

LABSTRACT – November 2018

Respiratory Virus Testing Algorithm

Audience

Healthcare providers who order respiratory virus testing for their patients.

Overview

This lababstract provides clinicians with the details of Public Health Ontario (PHO) Laboratory's respiratory virus testing algorithm. PHO Laboratory utilizes different testing algorithms for influenza and other respiratory viruses during the winter and summer seasons.

The winter algorithm takes effect on the first Monday of November and remains in effect until the first Sunday of May.

The summer algorithm takes effect on the first Monday of May and remains in effect until the first Sunday of November.

Note: Exact dates may vary due to influenza activity levels during the transition time periods.

What has changed for the 2018 – 2019 season?

With the 2018-2019 winter algorithm (starting Monday, November 5th, 2018), PHO Laboratory will conduct a staged implementation of a laboratory developed multiplex respiratory virus PCR (MRVP1) across four testing sites (Toronto, Ottawa, London and Timmins). MRVP1 will initially be implemented in Toronto, London* and Ottawa[@], and subsequently in Timmins.

MRVP1 detects influenza A, influenza A H3 subtype, influenza B, and respiratory syncytial virus (RSV). Specimens' testing positive for influenza A and negative for H3 subtype will be subsequently tested for influenza A (H1N1) pdm09 subtype. Timmins, servicing Northern Ontario, will use influenza A and B RT-PCR (followed by subtyping if influenza A positive) until MRVP1 is implemented for that region.

Regardless of the testing site, the same total complement of respiratory viruses will be tested during this staged implementation through the combination of real-time PCR and rapid viral culture methodologies.

* London services Southwestern Ontario

[@] Ottawa services Southeastern Ontario

Influenza testing available at PHOL (summer and winter).

Patient Setting ¹	Winter	Summer
In-patient (ICU/CCU ² or ward) Institutions (non-outbreak)	MRVP 1 ^{3,4} If flu A or B or RSV is detected ^{5,6} then no further respiratory viral testing will be performed. If flu A, B and RSV are negative, samples will be further tested by Rapid Viral Culture ^{7,8}	Rapid Viral Culture ^{7,8}
Institutional Respiratory Infection Outbreaks	Influenza Rapid Testing for up to 4 ⁵ outbreak samples, followed by MRVP 1 ^{3,4} If flu A or B or RSV is detected ^{5,6} then no further respiratory viral testing will be performed. If flu A, B and RSV are negative, samples will be further tested by Rapid Viral Culture ⁷	Influenza Rapid Testing on up to 4 ⁵ outbreak samples, followed by influenza A/B RT PCR (1 sample from each flu A-positive outbreak will be subtyped). If flu A or B is positive then no further testing will be performed. If flu A/B is negative, samples will be further tested by Rapid Viral Culture ⁷
Emergency Room patients ⁹	Testing not available ¹⁰	Testing not available ¹⁰
Ambulatory , including ambulatory influenza high risk patients ⁹	Testing not available ¹⁰	Testing not available ¹⁰
Not specified on requisition	Testing not available ¹⁰	Testing not available ¹⁰

Table footnotes:

1. Patient setting must be provided to help triaging of specimens. If patient setting is not provided, sample will NOT be tested.
2. ICU - Intensive Care Unit; CCU - Critical Care Units.
3. MRVP1 detects: influenza A, influenza A H3 subtype, influenza B, respiratory syncytial virus (RSV) A and B.
4. Timmins testing site will use Flu A/B RT PCR until subsequent implementation of MRVP1.
5. For outbreaks with special concerns, including requests for additional testing, contact PHO Laboratory's Customer Service Centre.
6. Specimens that are positive for influenza A and negative for H3 using MRVP1 will be subsequently tested for influenza A (H1N1) pdm09 subtype.

7. The Rapid Viral Culture system (R-Mix Too©) detects: adenovirus, influenza A, influenza B, respiratory syncytial virus (RSV), parainfluenza 1, 2 and 3, and human metapneumovirus.
8. CMV PCR for bronchoalveolar lavage (BAL)/bronchial wash/pleural fluid will be done if requested on the requisition.
9. Respiratory swab collection kits will not be supplied for these patient settings.
10. To assist with patient management when respiratory virus testing is not available, healthcare providers are encouraged to refer to PHO's respiratory surveillance reports for information on respiratory pathogen activity in Ontario (see 5 below).

