Labstract – November 2016

Respiratory Viral Testing Algorithm and Enhanced Surveillance - Update

To Health Care Providers:

Effective November 7, 2016, Public Health Ontario (PHO) will be updating its respiratory viral testing algorithm to provide the highest quality testing for clinical management and treatment decisions for high risk patients in Ontario.

What is new:
This simplified respiratory viral testing algorithm ensures highly sensitive nucleic acid detection-based multiplex respiratory viral PCR (MRVP) testing for all patients at high risk of complications from respiratory viral infection. This test:

- detects 16 respiratory viruses and 3 influenza A subtypes to enhance diagnostic capacity
- offers a significantly reduced testing turnaround time to ensure optimized laboratory testing for clinical management.

Secondary use of this data for public health surveillance, including the production of PHO's Ontario Respiratory Pathogen Bulletin is also enhanced by the multiple targets included in this testing algorithm.

To ensure the highest quality testing of patients requiring these results for clinical management, PHO's new respiratory viral testing algorithm and testing will be used for:

- patients admitted to hospital
- patients presenting to the emergency department
- patients undergoing bronchoalveolar lavage (BAL)
- high risk patients in outpatient settings including children <5 years and adults 65 years or older, and patients with underlying chronic conditions (See Table for a complete list of high risk conditions).
- Outbreak investigations

Respiratory viral testing in non-high risk ambulatory patients is of minimal clinical value for this patient group and will no longer be available at PHO. To assist with the assessment and management of non-high risk ambulatory patients, clinicians are encouraged to keep up-to-date on respiratory viruses and select bacterial pathogens circulating in Ontario by regularly reviewing PHO's Ontario Respiratory Pathogen Bulletin (ORPB) (produced weekly from November to April and biweekly from May to October). Findings are analyzed by all patient settings, including ambulatory settings, as well as by local Public Health Unit.

Current clinical guidelines recommend, during influenza season, that antiviral therapy be started empirically for patients with significant acute respiratory illness (e.g. requiring hospitalization), and in those at high risk of influenza complications/severe disease. For more information please refer to the Reference at the end of this document.

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These important changes to PHO's respiratory virus testing algorithm have been summarized in the Table on the next page.

Table. Respiratory viral testing algorithm for specimens received at PHO, effective November 7, 2016

Patient Setting[1] or Specimen Type	Test Provided	Comments
1. Inpatient Intensive care Unit (ICU)/ Cardiac Care Unit (CCU) a) BAL/bronch wash/pleural fluids b) Other respiratory samples - NPS/ throat	• MRVP[2] for samples from categories 1-5	Additional testing for each setting/specimen type • CMV shell vial will also be performed on BAL/bronch wash/pleural fluids.
2. Emergency department, inpatient (ward), or Institution eg. Long-term care facility, correctional facility		• No additional testing performed, unless specifically requested
3. Autopsy/biopsy a) lung tissue		• Lung tissue: CMV shell vial culture & Conventional virus culture will also be performed The following are available on request: • *Legionella* PCR • *M. pneumoniae/C. pneumoniae duplex* PCR
b) NPS/throat		• Autopsy NPS: Conventional virus culture will also be performed
4. Outbreaks		• Influenza rapid testing will also be performed (up to 4 samples) • **NOTE: MRVP testing provided on up to 4 samples per outbreak** • Once 4 OB samples had been tested or if there is one influenza positive from that outbreak then no further respiratory viral testing will occur for that outbreak
5. Bronchoalveolar lavage (BAL) regardless of patient setting		• CMV shell vial will also be performed
6. Ambulatory (e.g., healthcare provider's office, clinic, other community ambulatory settings)	• MRVP[2] for samples from patients at high risk[3] for influenza complications only • **No routine testing performed for patients who are not at high risk of influenza complications[3].**	Although respiratory viral testing is available for persons at high risk for influenza complications, not all patients in this category require testing, and should be reserved for situations when this will aid in clinical management (e.g., more significant acute respiratory symptoms which may require future referral to hospital) **The "influenza high risk"[3] box must be marked on the PHO General Test Requisition** (http://www.publichealthontario.ca/requisitions) **for testing to occur for patients in the ambulatory setting** The high risk indication for testing must also be provided. Common influenza high risk conditions include chronic respiratory disease, cardiac, neurologic, and renal disease, immunodeficiency, malignancy, diabetes, hemoglobinopathy. High risk patient groups include person's age< 5 and ≥65 years, pregnant, obese with BMI> 40, and aboriginal. See footnote 3 for a complete list of influenza high risk conditions.

Table footnotes:

1 - If patient setting is not provided, sample will NOT be tested.

2 - MRVP - multiplex respiratory viral PCR. The current MRVP assay detects influenza type (A and B), influenza A subtype (H1, H3 and (H1N1) pdm09), rhinovirus, enterovirus, RSV A and B, parainfluenza 1, 2, 3 and 4, adenovirus, bocavirus, human metapneumovirus and human coronaviruses 229E, NL63 and OC43. Please note this panel does not detect MERS-CoV. MRVP will not be performed on multiple submissions from the same anatomical site, or repeat submissions within 7 days of a previous sample being collected.

