Canada's Pandemic Influenza Preparedness: Laboratory strategy

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Abstract

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 outlines Canada's pandemic influenza laboratory strategy as described in the CPIP *Laboratory Annex*. Laboratory identification and characterization of an influenza pandemic virus is critical to detect the pandemic, develop a vaccine, detect antiviral resistance and inform surveillance functions such as monitoring the geographic spread of the disease. Key elements of the laboratory response will include ensuring there are adequate resources for all activities. Pre-analytical activities include the appropriate collection, transport to the laboratory, triaging and preparation of specimens. Analytical activities refer to the different testing methods for the detection of influenza, including maintaining the ability to culture influenza virus for genetic and antigenic characterization. Post-analytic activities include ensuring front-line and provincial public health laboratories work together to make data and specimens available for surveillance purposes. In the inter-pandemic period, it is important to develop the infrastructure, protocols and processes to enable rapid-response research during a pandemic. This is an evergreen document that will be updated regularly.

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Introduction

The ability to detect an influenza pandemic, as well as the development of a vaccine to protect the population and reduce pandemic spread, and to detect antiviral resistance which would limit the effectiveness of Canada's antiviral stockpile, depend on the identification and characterization of the novel virus that is involved. Laboratories perform this role through tests designed to distinguish a novel influenza strain from seasonal influenza and other respiratory viruses. These laboratory data are used to inform surveillance functions such as monitoring the geographic spread of disease and the impact of interventions.

Canada's pandemic influenza laboratory strategy is described in the Laboratory Annex (1) to Canadian Pandemic Influenza Preparedness: Planning Guidance for the Health Sector (CPIP) (2). It is informed by laboratory experience gained during the 2009 H1N1 pandemic, which made clear the importance of effective communication and coordination among all laboratory tiers and their counterparts throughout the duration of the pandemic response. This technical guidance document describes a scalable approach to the delivery of laboratory services in a pandemic, with triggers for action and other tools providing the flexibility needed to tailor laboratory activities to increased and variable demands for testing. It is directed toward clinical laboratory professionals in Canadian national, provincial and hospital laboratories, and to clinicians, epidemiologists and other stakeholders whose responsibilities intersect with those of these laboratories as well as interested others. This article summarizes the recently updated Laboratory Annex (1) of the CPIP. Summaries of the health sector planning guidance and surveillance strategy are also included in this issue of the *Canada Communicable Disease Report* (CCDR) (3,4).

Canada's pandemic influenza laboratory strategy

Objectives

Laboratory testing for the influenza virus in a pandemic has two broad purposes: population-based surveillance and diagnostic testing. Population-based surveillance involves detection and identification of the novel virus and differentiation from common strains, and includes determination of antiviral susceptibility and strain characterization that can be used to identify potential vaccine mismatch. Although diagnostic testing of patients with influenza-like illness (ILI) may not be indicated for the clinical management of people with uncomplicated ILI, testing will have a role in community-based surveillance of outbreaks, as well as timely diagnosis of hospitalized and high-risk patients to inform treatment and management of exposed contacts.

Canadian context

Laboratories accredited to perform the analytical activities required in a pandemic are maintained by federal and provincial jurisdictions—these include the federal National Microbiology Laboratory (NML), provincial public health laboratories (PPHLs) and front-line hospital laboratories. Collaboration, supported by a clear designation of roles and appropriate structures and processes, is necessary among laboratories in all jurisdictions to enable the rapid determination and delivery of public health response measures during a pandemic.

The Public Health Agency of Canada (PHAC), through the NML, is responsible for coordinating national laboratory surveillance and for reporting laboratory results internationally to the World Health Organization (WHO) and its partners. The NML plays a significant role in supporting PPHLs through specific laboratory functions such as genetic and antigenic characterization of seasonal and novel influenza strains and phenotypic antiviral susceptibility testing, as well as providing information and support to PPHLs to develop and validate diagnostic assays for new strains for decentralized use. PPHLs carry out primary detection assays and are responsible for having the capability to detect the emergence of a potential novel subtype. They provide a supportive role to front line laboratories and submit viral samples, patient specimens and limited epidemiological information to the NML through established surveillance systems. Front-line laboratories' responsibilities during a pandemic include testing to identify influenza in patient specimens and submitting diagnostic specimens to the PPHL for further characterization.

