinical data as well as postmarketing information.

Vaccine safety

The scale of the pandemic vaccination campaign and the EUND regulatory pathway warrants careful attention to vaccine safety to minimize risk and maximize the benefits of the vaccine. Pandemic vaccine safety is built upon the infrastructure and systems already in place for monitoring routine vaccines. Postmarket surveillance of adverse events following immunization (AEFI) is undertaken by PHAC and Health Canada with provincial and territorial partners and other key stakeholders. Despite the fact that

premarket regulatory application provides a significant amount of information, postmarket surveillance is critical to capture reports of serious and unexpected AEFIs. This information is then used to investigate the relevant vaccine and to enable regulatory action as needed. However, a vaccine released under EUND would have little or no postmarket data and existing surveillance activities undertaken by PHAC, Health Canada and provincial and territorial partners would require considerable scaling up.

In a pandemic, it is critical that AEFI information be quickly passed on to the federal Health Portfolio (e.g., Health Canada and PHAC), where reports can be aggregated and analyzed. A vaccine safety signal from an AEFI report could include an increase in frequency or severity of events known to be caused by influenza vaccine (e.g. allergic reactions) or a previously unknown adverse event (e.g. narcolepsy). Signals need to be quickly investigated so that the cause can be assessed and action taken as appropriate. Possible actions include updates to the product monograph, revisions to vaccine recommendations, changes to administration practices and quarantine or recall of a vaccine lot by Health Canada. Key needs for such enhanced safety monitoring and case report assessment include protocols for rapid field investigations, analytical capacity and knowledge of background rates of potential adverse events to compare observations with expectations.

Vaccine allocation, distribution and storage

An allocation plan (i.e. the amount of vaccine each province and territory receives) will be developed by the Vaccine Supply Working Group, an FPT forum to coordinate vaccine procurement and vaccination programs. Similar to pH1N1, distribution to the provinces and territories will be done on a per capita basis at the outset, beginning with the first lots available and continuing throughout the vaccine production cycle.

As with all vaccines, proper storage and handling guidelines must be followed. For example, the cold chain must be maintained throughout the distribution process. Detailed information is provided in the *National Vaccine Storage and Handling Guidelines for Immunization Providers* (10).

Vaccine uptake

To assist with the prompt distribution of pandemic vaccine, it is important to establish the most efficient use of care providers to administer the vaccine and to have a common infrastructure to capture surveillance data. Most provinces and territories have some type of a hybrid delivery model (with pharmacists, public health nurses and physicians administering vaccine) for seasonal influenza. In addition, each province and territory maintains its own information system, using electronic databases and/or paper-based systems, to track vaccination coverage. This incompatibility across systems has made tracking seasonal influenza vaccine challenging and may result in missing information. At the national level, PHAC monitors seasonal influenza vaccine uptake through the National Seasonal Influenza Immunization Coverage Survey and the Canadian Community Health Survey, but this has a significant lag time and would not be timely in a pandemic situation. In the event of a pandemic, interoperable information systems that allow multiple providers to access and enter vaccine records are needed to provide accurate and timely estimates of vaccine coverage. To close the gap in vaccination coverage and uptake monitoring, work is underway to develop provincial and territorial registries for both seasonal and pandemic influenza surveillance.

Discussion

Canada's pandemic influenza vaccine strategy is built on the strength of the seasonal influenza programs and informed by the lessons learned during pH1N1. Since pH1N1, Canada's pandemic vaccine strategy has been enhanced through a new pandemic vaccine contract with a domestic vaccine manufacturer; new regulatory processes that allow for expedited regulatory approvals; enhanced vaccine safety surveillance; and the ongoing efforts to develop vaccine registries.

Canada's vaccine strategy is always subject to change as a result of new developments. For example, plant-based vaccines are a new technology that may obtain market authorization as a prototype vaccine during the life of the current pandemic vaccine contract. Planners must take into account this possibility and the potential impact and cost these new technologies may have over time. Other new research developments may also signal the need to revise the strategy.

Conclusion

The pandemic influenza vaccine strategy is one element of Canada's pandemic preparedness strategy. It represents a continuing commitment on behalf of all FPT governments to work collaboratively and ensure Canada is ready to respond in the event of an influenza pandemic. Canada was well prepared for pH1N1 and, as a result of the lessons learned from the response, it is even better prepared now.

Conflict of interest

None.

