Role of COVID-19 Antigen Testing

NSW Health Pathology Discussion Paper
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Background

Nucleic acid testing (NAT), serology and virus culture are used for the diagnosis of COVID-19 (SARS-CoV-2) disease. NAT is highly sensitive and is the mainstay of testing. It does have a number of limitations: turnaround times (TATs) that may be variable and dependent on specimen transport; varying nucleic acid extraction requirements; reagent shortages and uncommon false positives. The ‘in-lab’ TAT is around six hours. Rapid NAT is also available – in NSW Health Pathology (NSWHP) the Xpert® Xpress SARS-CoV-2 NAT assay on the GeneXpert platform is used across NSW, with a TAT of less than one hour. However, the GeneXpert cartridges are in limited supply and are therefore reserved for priority patients.

Recently, SARS-CoV-2 antigen detection tests have been developed as a rapid alternative to NAT, and these are becoming available in Australia. They detect the presence of SARS-CoV-2 proteins in respiratory tract samples and can be potentially employed as rapid tests for COVID-19 diagnosis. They can be performed in the laboratory or at the point of care. A number of these tests have been granted Emergency Use Authorisation (EUA) by the US Food and Drug Administration (FDA). A number of COVID-19 antigen detection tests are currently included on the ARTG for supply in Australia, but this list is expanding.

Rapid antigen tests have been used for many years for the diagnosis of other respiratory viruses such as influenza and RSV. They usually use lateral flow or similar techniques and may or may not require a specific reader platform. They are less (approx. 70%) sensitive compared with NAT, and in NSWHP were replaced some years ago by the rapid GenXpert influenza/RSV NAT.

Key points

- COVID-19 antigen tests are immunoassays that detect presence of viral antigen specific to SARS-CoV-2. A positive result implies current infection.
- Rapid antigen tests may be easier to perform with quicker TATs (15-30 min) but are generally less sensitive compared with NAT in detecting the relevant virus.
- They are ‘single patient’ tests that cannot go on high-throughput automated systems, unlike current NAT.
- Evaluation data on rapid antigen tests for COVID-19 are limited, and verification is required before use by NSWHP.
- Some of the rapid antigen assays may not be compatible with upper respiratory tract specimens collected in the usual transport media. Some assays have suggested their use on blood, but antigenaemia is low and this is unlikely to be clinically relevant.
- Some antigen tests can not differentiate between SARS-CoV and SARS-CoV-2 (although SARS is not circulating).
- The positive and negative predictive values of COVID-19 rapid antigen tests that are less sensitive than NAT are dependent on the prevalence of COVID-19 in the community. Currently symptomatic COVID-19 disease prevalence in NSW is low.
- The reliability of rapid antigen tests is likely to be better when tested in early stages of infection (for example, within the first five days after symptom onset) when the viral load is higher.
The sensitivity and specificity of these tests in asymptomatic screening is uncertain.

Correlation of a positive rapid antigen test with NAT Ct values (as a measure of viral load) and SARS-CoV-2 culture (as a marker of infectivity) is currently uncertain.

In a low prevalence environment, positive rapid antigen test is likely to require confirmation with NAT to exclude a false positive result. A negative rapid antigen test in a clinically suspicious case will require NAT to exclude infection.

Remaining material from the assay may not be suitable for whole genome sequencing and virus culture, necessitating another sample collection.

Assay costs (including readers) need to be determined.

The PHLN is reviewing rapid antigen assay performance and indications. Given the low prevalence of disease in NSW, the State may be dependent on overseas (independent) evaluations.

Whilst some of these tests have been advertised the presence of any or adequate numbers of these tests has not been confirmed, nor supply chain security assured.

Whilst these tests are registered on the ARTG/TGA the validation studies relevant to Australia have not been fully addressed and resolved.

### Operational requirements

- A nasal or nasopharyngeal swab is required. Data on alternative samples e.g. saliva or lower respiratory tract samples are limited.
- Operator training is required.

### Possible uses

A sensitive rapid antigen assay (with high specificity) could be used:

- For screening in high-risk settings
- When community disease prevalence is high
- When testing someone with or without symptoms and within a reasonable timeframe of exposure to a newly confirmed case
- As part of ‘mobile’ response teams to cruise ships/ACFs/other ‘closed’ environments/remote locations
- When determining persistence of infectivity following a NAT positive case e.g. for release from quarantine/high level PPE/HCW getting back to work.

### Conclusions

COVID-19 rapid antigen tests are currently not considered by NSWHP to be suitable for widespread use, given the availability and reliability of high throughput and rapid NAT.

This may change in defined specific use cases as data on performance and assay availability and approval become available.

They do not replace NAT as the preferred method for COVID-19 diagnosis.
Future directions

- Ongoing monitoring of local and global (independent) literature on assay performance.
- Review the PHLN response to rapid antigen testing.
- Continue to tabulate new TGA listed assays.
- In line with evaluation of rapid antibody test kits, develop a laboratory evaluation plan for limited and selected assays (recognising that appropriate validation or verification is difficult with low COVID-19 caseloads).
- Discuss with NSW Health potential clinical and public health use, and financial considerations.
- Continue to monitor new assay techniques (eg: holographic imaging and artificial intelligence) that may be more suitable in certain screening situations.