Canadian Public Health Laboratory Network

PROTOCOL FOR MICROBIOLOGICAL INVESTIGATIONS OF SEVERE ACUTE RESPIRATORY INFECTIONS (SARI)

1.0 INTRODUCTION

Although the protocol for Severe Acute Respiratory Infections (SARI) was initially developed as a response to the 2003 SARS outbreak, its intended use is to facilitate the diagnosis of severe respiratory infections due to both unknown and known respiratory pathogens that have the potential for large scale epidemics. With both the novel coronavirus and the emerging H7N9 virus, a key factor is the determination of risk based on epidemiologic factors, which is in turn related to exposure in an "area of concern". The initial risk assessment must be done in concert with your local Ministry of Health (MOH). SARI alerts should trigger clinicians to "Think, Tell and Test

- **Think** about the possibility of an emerging respiratory infection(e.g. novel influenza A virus)
- **Tell** the local medical officer of health or local public health official
- **Test** for pathogen only after appropriate consultation and based on clinical symptoms

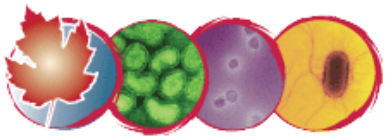
2.0 LABORATORY PROTOCOL (Figure 1)

Although the risk assessments will be modified as new information becomes available, at this time the probability that a severe acute respiratory illness is due to a novel coronavirus or H7N9 is extremely low. Therefore, in patients with no epidemiological risk factors the most common pathogens should be ruled out before considering an unusual or more highly virulent pathogen. This may be done at the local laboratory or the Provincial Public Health Laboratory (PPHL) depending on local capacity and expertise.

Specimens to be considered for collection include sputum, nasopharyngeal swab (NPS), bronchoalveolar lavage (BAL), endotracheal secretions, and throat swab. For pediatric patients, a nasopharyngeal aspirate is a suitable replacement to a NPS.

Pathogens that should be excluded on preliminary testing include:

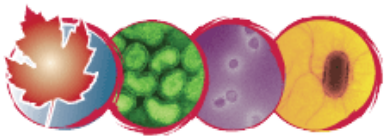
- **Conventional bacteria** (including *Mycoplasma pneumoniae, Legionella pneumophila*)
  - Specimen: sputum and urine
  - Testing: gram stain and routine culture ± Legionella.
    - *Mycoplasma pneumoniae* PCR,
    - Legionella urinary antigen
- **Conventional respiratory viruses** (e.g. human influenza, parainfluenza, respiratory syncytial virus, adenovirus, human metapneumovirus, rhinovirus/enterovirus, coronavirus)
  - Specimens: NPS, endotracheal secretions, BAL, +/- throat swab and sputum.



- NPS is the primary specimen type for respiratory viruses including seasonal influenza. However, based on our experience with pandemic H1N1, deeper specimens such as endotracheal secretions or BAL must be collected in cases of severe respiratory infection with negative NPS.
- A number of avian influenza A viruses, including H7N9, have been detected in throat swabs. Recently, H7N9 was only detectable in sputum specimen in 1 of 4 patients. While sputum and throat swabs are not ideal for most influenza viruses, until the ideal specimen for H7N9 can be identified, multiple specimens types should be considered in patients suspected of having avian influenza A viruses

– Testing:
  - Influenza A and B by RT-PCR with subtyping (H3N2 or H1N1) should be the primary method for detection of influenza (24 hour turnaround time (TAT)).
  - Respiratory multiplex RT-PCR for parainfluenza, human metapneumovirus, coronavirus, rhinovirus/enterovirus, adenovirus should be done on negative influenza specimens (48 hour TAT) when there is a clinical indication to detect noninfluenza viruses.
  - RIDTs should not be used to rule out influenza A. The sensitivity of currently available RIDT for human influenza strains is suboptimal. The performance characteristics of currently available commercial tests for detection of H7N9 are unknown, and likely to be poor based on the suboptimal sensitivity of these assays for other avian influenza strains.
  - Novel influenza A viruses and the novel coronavirus are classified as Risk Group 3 pathogens. Routine culturing of specimens from suspect patients should only be considered in PHLs with containment level (CL)3 facilities