Collaboration will be required to respond to uneven demand and capacity for testing in different regions of the country. Due to Canada's size and geographic population distribution, it is likely that a pandemic will affect different regions at different times and with varying severity, so that laboratories in more affected regions will experience a greater demand for testing. Testing is also more challenging in remote and isolated communities and requires collaboration between jurisdictions; for example, laboratories in British Columbia and Alberta carry out testing for the Territories, requiring logistical preparation for sample collection and transportation.

Key elements of the laboratory response

Pre-analytical activities

Pre-analytical activities are those that must be followed to ensure appropriate collection of specimens and their transport to the laboratory for testing. Different types of specimens and collection methods are often used to optimize the detection of influenza in patients with more severe disease. Transportation conditions and timing are important considerations for maintaining specimen integrity.

During the 2009 influenza pandemic, many laboratories underestimated the pre-analytic pressures associated with an increase in testing demand. Strategies are required to ensure adequate resources will be available to address this demand, such as increasing resources for accessioning specimens received by the laboratory (e.g., receiving, sorting, logging into the laboratory information system, labelling and processing). There should be a process in place in advance for triaging specimens during periods of high demand. Laboratories should also develop a process for aliquoting (dividing or apportioning) of specimens to allow for retesting a sample or submitting a sample to the NML as needed.

Analytical activities

There are several different testing methods available for the detection of influenza, each with specific time for results, sensitivities, ability to characterize subtypes, throughput and cost. The most widely recommended tests for detecting and characterizing influenza are nucleic acid amplification tests (NAAT), because of their performance, automation and scalability. Direct immunefluorescence assays (DFA) and indirect immune-fluorescence assays (IFA) methods can be used for detecting influenza A, but are not sufficient for subtyping and are less sensitive than NAAT methods. Although rapid influenza detection tests (RIDT), which are based on antigen detection, can provide results within 30 minutes, they cannot subtype and their poor sensitivity limits their usefulness in the management of individual patients; however, RIDT may be useful for monitoring outbreaks, or as an option for timely detection of influenza in remote communities. If antigen-based RIDT are used, the test limitations must be clearly understood by the end user. More rapid NAAT are becoming available; however, their performance in detecting novel viruses and their influence on patient outcomes requires further study. Serology tests are labour-intensive and not used routinely for diagnosis, but have been useful for epidemiologic and immunologic research.

Maintaining the ability to culture influenza virus is important as viral isolates are required for genetic and antigenic characterization, for monitoring of antigenic drift and for phenotypic antiviral resistance (AVR) testing; however, it is expected that novel influenza viruses will be risk group 3 pathogens that will restrict this activity to PPHLs with the appropriate containment level 3 laboratory licence. Ongoing genetic and antigenic characterization and antiviral resistance testing are an important part of routine surveillance. In addition, phenotypic and genotypic testing for antiviral resistance is also done through targeted testing of specimens from patients who are suspected of having a resistant virus. AVR testing informs guidelines for the use of antivirals, and can be an important adjunct in the clinical management of individual patients.

During an influenza pandemic, other respiratory viruses (such as parainfluenza or rhinovirus) can circulate in the population and cause significant illness. To ensure that morbidity and mortality are correctly attributed to the pandemic influenza, it is important to maintain some testing for other respiratory viruses even as resources become more limited.

Post-analytical activities

It is important to ensure front-line laboratories and PPHLs work together to make data and specimens available for surveillance purposes. If elevated testing demands require changes in laboratory testing methods, these changes need to be communicated to clinicians and other users of laboratory data, and their impact on surveillance or patient care made clear. A communication strategy should be developed during

seasonal influenza, to ensure that a process and infrastructure are in place to develop and disseminate messages in a pandemic. Laboratories also need to plan for archiving, storing and removing the large number of specimens that will be processed during a pandemic.

Quality assurance and quality control

Participation in influenza proficiency programs is essential for all laboratories performing influenza diagnostic work, and quality control activities should continue as a pandemic evolves. The NML provides proficiency panels assessing the performance of tests at PPHLs and other laboratories, and also transfers sequence information on influenza viruses to the PPHLs to ensure that the tests used to identify the novel subtype are effective. If, as occurred in the 2009 pandemic, a novel virus requires new testing protocols, PPHLs and the NML will work together to validate the accuracy of new methods or of commercially available assays.

