The challenges of establishing adequate capacity for SARS-CoV-2 testing

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The response to COVID-19 in Australia has been impressive, but our laboratory capacity must be used wisely

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19), has spread rapidly throughout the world from its origins in China in late 2019; the COVID-19 outbreak was declared a pandemic by the World Health Organization on 11 March 2020.[1] It is the seventh coronavirus known to have crossed from animals to humans, and may become the fifth to persist as an endemic human coronavirus.[2]

More than three and a half million laboratory-confirmed COVID-19 cases had been recorded around the world by early May 2020, including 6801 in Australia.[3] There has been no clear evidence of sustained community transmission in Australia, and the number of new cases is declining rapidly. Early diagnosis has been critical for successful contact tracing, isolation, and quarantining measures, and the impact of inadequate testing capacity has been seen in countries experiencing major crises, such as the United Kingdom.[4]

The sophisticated laboratory system in Australia has been regularly challenged in recent years by new pathogen threats, including SARS-CoV-1 in 2003 and pandemic H1N1 influenza in 2009. Since that period, nucleic acid detection, including polymerase chain reaction (PCR) assays, advanced sequencing techniques, and highly automated testing platforms have dramatically increased the capacity of Australian laboratories for rapid, large volume testing.

The laboratory response in Australia to COVID-19 was impressive. Testing capacity quickly reached many thousands per day, and the testing rate in Australia is consequently one of the highest in the world: by early May, about 2% of the population had been tested.[1,3,5]

In this issue of the *MJA*, Caly and colleagues describe the first clinical isolation of SARS-CoV-2 in a laboratory outside China, in late January 2020.[6] At that time, the non-availability of virus in Australia was delaying the evaluation of in-house PCR assays based on published SARS-CoV-2 sequences.[7] The Victorian Infectious Diseases Reference Laboratory promptly made inactivated virus available to laboratories, both here and overseas, as well as live virus to high containment (PC-3) laboratories for culturing. The sensitivity and specificity of the first local PCR assays were assessed with this virus.

Several in-house and commercial PCR-based assays for SARS-CoV-2 detection are now available. As they are new tests for a novel virus, they have not yet gained full approval by the Therapeutic Goods Administration (TGA) and require an emergency exemption under TGA regulations.[8] Data on test performance and interpretation is being accumulated and evaluated.

PCR assessment of upper respiratory tract swabs, and of lower respiratory tract samples when available, is recommended for COVID-19 diagnostic testing.[6] Testing protocols target several SARS-CoV-2 genes,[9,10] and include at least one specific SARS-CoV-2 assay and, in some cases, a *Sarbecovirus* assay (the *Betacoronavirus* subgenus that includes SARS-CoV-2 and the no longer circulating SARS-CoV-1).

SARS-CoV-2 is detectable in the upper respiratory tract from one or two days before the onset of symptoms until at least five days afterwards; estimates of peak shedding range between one day before and four days after symptom onset.[11–13] Upper respiratory tract virus levels decline sharply after seven days but may still be detectable in the lower respiratory tract, especially in patients who progress to pneumonia. Viral load is typically higher in people with more severe illness, in whom virus may also be detectable in serum and faeces.[13] Upper respiratory tract samples from some patients can be PCR-positive for 3–4 weeks, even after clinical recovery, but this probably reflects detection of non-viable virus.[14,15]

Viral culture can help determine whether potentially infectious virus is present. Prolonged high viral load in faeces has occasionally been reported, but viable virus has only rarely been cultured.[12,16] It is important to remember that the location of detectable virus and the pattern of virus shedding is influenced by the age of the patient population, and by the severity and duration of illness.

PCR testing is now widely available in private and public sector laboratories, and testing capacity in Australia is sufficient to meet the likely need. However, delivering timely results during peak demand periods has been challenging, and this problem may recur if there is a resurgence of virus transmission. Processing large numbers of samples within a short period can disrupt the normal workflow of testing laboratories, particularly during the development, evaluation, and implementation of new tests. Further, specimen collection and transport are slowed by the additional safety requirements, and testing in reference laboratories may bypass normal electronic reporting systems.

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Competing international demand for equipment and reagents is an ongoing problem, and the availability of testing in Australia may need to be restricted if there is a large increase in testing overseas. Many local laboratories have therefore retained diverse platforms that allow flexibility in the face of variable reagent supplies, but any changes required may affect capacity and workflow. Delivering testing outside laboratories in large urban centres remains challenging. Point-of-care PCR tests are becoming available,[10] but there will be similar problems of adequate and reliable supplies of equipment and reagents.

Laboratory-specific and commercial serological tests have been developed and their diagnostic role is being evaluated.[7,17] As serum antibodies appear several days after the onset of symptoms, these tests will not be suitable for diagnosing acute illness, but they may assist with retrospective diagnosis, the investigation of suspected cases of COVID-19 with negative PCR results, assessing immunity, and seroprevalence studies. Point-of-care serology tests should not be used for diagnosis until their performance has been properly evaluated.[7,10]

SARS-CoV-2 testing should be used wisely with regard to public health and clinical priorities for controlling the spread of the virus, and for ensuring the quality and sustainability of our testing capacity. This means working closely with our clinical and public health colleagues as testing capacity and demands change.

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