When influenza is circulating, laboratory confirmation of influenza is not needed before initiating treatment, as waiting until influenza is confirmed will delay initiation of therapy. Current clinical guidelines recommend that during influenza season, influenza antiviral therapy (e.g., oseltamivir or zanamivir) be started empirically for patients with:

- moderate, progressive, severe or complicated influenza, such as individuals who are hospitalized with influenza-like illness)
- high risk of influenza complications/severe disease.

For more information, please see the references provided with this document.

To understand the circulating respiratory pathogens and to assist with influenza antiviral treatment decisions, health care providers are reminded to regularly review PHO's [Ontario Respiratory Pathogen Bulletin \(ORPB\)](#). The ORPB is updated weekly and provides an overview of influenza and other respiratory viruses. Data on influenza positivity is also presented at the local public health unit level to provide jurisdiction-specific information.

Specimen Collection and Handling

Please check the specimen collection kit's expiry dates before use. Expiry dates on collection swabs and transport media (tube) may not be identical – please check both dates. Specimens collected in expired kits will be rejected. Specimen containers and supplies are provided to submitters for the exclusive purpose of submitting specimens to PHO for testing (http://www.publichealthontario.ca/test_directory).

NOTE: To maintain optimum viability, specimens should be stored and transported to PHO at 2-8°C within 48 hours of collection. If longer storage/transit time is anticipated, specimens should be frozen at -70°C or lower.

Additional respiratory viral services available at PHO

1. Influenza Antiviral Susceptibility Testing

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Currently circulating influenza A subtypes (H1N1pdm09 and H3N2) are universally amantadine resistant and almost all currently circulating influenza A and B viruses are oseltamivir susceptible. Resistance has been documented on rare occasions. Pre-pandemic seasonal influenza A (H1N1) was known to be amantadine susceptible, and almost universally oseltamivir resistant, but it has not been detected in Ontario since mid-2009.

Routine susceptibility testing is not required for clinical care, however a proportion of influenza-positive samples will be forwarded to the National Microbiology Laboratory for strain typing and antiviral susceptibility testing and limited susceptibility testing is also available at PHO.

Recommended criteria for antiviral susceptibility testing in Ontario are:

- Influenza developing during or soon after influenza antiviral prophylaxis (e.g., oseltamivir or zanamivir)
- Severely-ill patients (ICU) with laboratory-confirmed influenza not responding to influenza antiviral therapy
- Fatalities in patients with laboratory-confirmed influenza being treated with influenza antiviral therapy
- Persistent influenza viral shedding, defined as a repeat PCR test positive after 7 days or more of treatment. Repeat PCR testing could be undertaken for patients who are not responding to antiviral therapy. Immunocompromised patients are at greater risk for more severe disease, persistent viral shedding and development of antiviral resistance.
- Influenza A (H1N1) pdm09-positive outbreak samples (will be routinely tested at PHO)
- Positive test for influenza A in a traveller returning from an area where resistance is endemic

To request influenza susceptibility testing for a patient who meets any of the above criteria, please provide the relevant information on the laboratory requisition. To make a request on a sample already submitted to PHO, please contact our Customer Service Centre at 1-877-604-4567 or 416-235-6556 or your local PHO laboratory.

2. Testing for Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

MERS-CoV is a novel coronavirus that emerged in the Middle East in 2012. Patients with relevant clinical presentation and epidemiological risk factors for MERS-CoV infection, such as travel to certain countries in the Middle East or contact with a confirmed or probable MERS-CoV case, should be considered for MERS-CoV testing. For further information, please see the PHO MERS-CoV Test Information Sheet available at: [publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/Middle-Eastern-Respiratory-Syndrome-Coronavirus-\(MERS-CoV\).aspx](http://publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/Middle-Eastern-Respiratory-Syndrome-Coronavirus-(MERS-CoV).aspx)

3. Testing for Novel Influenza Viruses

a) Avian influenza viruses

PHO conducts testing for avian influenza (e.g., H5N1, H5N2, and H7N9) as required based on the information provided on the test requisition. Samples indicating travel to affected areas, or exposure to known cases, will be tested by real-time influenza A PCR (US CDC protocol) and if positive will be tested first for seasonal subtypes (H3N2, H1N1pdm09). If no seasonal subtype is detected, further testing for avian influenza subtypes will be conducted.

