PATHOLOGY
TECHNOLOGY
AUSTRALIA

Position Statement

Subject: **COVID-19 Rapid Testing**
Originally Published: **20 October 2021**
This Revision Published: **11 August 2021**

A fast-moving pandemic needs a fast test - saving lives and livelihoods

---

The high-quality rapid antigen tests are available in Australia and have a role to play in our fight against COVID-19. These tests may best be deployed for repeat testing (every 3 days) in screening at-risk cohort and in essential workplaces to rapidly detect and isolate infected individuals. Thus, keeping workers safe and the economy running smoothly. PCR testing will remain the gold standard and will continue to complete high volume testing. However, as we are challenged by faster moving and more virulent strains of the virus, we need to adapt our testing to a faster turn-around-time and faster detection. Repeat rapid antigen testing is a potential candidate to assist in the move from case detection to suppressing transmission – saving lives and livelihoods.

Background

Nucleic Acid Testing such as RT-PCR and genome sequencing have been mainstays in diagnosing and monitoring COVID-19. These tests are performed on high volume testing platforms in our main pathology laboratories and at the point of care in regional and remote settings. The turnaround time for PCR tests ranges from about 1 hour for point of care devices, up to between 48 and 72 hours in laboratories - when testing numbers are high. These tests require technology of medium to high complexity and the operators need to be well trained. The Delta variant is more challenging to manage due to it being 55% more transmissible (than the Alpha strain)[1] and having a higher viral load (up to 1000 times higher than previous variants)[2].

Antigens are the entities that stimulate the human body immune response and are the target to which antibodies bind. In the case of the SARS-CoV-2, the antigenic components are the spike and nucleocapsid proteins that coat live virus.

Rapid antigen tests are available and registered for use in Australia. These tests have relatively high sensitivity (true positive rate), between 84 and 97%, and very high specificity (true negative rate), >99%. The test is performed by lateral flow immunoassay – either colourimetric or fluorescent - and formats include human and machine readable. These tests can be performed on-site, with results available in 10 to 30 minutes, require no complex equipment and are about 20% of the cost of PCR tests. These tests are similar in look to pregnancy tests available at most pharmacies.

COVID-19 ***antibody*** testing is also available for assessing the level of antibodies circulating in the blood of individuals post infection and to assess people's immune status after vaccination.

When assessing the immune status of an individual it is important to know if their measurable antibodies and capable of killing the virus (referred to as neutralizing antibodies). Also important in assessing immunity is the extent to which the body's T-cells (the cells that retain the memory of antigens the body has encountered) have been activated and their ability to re-produce the relevant antibody when challenged.
Technology and tests are available to detect and quantitate antibodies, and their neutralising ability, and T-cells.

Specific comments on COVID-19 Rapid Antigen Testing

- Rapid antigen tests are based on technology that has been in professional use for decades. The technology is well understood, stable and reliable when sourced from high quality manufacturers. The test consists of a lateral flow immunoassay that uses antibodies to detect specific viral proteins.
- COVID-19 antigen tests are generally performed on a nasopharyngeal swab, near nasal swabs or on saliva samples to detect the presence of viral protein. Testing can be performed in the laboratory, on automated immunoassay platforms, or at the point of care using a Rapid Antigen Tests.
- Rapid antigen tests, whether read by eye or by machine, have approximately the same turnaround times. Reading the tests by machine can improve accuracy and consistency, and have options to digitise and transmit the result. Mobile phone Apps that use photo-recognition of the test are now available and will help standardise results and enable upload to a patient's file.
- Rapid antigen tests are less sensitive than most PCR testing. Both the WHO and FDA have set a minimum acceptable clinical sensitivity limit at 84% and 80% (respectively). None of the tests registered so far in Australia have clinical sensitivity below 80%, the highest being 97%.
- While the clinical sensitivity of rapid antigen tests is slightly lower than that of PCR, several factors need to be recognised:
    - The serial interval— the time from illness onset in a primary case (infector) to illness onset in a secondary case (infected)— has been determined to be between 3 and 5 days[3]. Meaning that high frequency testing (every 3 days) would be required to quickly detect and reduce transmission in any specific cohort.
    - Rapid antigen testing has the capability of delivering fast, actionable results. Mina and Larremore *et al* 2020 have published detailed modelling which clearly shows that frequency of testing and speed to act are only marginally improved by increased sensitivity[4]. That is, improvements in testing sensitivity do not alter the outcome greatly.
    - The NEJM[5] has recently published a Perspective piece questioning, not how well we can detect COVID-19 in single samples, but how effectively infections can be detected in a population by the repeated use of a given test.
    - A real-world study funded by the USA NIH, and performed at the University of Illinois, demonstrated that rapid antigen testing performed every 3 days on asymptomatic individuals yielded the same sensitivity as PCR (greater than 98%) and gave results faster, so appropriate action could be taken. Importantly this study demonstrated that rapid antigen tests are most effective at detecting live virus at viral loads likely to be transmissible.[7]

