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Newsletter

SARS-CoV-2 Antigen Tests

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Laboratory testing and vaccination are the cornerstones to successfully stopping the spread of the SARS-CoV-2 virus that causes COVID-19.

Testing is used for diagnosis of SARS-CoV-2 infection in those people with suggestive symptoms, to screen individuals in order to identify pre-symptomatic or asymptomatically infected individuals that may unknowingly be transmitting the virus to others and for surveillance to understand the spread of the virus in particular groups of people or geographic areas.

Both SARS-CoV-2 antigen (Ag) and PCR tests are viral tests for the diagnosis of infection with SARS-CoV-2. Viral tests can also be used as screening tests to identify infected individuals that need to isolate from others to decrease transmission.

RT-PCR (real-time reverse transcriptase polymerase chain reaction) tests

- are very sensitive and specific.
- they detect one or more SARS-CoV-2 genes indicating a current or recent infection.
- because these tests are so sensitive, viral RNA may be detected in people that have been infected even after they are no longer ill, sometimes up to 30 days after infection.
    - It has been shown that the infectiousness of the virus drops dramatically after day 10-14 and so this is the reason why retesting is not indicated in individuals that have recovered from infection, are asymptomatic and have completed their full isolation period.
- PCR tests are done in laboratories by trained laboratory personnel.
- Results are qualitative i.e. positive or negative and Ct values differ between kits and laboratories and are not directly correlated to clinical infectivity or stage of infection.

Antigen tests

- are immunoassays that can identify specific viral antigens
- all antigen tests are not equal, and their performance depends on the antigen that has been used in the test design, the verification of tests done against the gold standard for diagnosis the RT-PCR as well as operator skill
- the specificity of Ag tests is the same as PCR tests, but they have slightly lower sensitivity
- sensitivity of Ag tests depends on the stage of infection that the test is administered and is better in symptomatic individuals.
    - Sensitivity in asymptomatic individuals is around 60%
    - Sensitivity in symptomatic individuals is around 80%
- Antigen tests can be used to make quick decisions about symptomatic individuals in hospitals triage and to control the spread of infection in other conger gate settings (care homes, prisons etc.)

- In some countries because these tests are cheaper, they can be used more frequently. Repeated or serial testing is done to compensate for the lack of sensitivity in certain settings, including work places, universities and schools

Table 1 *Summary the performance characteristics and advantages/disadvantages of SARS-coV-2 PCR and Antigen tests.*

	PCR	Antigen
Indications	Detect current or recent infection Asymptomatic/Pre-symptomatic	Detect current infection
What does it detect?	Viral RNA	Viral antigens
Specimen	Nasal,nasophyngeal, orophyngeal, sputum, saliva	Nasal, nasophyngeal
Turn Around Time	1-2 days	15-30 mins
Advantages	Most sensitive method No need to confirm results	Short turnaround time Allows quick identification of infected people if they are symptomatic preventing further transmission in hospitals or other settings where people are together Performance comparable to PCR in symptomatic individuals
Disadvantages	Longer turnaround time Higher costs	May need confirmatory testing Less sensitive compared to PCR in asymptomatic individuals

In South Africa, antigen testing is recommended when a quick decision is needed regarding COVID in a symptomatic patient and there is no time to do a PCR or no access to a PCR test. The short turnaround time makes it very useful to triage patients in hospitals and emergency rooms when there is no time to wait for a PCR result, examples are for women is in labour or for patients that requires emergency procedures or surgery. The performance of antigen tests improves when the prevalence of infections is high. So, they can also be used to identify infected individuals during peaks of COVID activity.

References

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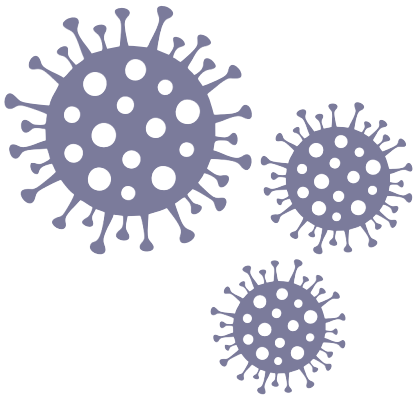

SARS-CoV-2 Variants

All viruses change their genetics over time as they circulate through human populations. These changes occur to help the virus survive better and escape immunological responses generated by the host to protect against the virus.

