COVID-19 DIAGNOSTICS: KNOW HOW TO INTERPRET

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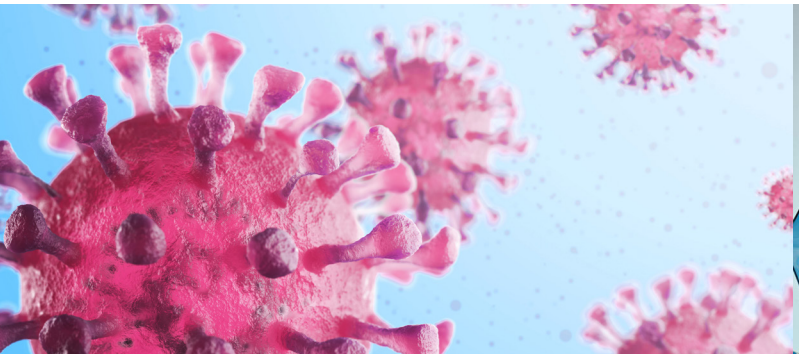

BACKGROUND INFORMATION

Virus isolation, viral detection, and amplification of nucleic acid (PCR) are methods that provide the highest degree of confidence in viral diagnostics result. A COVID-19 Nucleic Acid Real-Time Reverse Transcription Polymerase Chain Reaction (RT-PCR) Test is used for qualitative detection of nucleic acid from SARS-CoV-2. Specimens used in this test are taken from the nasopharynx (behind your nose and above the back of your throat) and oropharynx (the part of the throat at the back of the mouth behind the oral cavity). However, this **test requires specialised technical skills and equipment, is time-consuming and costly, and may produce false negatives.**

Table 1: Detection Results of Clinical Specimens by Real-Time Reverse Transcriptase–Polymerase Chain Reaction

Specimens & values	Bronchoalveolar lavage fluid (n=15)	Fibrobronchoscope brush biopsy (n=13)	Sputum (n=104)	Nasal swabs (n=8)	Pharyngeal swabs (n=398)	Feces (n=153)	Blood (n=307)	Urine (n=72)
Positive test result, no (%)	14 (93)	6 (46)	75 (72)	5 (63)	126 (32)	44 (29)	3 (1)	0
Cycle threshold, mean (SD)	31.1 (3.0)	33.8 (3.9)	31.1 (5.2)	24.3 (8.6)	32.1 (4.2)	31.4 (5.1)	34.6 (0.7)	ND
Range	26.4-36.2	26.9-36.8	18.4-38.8	16.9-38.4	20.8-38.6	22.3-38.4	34.1-35.4	
95% CI	28.9-33.2	29.8-37.9	29.3-33.0	13.7-35.0	31.2-33.1	29.4-33.5	0.0-36.4	

Abbreviation: ND, no data.

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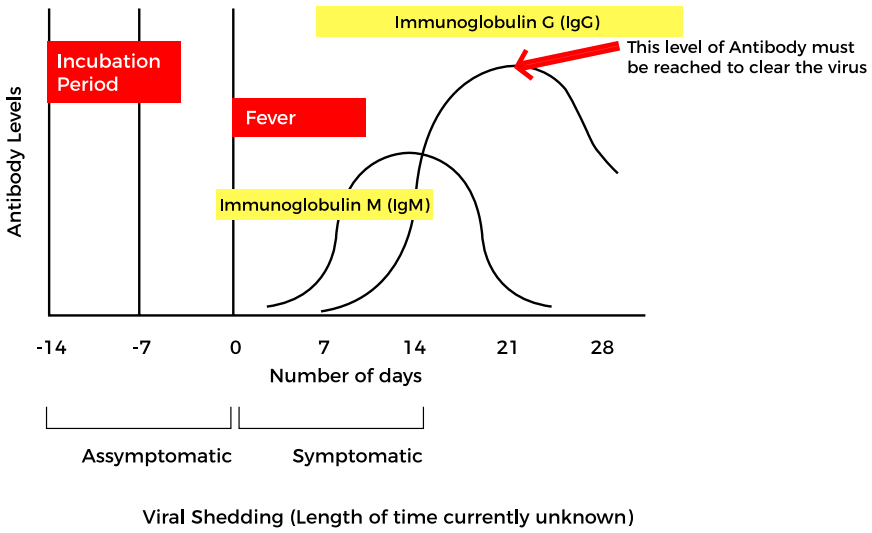

Figure 1: Production of antibody levels at different stages of COVID-19 infection. A negative diagnostic result does not indicate that the person is negative.

RESULT ANALYSIS AND RECOMMENDATION

- RT-PCR's limitations means it is not the best for field work; new commercial kits are available, but these are costly and are not completely validated.
- The table shows that different levels of COVID-19 was detected from different specimen types; this shows that specimen type is important.
- Bronchioalveolar lavage fluid provided the highest concentration (93%) but it requires trained personnel to extract and hence not recommended.
- Because the virus is transmitted via respiratory droplets, the best alternative specimens are sputum and nasal swabs (72% and 63% positivity, respectively)
- However, there is a lower positivity rate that also depends on time of collection. Therefore, a minimum of two tests are needed to confirm negativity and the tests should be carried out 5-7 days apart.

- **Any negative must be verified as a true negative.**
- **Asymptomatic patients or those with mild symptoms can still spread the virus.**

COMPLEMENTING VIRUS DIAGNOSTICS WITH SEROLOGY

- COVID-19 IgM and IgG testing are used to detect IgM and IgG antibodies. This is based on the host response following a SARS-CoV-2 infection (as shown in Figure 1).
- IgM provides the first specific defence, an indicator of a current infection; IgM appears within four to 10 days of exposure and can remain for up to two weeks or more.
- IgM will later be replaced by IgG; IgG provides lasting immunity, an added advantage that indicates a lasting or cross-immunity.
- A serology test supplements the diagnosis of COVID-19; it does not replace the RT-PCR Test.
- Even though serology testing does not confirm infection, it provides an evidence of recent infection. This is an important immunological evidence for physicians that is also useful for monitoring during treatment.

IMPROVING DIAGNOSTICS: THE WAY FORWARD

- There is an urgent need for a test to quickly identify infected patients to prevent virus transmission and assure timely treatment of patients.
- Researchers and pharmaceutical companies are developing PCR kits, antigen and serological tests. Professor Jackie Ying from NanoBio Lab, Singapore showed that the use of nanoparticles and dyes can speed up testing.
- Even though her test is not commercially available yet, a collaboration with Malaysian labs could provide the data on accuracy that is necessary to speed up its recommendation to be used in COVID-19 diagnosis.
- Another test kit developed by a South Korean company detects the antigen in 10 minutes using monoclonal antibodies.
- User places swabs of nasal discharge into the lateral flow cassette; results can be obtained within 10 minutes with an accuracy of 85%.
- The Korean test kit needs further evaluation; it is useable but should be used as a quick test to complement a PCR Test.

IMPORTANT TAKEAWAY MESSAGES

- Performing only a single test to diagnose COVID-19 could lead to a **false-negative result** or misdiagnosis.
- Therefore, to ensure that those who are negative are true negatives, **DUAL SAMPLING** must be done; a **second sample taken seven days apart will confirm this.**
- Implementing a diagnostic workflow that follows the disease's time frame will provide a comprehensive diagnosis.

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