  - If a test has 95% sensitivity, it detects 95% of the positive cases regardless of the prevalence. In a very low prevalence setting, say 100 individuals in 1 million infected, 95 of those would be detected, leaving 5 individuals in 1 million not detected at the first testing encounter. In a repeat testing environment, there is a high likelihood that positive cases will be detected in subsequent tests (depending on the test frequency).

- Rapid antigen tests are most likely to be used for repeat testing (every 3 days) to screen workers in high risk and essential workplaces. The USA CDC recommends that high frequency testing "could quickly identify persons with a SARS-CoV-2 infection to inform infection prevention and control measures, thus preventing transmission"[6].
- All the rapid antigen tests registered so far with the TGA have extremely high specificity (extremely low false positive rates of less than 1 per 100). It will be difficult for the clinical specificity of rapid antigen tests to reach 100% as the gold standard PCR test (against which rapid antigen tests are measured) has a measurable false positive rate itself.
  - With a prevalence of COVID-19 in Australia is less than 0.001% and an average specificity of rapid antigen tests in Australia above 99.2% the false positive rate of rapid antigen tests is less than 1 in 2 million tests. Effectively, these tests are excellent for ruling out a current infection.
  - From a Public Health testing perspective, the positive cut-off of the test is optimised to minimise false negative results. This is done at the expense of false positives. False positives, in this sense, are of less consequence to the public health interest. However, false positives can have significant impact on an individual and their close contacts, on contact tracing resources and related workplaces. All positive rapid antigen tests would be immediately verified by a PCR test.
  - In a repeat testing workplace environment, false positives will have a much lower impact than in the general population. If staff at at-risk and essential worksites are tested frequently and prior to commencing their work, the need to shut down a site is significantly reduced.
- There are now studies using rapid antigen tests which demonstrate excellent performance detecting infection up to about day 7 post symptoms (approximately 10 days post infection). The performance of rapid antigen tests declines between day 7 and 10, post symptoms, when PCR can still detect small quantities of viral RNA. We know, from comparing the Ct scores from PCR tests, performed on samples collected at the same time (as the antigen test), that high Ct scores correlate with low viral load and low viral antigen levels. It is debatable whether the virus is still infectious at this late stage.
- A study performed at the Peter Doherty Centre in Melbourne demonstrated that a rapid antigen test had 99.96% sensitivity and 99.97% specificity during the first 7 days of infection.[8]
- As viral load declines so do the viral antigen levels. Evidence suggested that somewhere between day 7 and 10, post onset of symptoms antigens become undetectable (by some rapid antigen tests). At this point, the individual is 10 to 13 days post actual infection day.
- These rapid antigen tests, when used for repeat testing of workers in at-risk and essential workplaces, will almost always be testing people in early phase infection where these tests perform extremely well.

- Evidence shows that rapid antigen tests detect both symptomatic and asymptomatic individuals up to 7 days post symptoms.[7]
- Asymptomatic individuals have been shown to have similar viral loads to those with symptoms. There is evidence, however, to suggest that asymptomatic individuals transmit virus at a lower rate than symptomatic individuals. WHO data[9] shows that between 14 and 20% of Australians with COVID-19 are asymptomatic and even at a lower rate of transmission, they could be a significant cause of community transmission of unknown origin.
- Lower limits of detection for these tests have been determined and are usually quoted in the product instructions for use; usually expressed as lowest $TCID_{50}$/mL detected.
- Many manufacturers calibrate the lower limit of antigen detection to the low end of where viral load is thought to become transmissible.
- Rapid antigen tests are very specific for antigens of the SARS-CoV-2 virus and do not cross react with other human coronaviruses or the common influenza and adenovirus strains.
- Data capture and reporting of rapid antigen tests is now available via mobile phone Apps and for some devices, via portable test reader. Methods for minimising fraudulent testing are now available via photo-recognition, barcoded devices and geolocation/geofencing software.
- Self-collection of samples is now realistic via a TGA approved Australian device called the Rhinoswab. This device has been shown to collect larger amounts of viral material than the traditional nasopharyngeal swab and could provide even higher sensitivity for rapid antigen tests than currently observed. Standardised self-collection will facilitate the next step in COVID-19 outbreak management, that being home quarantine and home testing.