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Increase in MenW in the Netherlands and an atypical presentation

Source: Russcher A, Fanoy E, van Olden GDJ, Graafland AD, van der Ende A, Knol MJ. **Necrotising fasciitis as atypical presentation of infection with emerging *Neisseria meningitidis* serogroup W (MenW) clonal complex 11, the Netherlands, March 2017**. Euro Surveill. 2017;22(23):pii=30549. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2017.22.23.30549. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=22813.

In March 2017, a patient with necrotising fasciitis caused by *Neisseria meningitidis* serogroup W (MenW) clonal complex 11 was diagnosed in the Netherlands. Unusual and severe presentations of MenW infections are common in the current European epidemic. In the Netherlands, the incidence of MenW infections increased 10-fold, from an average of 0.03 per 100,000 population in 2002–2014 to 0.29 in 2016. Awareness of atypical presentations enables timely adequate treatment and public health action.

Case description and microbiological findings

In March 2017 (day 0), a man in his early sixties consulted his general practitioner (GP) because of a painful, red and swollen ankle since 1 day. Five days before his GP visit, he had experienced a fever that lasted 2 days and was accompanied by nausea and vomiting, from which he recovered spontaneously. The GP diagnosed a first episode of gout and prescribed a non-steroidal anti-inflammatory drug (NSAID). One day later (day 1), the patient visited the emergency department of a local hospital as the redness had spread and now covered his left lower leg up to the knee. Blistering was present on the ankle. Physical examination also revealed a red, painful area on his right elbow that the patient had been unaware of up until that moment. Prior to this illness, the patient had not travelled abroad, had generally been in good health and had an unremarkable medical history.

Emergency surgery was performed immediately because of the clinical suspicion of a necrotising fasciitis. During surgery, extensive necrosis of subcutis and fascia of the lower leg was present and a fasciectomy of the total lower leg was necessary. Intraoperative Gram-staining of fascia tissue of both the leg and elbow showed the presence of Gram-negative diplococci … Typing at the Netherlands Reference Laboratory for Bacterial Meningitis revealed a serogroup W subtype P1.5,2:F1–1 belonging to the hypervirulent clonal complex 11.

Ongoing transmission of *Candida auris* in the United States

Source: Tsay S, Welsh RM, Adams EH, et al. **Notes from the Field: Ongoing Transmission of *Candida auris* in Health Care Facilities — United States, June 2016–May 2017**. MMWR Morb Mortal Wkly Rep 2017;66:514–515. Availailable from: DOI: http://dx.doi.org/10.15585/mmwr.mm6619a7 (summary).

In June 2016, CDC released a clinical alert about the emerging, and often multidrug-resistant, fungus *Candida auris.* As of May 12, 2017, a total of 77 U.S. clinical cases of *C. auris* had been reported to CDC from seven states: New York (53 cases), New Jersey (16), Illinois (four), Indiana (one), Maryland (one), Massachusetts (one), and Oklahoma (one) . Screening of close contacts of these patients, primarily of patients on the same ward in health care facilities, identified an additional 45 patients with *C. auris*, resulting in a total of 122 patients from whom *C. auris* has been isolated.

Among the 77 clinical cases, median patient age was 70 years (range = 21–96 years), and 55% were male. *C. auris* was cultured from the following sites: blood (45 isolates), urine (11), respiratory tract (eight), bile fluid (four), wound (four), central venous catheter tip (two), bone (one), ear (one), and a jejunal biopsy (one). Antifungal susceptibility testing at CDC of the first 35 clinical isolates revealed that 30 (86%) isolates were resistant to fluconazole (minimum inhibitory concentration [MIC] >32), 15 (43%) were resistant to amphotericin B (MIC ≥2), and one (3%) was resistant to echinocandins (MIC >4). Most (69, 90%) clinical cases were identified in the New York City metropolitan area (53 in New York and 16 in New Jersey). Nearly all patients had multiple underlying medical conditions and extensive health care facility exposure. Epidemiologic links have been found between most cases.

CDC has worked with state and local partners to develop and share infection control recommendations to help curb the spread of *C. auris*. Current recommendations for *C. auris*–colonized or infected patients include 1) use of Standard Precautions and Contact Precautions, 2) housing the patient in a private room, 3) daily and terminal cleaning of a patient's room with a disinfectant active against *Clostridium difficile* spores (an update from previous disinfectant recommendations), and 4) notification of receiving health care facilities when a patient with *C. auris* colonization or infection is transferred. Accurate identification of *C. auris* and adherence to infection control practices, coupled with ongoing public health surveillance and investigations, are needed to halt the spread of *C. auris.*

CCDR

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