Biosafety considerations

Laboratories need to observe biosafety protocols to prevent exposure to a novel virus in the laboratory when samples are tested. The Centre for Biosecurity at PHAC will provide guidance on the way that specimens of a novel virus should be handled; guidance will be updated as further knowledge is gained about the virus (5).

Integration of laboratory functions with other CPIP components

Laboratories and public health decision makers should work together in the interpandemic period to ensure an awareness and understanding of laboratory functions, including the unique requirements associated with influenza detection in a pandemic, and the important role of the laboratory in the response to a pandemic. In addition, data sharing between laboratories and between Provinces/Territories and PHAC during a pandemic is critical. Data-sharing agreements should be in place before a pandemic to facilitate data transfer and must include intellectual property, copyright and other publication issues.

There are several key linkages and interrelationships with laboratory activities that contribute to an effective and coordinated pandemic response. To ensure the comparability and correct interpretation of data, epidemiologists must understand the details of laboratory testing (e.g., testing algorithms, sensitivity and specificity of the tests used); just as laboratories need to understand which data the epidemiologists need for risk assessments and analysis of pandemic progression. The use of existing surveillance infrastructure for seasonal influenza and other respiratory viruses and the development of data sharing agreements during the interpandemic period provide optimized surveillance capacity in a pandemic (6). Laboratories should communicate changes made to laboratory testing practices, including changes in collection requirements and test performance to clinicians and other end users so that clinicians understand how changes may influence and limit patient management. Community planners must collaborate with laboratory experts and Provinces/Territories to develop new ways of providing testing in First Nations' or other remote and isolated communities and of communicating information among partners. Geographic location and weather conditions may be important considerations in planning the transport of specimens to a laboratory, as these specimens are both time- and temperature-sensitive. Finally, laboratories should put in place the necessary processes to communicate with vendors to rapidly access supplies of commercial assays and reagents to support the laboratory response.

Research needs

In the inter-pandemic period, it is important to develop the infrastructure, protocols and processes to enable rapid-response research during a pandemic to help address knowledge gaps about influenza prevention, treatment and control strategies. In light of their role in supporting such research, laboratories should be involved in this advanced planning. Laboratories should also undertake advanced planning for the infrastructure they would require to support such research. Preparation for research should be encouraged through rapidly-conducted influenza studies during interpandemic influenza seasons.

Discussion

The CPIP laboratory strategy uses testing algorithms and collaborative and data-sharing arrangements that form the seasonal influenza testing and surveillance system, and has been updated to incorporate lessons learned in the 2009 H1N1 pandemic. Challenges remain, however, and are noted as suggestions for improvements in preparedness that laboratories in all jurisdictions should consider during the interpandemic periods.

A primary challenge is the anticipated increase in demand for testing in a pandemic—which could be more than ten-fold over peak seasonal demand. Plans should be developed in the interpandemic period to manage this demand and include those relating to operational functions such as policies for hiring and training staff to meet increased demand, consideration of the processing of high volumes of specimens and plans to meet demands for laboratory supplies. Front-line laboratories should use this period to strengthen their diagnostic capacity, while Provinces/Territories should utilize the criteria established by PPHLs to prioritize testing, so that reporting at the national level is consistent.

Communication strategies could also be strengthened during the interpandemic period, to enable more timely exchange of data, particularly with respect to greater coordination between PPHLs and front-line laboratories in the communication of surveillance data. Linkages within the Canadian Public Health Laboratory network (CPHLN) (7) and similar groups, as well as support for ongoing meetings, should be maintained throughout the interpandemic periods to facilitate the CPHLN's ongoing effectiveness in coordinating the national response to testing, as it did during the 2009 pandemic (8).

The CPHLN continues to monitor developments in laboratory contributions to pandemic influenza preparedness and response. The CPHLN, in consultation with the Pandemic Influenza Laboratory Preparedness Network (PILPN), review laboratory

protocols to ensure Canadian laboratories are able to detect a new influenza virus if it appears in the country. CPHLN also oversees reviews of the *CPIP Laboratory Annex* and incorporates any new developments that arise.

Conclusion

Laboratory testing is a critical function in a response to an influenza pandemic, contributing to both epidemiological surveillance work and to clinical support of affected individuals. It benefits from the systems and structures that are used and refined each year with seasonal influenza and other respiratory viruses, but will need to anticipate and scale activities to meet the needs of a pandemic.

Authors' statement

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Conflict of interest

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