Recommendations

Rapid antigen tests of suitable sensitivity, approved by the TGA, will have a role to play in the COVID-19 testing regimen deployed in Australia. These tests will best be deployed for high frequency testing – every 3 days - in at-risk and essential workplaces to rapidly detect and isolate infected individuals. Thus, keeping workers safe and the economy running smoothly.

The evidence is now very strong that repeat testing in at-risk cohorts and taking rapid action to isolate positive cases, is the best method of suppressing transmission.

Our recommendations:

1) Urgent implementation of multiple pilot programs for rapid antigen testing in healthcare, aged care, quarantine services, airline services, construction, food services and distribution.
2) The state-based home quarantine pilot studies to include rapid antigen testing using suitable self-collection device.
3) In doing so, develop the quality frameworks and guidelines for sustainable use of such testing.
4) TGA conditions on the supply and use of approved rapid antigen tests be modified to enable supply and use by a broader range of health professionals.

5) States and Territories that have banned the use of rapid antigen tests reverse these bans, or at least identify the conditions under which such testing is permitted.
6) Funding for rapid antigen testing is provided either via an MBS item number or purchased and supplied by commonwealth or state authorities (or other suitable method).

References

1. Predicted dominant variant Delta of SARS-CoV-2 before Tokyo Olympic Games, https://doi.org/10.1101/2021.06.12.21258835;
2. Nature News 21 July 2021: How the Delta variant achieves its ultrafast spread (nature.com)
3. Serial interval of novel coronavirus (COVID-19) infections
   IJID 93 (2020) 284-286
   Hiroshi Nishiuraa,b, *, Natalie M. Lintona , Andrei R. Akhmetzhanova
   https://www.ijidonline.com/article/S1201-9712(20)30119-3/pdf
4. Test sensitivity is secondary to frequency and turnaround time for COVID-19 surveillance
   Daniel B. Larremore, Bryan Wilder, Evan Lester, Soraya Shehata, James M. Burke6,
   James A. Hay, Milind Tambe, Michael J. Mina, and Roy Parker
   https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7325181/
5. Rethinking Covid-19 Test Sensitivity — A Strategy for Containment
   Michael J. Mina, M.D., Ph.D., Roy Parker, Ph.D., and Daniel B. Larremore, Ph.D.
   DOI: 10.1056/NEJMp2025631
6. Interim Guidance for Antigen Testing for SARS-CoV-2
   https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html
7. NIH-funded screening study builds case for frequent COVID-19 antigen testing | National Institutes of Health (NIH) www.nih.gov/news-events/news-releases/nih-funded-screening-study-builds-case-frequent-covid-19-antigen-testing
8. Multi-site assessment of rapid, point of care antigen testing for the diagnosis of SRAS-CoV-2 infection in a low-prevalence setting www.thelancet.com/journals/lanwpc/article/PIIS2666-6065(21)00024-9/fulltext
9. Estimating the extent of asymptomatic COVID-19 and its potential for community transmission www.medrxiv.org/content/10.1101/2020.05.10.20097543v3

About Pathology Technology Australia

Pathology Technology Australia represents the manufacturers and suppliers of over 95% of all testing and technology used in commercial pathology laboratories, hospitals, community and primary care.
Our members develop and manufacture tests and the testing technology, train doctors and scientists in the use of this technology, provide technical support and maintain the supply chain - all of which makes pathology possible. The member companies of Pathology Technology Australia strive to provide the most up to date tests and testing technology that deliver the highest quality, accessible and affordable healthcare services to all Australians.