

Specimen Collection Site: Literature Review as of September 10, 2020

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Considerations

With students and staff returning to campus, there will be increased interest in testing everyone for COVID-19. Currently, the gold standard is a nasopharyngeal swab which constitutes inserting a swab through the nostril a distance equal to the opening of the ear and leaving/swabbing for a few seconds. The sensitivity of nasopharyngeal swabs (NP) is not 100% but remains high. In studies of influenza, NP sensitivity ranges from 68%-95% and increases even more when combined with a second specimen.¹ NP can also be uncomfortable for the patient and requires a healthcare worker to perform the swab. Due to this, there has been interest in determining whether other biological samples could be used instead with less discomfort and possibly self-collected by the patient. To investigate this, a review of the literature was completed.

In general, the other biological samples that have been explored in the literature are oropharyngeal swabs, saliva, sputum, self-collected nasal and throat, and feces. Some have also looked at detecting COVID-19 via urine or blood but these samples rarely test positive for known COVID-19 cases.²⁻⁴ The literature is quite mixed on whether a specific sampling site is truly better than a NP, and most studies compare results to NP samples of the same patient.

Overall, these studies cited below are small and are mostly completed on patients who are hospitalized with COVID-19. Those presenting to healthcare facilities with possible symptoms of COVID-19 differ dramatically from asymptomatic or pre-symptomatic individuals in the greater population. This should be taken into consideration when interpreting the sensitivity of differing collection sites. Another consideration is the viral load of patients when they are tested. Viral load increases after symptom onset and after approximately 1 week begins to lower.⁵ Additionally, higher viral loads have been detected within nasal versus the throat, which also has implications for the specimen collection site. These should be recognized when considering the results presented below.⁵

Another important facet of current COVID-19 testing is the fact that many testing protocols are developed locally in hospital and commercial laboratories. Information about these tests is not readily available and was not included in this literature review. Locally developed tests carry their own sensitivities and specificities and should be evaluated within their communities.

Oropharyngeal Swabs

Oropharyngeal swabs (OS) are done by inserting the swab into the patients mouth and rubbing it along the tonsillar pillars. These still require a healthcare worker to perform the swab and can sometimes be uncomfortable. Some studies have found that OS tend to be less sensitive than a NP when both are collected.^{2,6,7} Other studies have demonstrated concordant results between

OS and NP.^{3, 8} One pre-print found that when combining OS with a less invasive nasal sample using a more available OS swab, sensitivity increased.⁹ This may be a viable path to explore where numerous, more tolerated sites are sampled and combined to use for testing of COVID-19.

Saliva

Most of the literature examines saliva specimens in comparison to NP. Saliva specimens are ideal in that they can easily be self-collected, pose no risk to healthcare workers, and are not uncomfortable.¹⁰ Some studies have found saliva to be less sensitive than NP, but this may be attributable to when testing was done in relation to symptom onset.¹¹⁻¹⁵ Saliva has been shown to be similar to NP in that viral titers decrease in saliva over time after symptom onset.^{16, 17} This is important because if saliva testing (or NP testing) is done long after symptom onset, there is the possibility for a negative test even though the patient may have COVID-19. Other studies, though, have found saliva samples to be equally as sensitive as NP, with an occasional study finding saliva to be more sensitive.^{16, 18-21} Overall, though, saliva samples have high sensitivity and specificity when compared to NS, generally >80% and >95%, respectively, and may be a good, non-invasive alternative to NP swabs.^{22, 23, 24}

Sputum

Sputum is a mix of saliva and mucus coughed up from the respiratory tract. Sputum samples are similar to saliva in that they can be self-collected and are not uncomfortable but producing sputum for a test absent a respiratory infection may not be viable. Of two small studies, sputum specimens performed similarly to NS.^{6, 25}

Self-Collected Nasal and Throat

Another alternative is patient-collected nasal and throat swabs and saliva samples. This involves the patient swabbing the inside of their own nostril and back of the mouth and spitting in a tube. These methods are safe for healthcare workers since they are not involved and also can be more tolerated than NP or OS due to the swab not going as deep. When these swabs are done, studies have found them to be quite sensitive, generally >90%, and accurate when combined together.^{8, 9, 26-30} Self-collected saliva samples were found to be consistent, and in some cases superior when compared to healthcare worker collected NT swabs from COVID-19 suspected participants.³¹

Based upon the literature, NP is still the gold standard for COVID-19 testing. But considering testing large populations and discomfort, NS may not necessarily be the best choice. Other samples such as saliva or self-collected nasal and throat swabs have high concordance with NP and should be considered when thinking about testing many people. It also seems beneficial to include multiple samples (i.e.: both throat and nasal swabs) to increase sensitivity when testing many people. Additionally, some are beginning to investigate group pooling of samples to help

reduce the burden on labs and the supply chain. This may be another avenue to explore when thinking about testing many people.

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