Questions

Q1 Rapid Diagnostic Testing (RDTs) for SARS-CoV-2

Which *one* of the following statements about rapid diagnostic testing (RDTs) for SARS-CoV-2 is *false*?

- ❍ 1. Nucleic acid amplification tests can remain positive for months after infection.
- ❍ 2. Antigen-based RDTs can detect infection within 5 to 7 days after symptom onset.
- ❍ 3. Home-based RDTs are just as accurate when performed by untrained persons.
- ❍ 4. Testing is generally not useful in the first 48 hours after exposure.

Educational Point: Limited access to diagnostic testing in underserved communities and incomplete reporting of Covid-19 data to the WHO mean that official numbers, although staggering, probably represent a fraction of total infections and deaths from the Covid-19 pandemic.

Globally, clinical laboratories have performed approximately 3 billion molecular diagnostic tests for SARS-CoV-2.

Diagnostic testing for acute SARS-CoV-2 infection can be performed with either molecular nucleic acid amplification tests (NAATs) or antigen-based assays, and both are available as rapid diagnostic tests (RDTs). Molecular NAATs detect the presence of viral gene targets, including the N, S, and E genes and the open reading frame 1ab *(ORF 1ab)*.

Reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assays are the most widely used diagnostic SARS-CoV-2 NAATs worldwide. Antigen-based tests, also called immunoassays, detect domains of the surface proteins, including the nucleocapsid, spike, and receptor-binding domains, that are specific to SARS-CoV-2. Although both techniques are highly specific, NAATs are generally more sensitive than antigen-based tests because they amplify target genomic sequences. Tests to detect host IgG or IgM antibodies to SARS-CoV-2 should not be used to diagnose acute infection.

The clinical performance of diagnostic SARS-CoV-2 testing extends beyond pathogen targets such as viral proteins and RNA and includes clinical characteristics (e.g., the patient's viral load and the time since exposure or symptom onset), operational testing attributes (e.g., the specimen type, swab technique, transport conditions, and laboratory technique), and analytic test properties (e.g., sample preparation and signal amplification). **Although NAATs are highly sensitive and accurate, they can remain positive for weeks to months after infection.** Viral culture studies suggest that SARS-CoV-2 may be capable of replicating only for 10 to 14 days after symptom onset, so NAATs may detect remnant viral RNA well past the time period of recovering replication-competent virus. Conversely, antigen-based assays remain positive for 5 to 12 days after symptom onset and perform better in persons with a high viral load, which correlates with disease severity and death. Thus, antigen-based tests may correlate better with replication-competent SARS-CoV-2 than molecular tests and may provide information about potential transmissibility.

All antigen-based RDTs are approved for use in symptomatic persons and provide results in 10 to 30 minutes.

Although direct-comparison studies are limited and often retrospective, antigen-based RDTs have a lower sensitivity than molecular RDTs, as compared with a reference standard of laboratory-based RT-PCR tests, particularly among persons who have a low viral load or no replication-competent virus. However, **antigen-based RDTs can detect infection early in the disease course (within 5 to 7 days after symptom onset)** when viral loads are high (i.e., a low RT-PCR cycle threshold); these high viral loads account for most transmissions. Studies have shown varying degrees of clinical accuracy (sensitivity, 36 to 82%; specifically, approximately 98 to 100%) when various antigen-based RDTs are used for screening asymptomatic persons.