- If more invasive samples are collected they should be processed for a wide range of pathogens:
  – Bronchial-alveolar wash for all cultures (bacteria, viruses, mycobacteria, fungi)
  – Open lung biopsy – for all cultures, RT-PCR and histology (ensure specimen is NOT PUT IN FORMALIN)



WHEN TO SUSPECT THE NOVEL CORONAVIRUS (MERS-CoV):

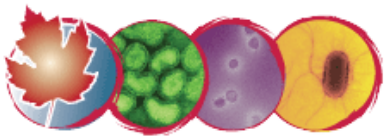
Limited data suggests that MERS-CoV can present as a co-infection with other viral pathogens. As such, in addition to specimens that are negative for conventional pathogens, those that do have other identified pathogens **but are consistent with suspect cases of novel coronavirus based on the PHAC case definition** should be tested for the MERS-CoV. The details regarding testing and some control materials for method development are available from the National Microbiology Laboratory (NML). To date only a few PPHLs have developed the capacity to test for this pathogen in-house. All other PPHLs will forward the suspect specimens to the NML for further testing.

WHEN TO SUSPECT A NOVEL INFLUENZA VIRUS (including H7N9):

Influenza viruses that are positive on the initial influenza identification test but cannot be subtyped using RT-PCR should be further characterized. Laboratories that have the capacity to further characterize the specimens by sequencing methods (e.g. sequence the M gene) to determine the subtype of the virus will do so. Those that lack this capacity will rely on the NML for further characterization. However, given that subtyping assays are usually less sensitive than the identification assays, weak positives may not be able to be typed. Based on local experience, each laboratory should evaluate these on a case by case basis in concert with their local clinicians and Public Health colleagues.

Influenza positive specimens outside the influenza season or obtained from patients with a history of exposure animals (e.g. pigs or chickens), should be routinely submitted to the NML for characterization

NOTE: *While initial analysis of in-house assays used by many labs suggest they should be effective in identifying H7N9, it is difficult to determine the effect on the sensitivity of testing. This is particularly true of the performance of commercial assays whose primer sequences are not known.*



IF A FRONT LINE LABORATORY SUSPECTS A NOVEL RESPIRATORY PATHOGEN: The initial tests (as outlined above) would be similar but supplemental testing will be required at the PPHL. The Laboratory should communicate with the clinician to ensure that the following specimens are collected:

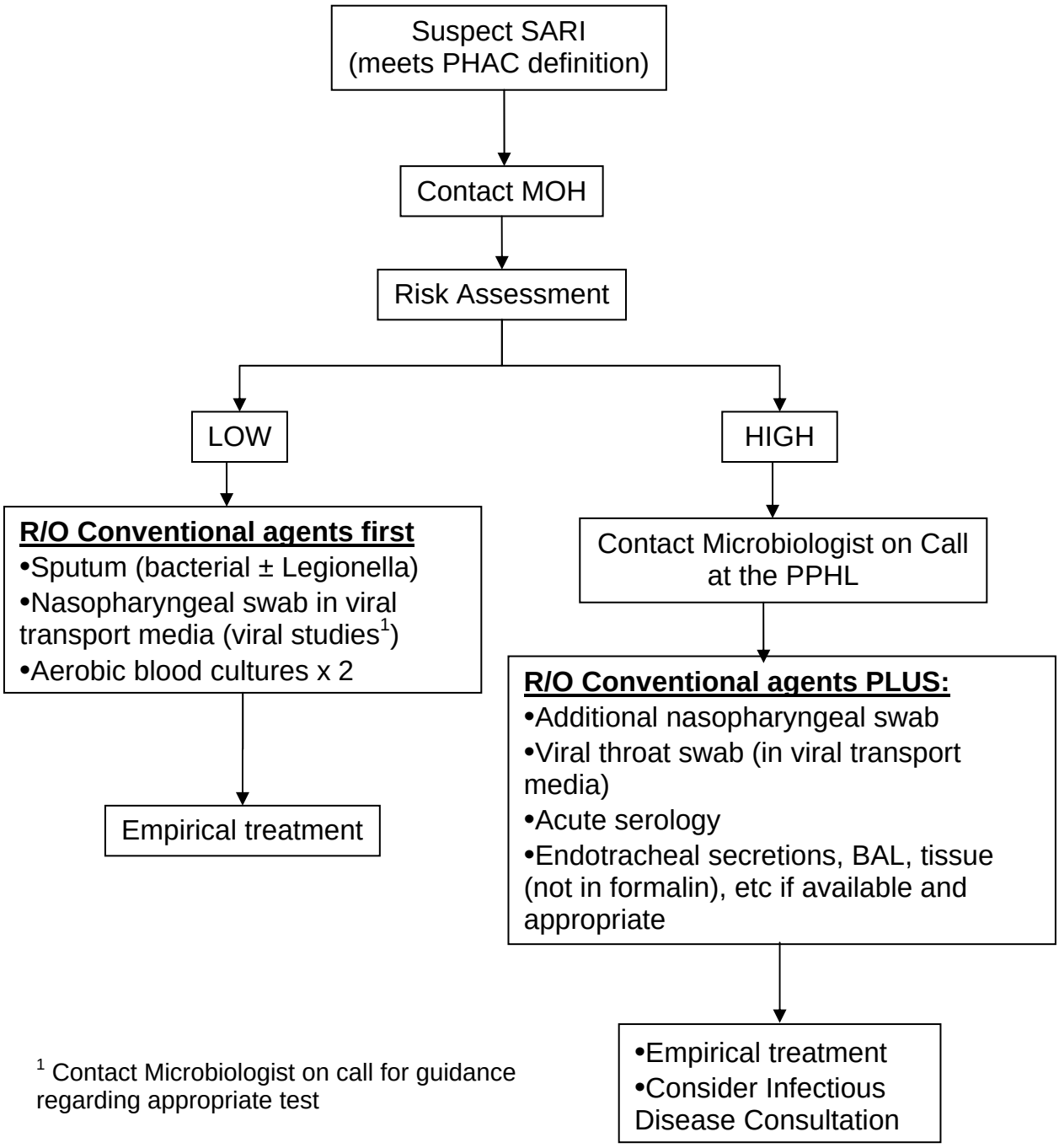
- A second NPS/endotracheal aspirate or BAL to be used for confirmation by the NML
- A viral throat swab (in viral transport media) – A number of avian influenza A viruses including the H7N9 have been detected in throat swabs. Until the ideal specimen can be collected multiple specimens types should be considered
- Acute and convalescent sera
- Conjunctiva swab if clinically appropriate (in viral transport media)

IF A PHL SUSPECTS A NOVEL RESPIRATORY PATHOGEN:

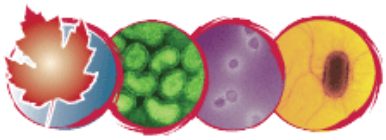
- The PPHL should notify the MOH immediately when a suspect specimens is identified
- All specimens with suspected novel respiratory pathogens (as outlined below) must be forwarded to the NML for confirmatory testing
- Specimens suspected to contain a novel respiratory virus should be handled using CL2 with enhance PPE if manipulated outside a BSC.

Figure 1:

•**Think** about the possibility of an emerging respiratory infection, e.g. novel influenza virus
•**Tell** the local medical officer of health or local public health official
•**Test** for pathogen only after appropriate consultation and based on clinical symptoms



[1] Contact Microbiologist on call for guidance regarding appropriate test



3.0 TRANSPORTATION OF SPECIMENS

If the case has been linked to another proven case of a novel respiratory virus, or has strong epidemiological evidence to link it with avian influenza, then please handle the specimen in the manner prescribed below; otherwise treat specimens as routine clinical specimens:

Transport by Land:
If the suspected agent is classified as Risk Group 3,use a Type 1A package.
(There is a modification possible for transport by air,see below.)

Other requirements of the TDG regulations such as training, labeling, marking and documentation apply.

Transport by Aircraft:
The International Civil Aviation Organization (ICAO) Technical Instructions (TI) with some additional provisions of the TDG Regulations, may be used for the transportation of diagnostic specimens by aircraft. Consignments prepared this way may be transported by road to and from the airport as well.

Under the ICAO TI, the shipping name DIAGNOSTIC SPECIMEN, UN3373 must be used for all diagnostic specimens if they may contain influenza Risk Group 3 agent. Diagnostic specimens are exempted from other requirements in the ICAO technical instructions if they are packaged in packaging of good quality, capable of passing a 1.2m drop test. A Type 1A package meets these requirements. A Type 1B package may only be used if it meets the additional ICAO requirements regarding cushioning of the secondary receptacle, drop test and pressure retention capability.

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