3 - Following the Association of Medical Microbiology and Infectious Disease (AMMI) Canada guidelines, patients at high risk for respiratory viral infection complications include the following –

• Asthma and other chronic pulmonary disease, including bronchopulmonary dysplasia, cystic fibrosis, chronic bronchitis and emphysema
• Cardiovascular disease (excluding isolated hypertension; including congenital and acquired heart disease such as congestive heart failure and symptomatic coronary artery disease)
• Malignancy
• Chronic renal insufficiency
• Diabetes mellitus and other metabolic diseases
• Hemoglobinopathies such as sickle cell disease
• Immunosuppression or immunodeficiency due to disease (e.g., HIV infection, especially if CD4 is <200×106/L), or iatrogenic, due to medication
• Neurologic disease and neurodevelopmental disorders that compromise handling of respiratory secretions (cognitive dysfunction, spinal cord injury, seizure disorders, neuromuscular disorders, cerebral palsy, metabolic disorders)
•Children younger than 5 years of age*
• Individuals 65 years of age or older
• People of any age who are residents of nursing homes or other chronic care facilities
• Pregnant women and women up to 4 weeks post-partum regardless of how the pregnancy ended
• Individuals <18 years of age who are on chronic aspirin therapy
• Obesity with a BMI >40 or a BMI >3 z-scores above the mean for age and gender
• Aboriginal peoples

* Children who are two through four years of age also have a higher rate of complications compared to older children; however, the risk for these children is lower than the risk for children younger than two years of age.

1. Specimen Collection and Handling

Please check specimen collection kit (http://www.publichealthontario.ca/test_directory) expiry dates before use. Expiry dates on collection swabs and transport media may not be identical – please check both dates. Specimens collected in kits that have expired dates will be rejected. Specimen containers and supplies are provided to submitters exclusively for samples that are to be tested by the PHO.

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.

2. Influenza Antiviral Susceptibility Testing

Currently circulating influenza A subtypes (H1N1pdm09 and H3N2) are universally amantadine resistant and almost all currently circulating influenza A and B viruses are universally oseltamivir susceptible. Resistance has been documented in 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 resistance 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 resistance testing and limited antiviral susceptibility testing is also available at PHO.

Recommended criteria for antiviral susceptibility testing in Ontario are:

- Influenza developing during or soon after Neuraminidase inhibitor (e.g., oseltamivir or zanamivir) antiviral prophylaxis
- Severely-ill patients (ICU) not responding to therapy
- Fatalities
- Persistent viral shedding, defined as a repeat PCR test positive after 7 days or more of treatment. This could be undertaken for:
    - Immunocompromised patients
    - Patients not responding to antiviral therapy
- influenza A(H1N1)pdm09-positive outbreak samples (will be routinely tested at PHO)
- Positive test for influenza A in a traveller returning from 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.

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

MERS-CoV is a novel coronavirus that emerged in the Middle East in early 2012. Patients with relevant clinical presentation and epidemiological risk factors for MERS-CoV infection, such as travel to 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

4. Testing for Novel Influenza Viruses

a) Avian influenza virus

PHO conducts testing for avian influenza (e.g., H5N1, H5N2, H7N9) as required by 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 for seasonal subtypes (H3N2, H1N1pdm09).

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

Information on influenza A/H5N1 is available at:http://www.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 among persons with direct 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 season is established.

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

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

5. Testing for Enterovirus D68

Information about testing for enterovirus D68 (EV-D68) testing, is available at: http://www.publichealthontario.ca/en/BrowseByTopic/InfectiousDiseases/Pages/Enterovirus-D68.aspx.

PHO Reports and Studies:
PHO routine surveillance reports are available on the PHO website at http://www.publichealthontario.ca/en/DataAndAnalytics/Pages/DataReports.aspx

- **Laboratory-Based Respiratory Pathogen Surveillance Report** summarizes all respiratory viral testing done at PHO
- **Ontario Respiratory Pathogen Bulletin**
- **Monthly Infectious Disease Surveillance Report**

Sentinel Practitioner Surveillance Network (SPSN) (formerly the Vaccine Effectiveness (VE) Study)

- **The SPSN** performs molecular viral testing on patients with influenza-like-illness visiting community-based sentinels across Ontario. SPSN sentinels are the only community practitioners who are exempt from laboratory testing restrictions as SPSN specimens are tested for influenza and other respiratory viruses (by molecular methods or culture). Ontario SPSN information and reports to sentinels, as well as information for practitioners interested in contributing to the study, can be found at: http://www.publichealthontario.ca/en/BrowseByTopic/InfectiousDiseases/Studies/Pages/VE-study.aspx

Reference:

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

For further information:

- Contact our Customer Service Centre at 416-235-6556 or 1-877-604-4567 (toll-free), or by email at CustomerServiceCentre@oahpp.ca
- For PHO specimen collection information and previous Labstracts, refer to http://www.publichealthontario.ca/labs
- The current version of the PHO General Test Requisition and other forms are available at http://www.publichealthontario.ca/requisitions
- To subscribe to future Labstracts, email labstracts@oahpp.ca
- To register for Autofax and receive laboratory reports by fax directly from our laboratory information system as soon as they are released, contact the Customer Service Centre.