Title: Essential COVID-19 information on the variability of testing using nasal, nasopharyngeal and throat swabs for SARS-CoV-2

Question: How do the testing characteristics for the AHS lab-developed tests for COVID-19 differ between samples collected from nasal, nasopharyngeal and throat swabs?

Context:
- When this review started, there were three devices in use for collecting samples for COVID-19 testing:
  1. FLOQSwab and Universal Transport Medium (for nasopharyngeal (NP) swabs)
  2. APTIMA® Unisex Swab Specimen Collection Kit (throat or deep nasal swabs)
  3. APTIMA® Multitest Swab Specimen Collection Kit (throat or deep nasal swabs)
- While this review was ongoing, recommendations for swabbing changed and AHS and APL no longer recommend nasal swabbing as a sample collection method.
- AHS uses a validated lab-developed real-time reverse transcriptase – polymerase chain reaction (RT-PCR) assay to test for the presence of SARS-CoV-2.
- There was a recent safety incident where a patient with a history and symptoms consistent with COVID-19 was taken out of isolation and off of contact precautions due to negative test result, raising questions about the negative predictive value of COVID-19 testing.
- Clinicians have raised questions about variability in testing characteristics (e.g. sensitivity, specificity, negative predictive value) depending on the anatomical site from which the sample was taken.

Recommendation – Provided by: AHS COVID-19 Scientific Advisory Group

1. Based on the evidence, false negative samples are infrequent but do occur and would appear to result from insufficient sample collection, emphasizing the importance of proper collection of samples.
2. A program should be devised to identify false negative test results and correlate to clinical cases of COVID-19. To calculate the clinical sensitivity of the test, a consistent case definition and a standard for confirming positive cases will be required. The current lack of a gold standard for confirming positive cases is a significant challenge.
3. Nasopharyngeal swabs are preferred for COVID-19 sample collection. When this is not possible, for instance due to potential shortages in NP swabs, throat swabs can be used but more evidence is needed to ensure that throat swabs are equivalent in quality to NP swabs for the purposes of COVID-19 testing. Instructions for collecting an NP or throat swab can be found here and are appended to the lab bulletin here.
4. The operational implications of throat swabs must be considered. For example, throat swabbing often elicits a cough from the patient. Staff at assessment centres must be prepared for these reflexes and be equipped with the proper PPE.
5. Information should be distributed to remind clinicians that a negative PCR can occur and a negative result does not mean that the case is a true negative, especially when there is a high probability of disease. Clinical judgement and multiple lines of evidence (such as clinical signs and symptoms, medical imaging results, and contact with lab confirmed cases) should be considered when
making decisions for patient care and staff protection.

Summary of evidence:

- The analytical validity of the lab-developed test used in Alberta is not in question, as confirmatory testing by the Canadian National Microbiology Lab (NML) showed that the Alberta test was 100 per cent accurate, and analytical specificity of PCR testing has been reported to be 100 per cent given the methodology – at least when done during active infection phase.

- However, problems with swab collection have been noted, and it is unknown how the anatomical site of sampling and the timing of the sample relative to the disease progression affects the likelihood of RNA detection in a person who is infected with SARS-CoV-2.

- There is very limited data regarding the negative predictive values and clinical sensitivity and specificity of commercially developed molecular tests for SARS-CoV-2. What data that exists publicly is a different assay from what is used in Alberta and comparisons should be made with caution.

- Studies comparing RNA detection from different sites used samples collected from any of the following sites: nasopharynx, nose, throat, sputum, or bronchoalveolar lavage fluid. The evidence was mixed with respect to the superiority (or inferiority) of nasal swabs compared to throat swabs. A small study (n=30) that is ongoing in Alberta indicates that NP and throat swabs may be equivalent while nasal swabs may have lower sensitivity. It is suspected that this is related to a lack of familiarity with deep nasal swab collection and poor collection technique, though this is based on anecdotal evidence.