Viruses adapt quickly because they replicate so fast and they have relatively imperfect self-regulatory enzymes that don't correct some chance genetic changes. Because of this, many of these genetic changes usually make the virus less fit to survive and the new viruses lineages will never emerge and simply die out. But some of the changes may be lucky and confer a survival advantage to the virus by creating a slightly different virus that can more successfully evade the host immune response.

With SARS-CoV-2, the virus that causes COVID-19, we have had the scientific capability to track the genetics of the virus very closely. Like most beta coronaviruses, SARS-Cov-2 has got relatively good self-regulatory enzymes and so genetic mistakes are corrected quickly. Global and national efforts have been able to sequence circulating SARS-CoV-2 viruses identifying genetic lineages of circulating SARS-CoV-2 viruses in specific geographical and community settings. The genetic changes that are important for the virus and which confer some advantages to it are changes in the spike (S) protein at the point where it interacts with human cells, the receptor binding domain (RBD). WHO has classified the new virus lineages into 2 groups

1. *Variants of interest (VOI)*
   - This is a variant that has detectable changes to the spike protein RBD that may influence how the virus will react with antibodies generated by previous infecting viruses or vaccination
   - Variant may have new characteristics that suggest increased transmissibility, severity of disease or diagnostic test or therapeutic agents could be evaded.
   - Cause significant community transmission or clusters of transmission in multiple countries
   - Require intensified surveillance and laboratory characterization
2. *Variants of concern (VOC)*
   - SARS-CoV-2 virus that meets the criteria for VOI
   - And in addition, has been shown through comparative assessments to have a significant on diagnostics, treatments or vaccines
   - Evidence of
     - Increased transmissibility
     - Increased virulence or change in clinical disease or presentation

A report on the 1 July, generated by the Network for Genomics Surveillance (NGS-SA) a consortium of South African scientists that collect and sequence viruses circulating in the country showed a shift in the SARS-CoV-2 variants in their sample of sequenced viruses showed that the beta VOC was the dominant variant accounting for 70% of the sample characterized in May (n = 739). In June the surveillance sequencing data showed that 49% of circulating viruses belonged to the delta VOC i (n=603). No lambda was detected at all.

Although limited in extent this surveillance of sequenced viruses does show that the delta VOC is likely to become the dominant variant in South Africa.

The delta VOC has got some important characteristics that make it harder to control. It is more transmissible. The virus does this by causing fusion of cells when it engages the ACE-2 receptor to enter human cells. This increased transmissibility is measured by the R0 in infectious diseases. The R0 is the number of new infections that occur from one infected case. The initial circulating SARS-CoV 2 virus from Wuhan had a R0 of 2.3, meaning 2 other people would become infected with the virus if they had contact with one infected person. The delta VOC R0 is 5 almost double the original Wuhan virus, meaning 5 other people will become infected from one case. This is illustrated in Figure 2 which compares the R0 calculations for SARS-CoV-2 variants and other viral infections.

There has also been a shift in the presenting symptoms of the delta variant. Many publications have shown that sore throat (pharyngitis/laryngitis), headache, runny nose are common presenting symptoms with this variant. The progression of the disease is the same and but severity of the COVID is not different for the delta variant compared to the beta variant. In addition, the clinical management of the variants remains the same. There is one minor difference, the effectiveness of antibody immunotherapy, some of the monoclonal antibody preparations which are not even available in South Africa at this time, cannot be used with the delta variant.

There is just a little bit of good news though, the genetic changes of the delta variant have not changed the effectiveness of most available SARS-CoV-2 vaccines. Researchers were quickly able to demonstrate that vaccination with the commonest available SARS-CoV-2 vaccines (J&J, Pfizer, Moderna, Astra Zeneca) all still provide protection against severe COVID disease, hospitalization and death.

References

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