Clinical Update: Serology testing for COVID-19 in NSW

7 September 2020

What is serological testing for COVID-19?
Serological testing detects pathogen-specific antibodies in a person’s blood after infection. The presence of these antibodies indicates a measure of the in vitro immune response to the SARS-CoV-2 virus, the causative organism for COVID-19. In COVID-19, the identification of SARS-CoV-2-specific antibodies indicates recent or past infection with the virus. In addition, the identification of different classes of antibodies e.g. IgG, IgM, IgA can be used to give an approximate timing of when the patient may have contracted COVID-19 disease.

Importantly, the longer term immune response to COVID-19 remains uncertain at this stage with scientific evidence related to this still emerging. Hence the implications of a “positive” SARS-CoV-2-specific antibody result may be difficult to assess, excepting that it indicates an immune response to the virus. Further, it is not known if the detection of antibody means the individual is protected from re-infection, or how long such immunity might last.

When should serological testing be considered?
Serology may be considered for:
- Patients who have symptoms consistent with COVID-19 but:
  - who are PCR-negative, OR
  - who were not tested by PCR OR
  - have unexpected positive or inconclusive PCR results
- Patients who were or are part of an outbreak investigation
- Surveillance of front line health care workers
- Surveillance of the population in sero-epidemiological studies
- Estimating time of infection to define infectious period, where this is not evident from the exposure history or clinical illness
- Making a retrospective diagnosis in individuals who have recovered from infection prior to testing.
- At the specific, explicit request from the Ministry of Health for Public Health concern

How is serological testing being used?
Currently, priority is being given to sera from patients identified by Health Protection NSW as requiring serologic testing to inform their public health response. If a requesting clinician would like testing expedited, they should contact their local Public Health Unit or Clinical Microbiologist.

What methods are used for serological testing in NSWHP?
Serological testing may be conducted by several methodologies comprising:
- automated high-throughput instruments, which at present perform IgG or total antibody assays and
- confirmatory assays based on well-established reference methodologies.

Commercial automated assays, that measure total antibody or subclass antibodies, such as IgG, are being instituted within NSWHP after undergoing comprehensive evaluation. NSWHP is committed to monitoring developments in this area and adjusting assays when necessary.

NSWHP has developed an in-house immunofluorescence assay (IFA) for SARS-CoV-2, which detects IgG, IgA and IgM antibodies to this virus, as well as neutralising antibody assays. IFA testing allows detection of different antibody classes and is useful in understanding the timing of infection. The IFA can be used to screen for antibodies as well as being used as a confirmatory assay.

Rapid point of care antibody assays have been evaluated but are not recommended for use in NSWHP because of inferior performance. This aligns with international experience. NSWHP is committed to continuing to monitor developments in this area.
**What sample is required for serological testing?**
The required sample is at least 8-10ml of blood collected in a serum separating tube (SST), requested for ‘COVID-19 serology’. Depending on the timing of symptom onset, acute and convalescent samples at least 14 -21 days apart should be obtained. The suggested timing of a convalescent sample for high throughput assays is 21 days, although the immunofluorescence assay may detect antibodies as early as 14 days from infection. The timing of a convalescent sample will be indicated upon the report issued at initial testing.

**What information is required on the serology request form?**
Please supply information on one or more of
- Date(s) of onset of symptoms consistent with COVID-19
- Travel history (if relevant) and dates thereof
- History of contact with person with COVID-19 or suspected COVID-19 and dates
- COVID-19 PCR results if known and the collection date of the positive PCR
- Specify if patient is a Health Care Worker
- Indication for testing (see above)

**What method will be used to perform serological testing?**
- This will depend on the laboratory to which the blood sample is sent. Testing platforms may change over time as further evaluations are conducted.
- COVID-19 serology assays are available via John Hunter Hospital, Royal North Shore Hospital, Royal Prince Alfred Hospital, Concord Hospital, Randwick campus, Liverpool Hospital, Westmead ICPMR.
- Laboratories that conduct automated high throughput instrument assays will, after testing by these platforms, send **samples with a positive result for the IFA confirmatory assay** at NSWHP-Westmead ICPMR. A neutralisation test will be performed if required.

**How should serological test results be interpreted?**
Whilst data indicates that SARS-CoV-2-specific antibodies may be detected from day 12 after the onset of illness their appearance may be delayed for as long as 21 days.

**NOTE:** different assays have different sensitivity in detecting antibody early in infection. **Hence absence of antibody or a negative result does NOT exclude infection.**

All initial positive results from automated high throughput assays, such as Roche ECLIA or ABBOTT CMIA, should be interpreted as “provisionally positive” until confirmatory results are available. This advice is modified where antibody is detected following seroconversion (a change from seronegative to seropositive), or a fourfold rise in SARS-CoV-2-specific antibodies between acute and convalescent sera (obtained once patient is recovered), is identified. In these circumstances the patient is classified as a **confirmed case of COVID-19.**

If neutralising or SARS-CoV-2-specific IgG antibodies are detected in a person with a compatible clinical illness and is a close contact of a confirmed or probable COVID-19 case this is classed as a probable case of COVID-19.

**It is uncertain whether detectable antibodies indicate immunity to COVID-19 infection, and their presence should NOT be taken to infer protection from COVID-19 reinfection.**

**For further information, please contact:**
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