In April, 2013, the World Health Organization (WHO) confirmed emergence of a novel avian influenza A (H7N9) virus in China. Ontario Ministry of Health and Long-Term Care guidance, including laboratory testing information, is available at:

health.gov.on.ca/en/pro/programs/emb/avian/workers.aspx

Influenza A (H5N1) infections in humans have been infrequently reported since 2003 with cases occurring in Asia, and later in Africa, Europe, and the Middle East, mostly due to exposure to infected birds or their environment. Information on influenza A (H5N1) is available at:

health.gov.on.ca/en/news/bulletin/2014/hb_20140110_1.aspx

b) Surveillance and testing for variant (swine origin) influenza viruses in humans

PHO conducts surveillance for variant influenza viruses, such as H3N2v, which have caused several hundred infections in the United States in recent years, with a peak in 2012, among persons with swine contact (e.g., children exposed at agricultural fairs, swine workers). Only limited human-to-human transmission has been documented. Screening will be done by real-time PCR for the swine nucleoprotein (NP) gene on all early and late season influenza A viruses of subtype H3 and a proportion of all other H3 subtype influenza A-positive samples once the influenza season is established.

This testing is also available on request in person(s) who develop acute respiratory illness following direct contact with swine or their environment.

NOTE: Samples that do not subtype for seasonal influenza will be tested for a panel of avian and/or swine influenza viruses.

4. Testing for Enterovirus (including EV-D68 and other serotypes)

EV-D68 circulated in Ontario in the summer/fall of 2014, and to a lesser extent in 2016. As of August 2018 several cases of EV-D68 were detected in Ontario. Information about non-polio *enterovirus*, including D68, is available at:

www.publichealthontario.ca/en/BrowseByTopic/InfectiousDiseases/Pages/Enterovirus-D68.aspx.

Information on specimen collection and testing for enterovirus can be found at:

<https://www.publichealthontario.ca/en/ServicesAndTools/LaboratoryServices/Pages/Enterovirus.aspx>

5. PHO Surveillance Reports and Network:

PHO routine surveillance reports are available on the PHO website at

- [Ontario Respiratory Pathogen Bulletin](http://www.publichealthontario.ca/ORPB) (<http://www.publichealthontario.ca/ORPB>)
- [Laboratory-Based Respiratory Pathogen Surveillance Report](http://www.publichealthontario.ca/LabPathogenReports) summarizes all respiratory viral testing done at PHOL (<http://www.publichealthontario.ca/LabPathogenReports>)

Sentinel Practitioner Surveillance Network (SPSN)

- The SPSN performs molecular respiratory viral testing on patients with influenza-like-illness visiting community-based sentinel health care providers across Ontario, as well as in other provinces. SPSN sentinels are the only community practitioners who are exempt from laboratory testing restrictions. Specimens collected by SPSN sentinels will continue to be tested for influenza and other respiratory viruses (by molecular methods or culture). General information on Ontario's SPSN, and information for practitioners interested in contributing to the network, can be found at:

publichealthontario.ca/en/BrowseByTopic/InfectiousDiseases/Studies/Pages/VE-study.aspx

References

1. Aoki FY, Allen UD, Stiver HG, et al. [The use of antiviral drugs for influenza: A foundation document for practitioners](#). Can J Infect Dis Med Microbiol Suppl C Autumn 2013;24: 1C-15C
2. AMMI Canada Guidelines. Available at: <https://www.ammi.ca/?ID=122>
3. Antiviral Medications for Influenza: Information for Healthcare Providers. Available at: publichealthontario.ca/en/eRepository/Antiviral_Medication_Influenza_Fact_Sheet.pdf

For further information

- Contact the PHOL Customer Service Centre at 416-235-6556 or 1-877-604-4567 (toll-free), or by email at customerservicecentre@oahpp.ca
- For PHOL specimen collection information and previous Lababstracts, refer to publichealthontario.ca/Labs
- The current version of the PHOL General Test Requisition and other forms are available at publichealthontario.ca/Requisitions
- To subscribe to future Lababstracts, [register on our website](#)
- To register for Autofax and receive laboratory reports by fax directly from our laboratory information system as soon as they are released, contact the PHOL Customer Service Centre