Petersburg Medical Center
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PCR vs Antigen Testing:

Antigen tests are what we consider to be the rapid tests. These tests have antibodies bound to a paper strip and are directed against the viral proteins (antigen). After the sample is added, fluorescent tags or dyes are added to the paper which bind the antibody-antigen complex and show the positive result. If there is no viral antigen present, the tag cannot bind, and no signal will be emitted. These tests are fast and inexpensive but are dependent on how well samples are collected and whether there is enough virus being shed at the moment of collection to emit a strong enough signal for a positive result. These tests are only FDA approved (EUA) for testing symptomatic individuals, not for screening asymptomatic people.

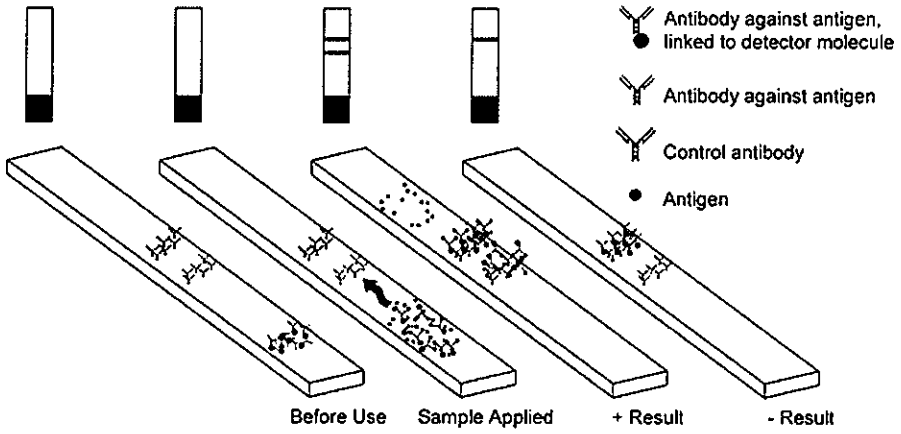

FIGURE 1- RAPID ANTIGEN TESTING. HTTPS://ASM.ORG/ARTICLES/2020/APRIL/COVID-19-TESTING-FAQS

Molecular tests (PCR) are much more sensitive but take longer and are much more complicated to perform. Viral RNA is extracted and made into complimentary DNA. Primers (short complimentary sequences to the DNA) that have a fluorescent probe bind and allow DNA polymerase to copy the sequence. As the DNA sequences are copied, the probe is cleaved, and a fluorescent signal is produced. The process will create millions of copies and with each new cycle, the signal intensity increases. If the signal reaches a pre-set value, the test is positive. If the signal fails to reach the required intensity, the test is negative. The PCR test is 20,000 times more sensitive than the antigen test at detecting Coronavirus.

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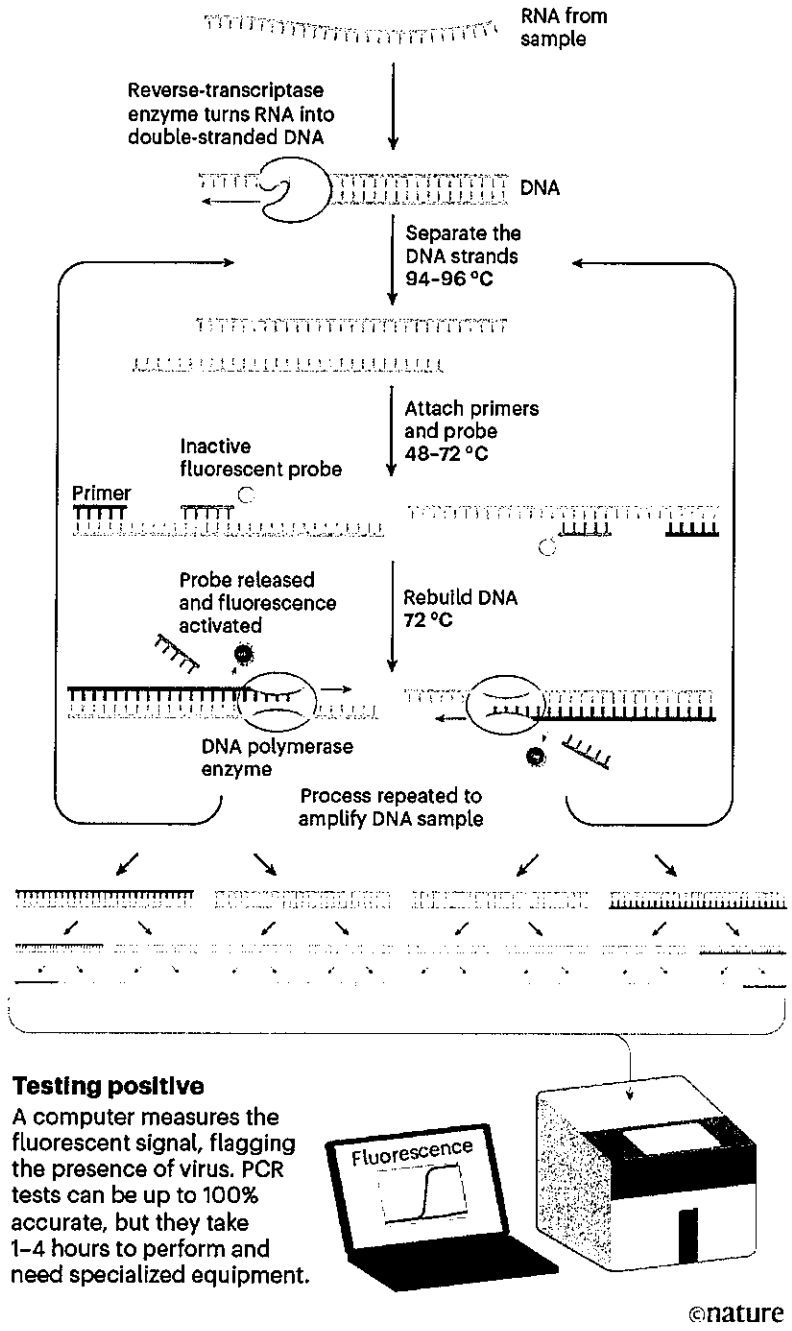

Nik Spencer/*Nature*

FIGURE 2- PCR. HTTPS://WWW.NATURE.COM/ARTICLES/D41586-020-02140-8

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False Negative and Positives

False negatives are possible if:

1) A patient is not shedding adequate viral DNA because testing is done too soon or too late, or
2) If a specimen has not been collected properly to obtain an adequate amount of fluid-containing virus

False positives are possible if:

1) Cross contamination occurs between patient specimens due to insufficient cleaning of the workspace or instrument, or inappropriate use of PPE.
2) The test is not performed according to the manufacturer instructions
    a. Wrong amount of reagent added or reading the test at the wrong time are a couple of examples.

    Laboratories are bound by strict quality control practices to prevent these issues.

With respect to Ct values:

The Ct cutoff value for tests are determined by the manufacturer of the test, not by individual labs. The manufacturer determines the cutoff by using known positive and negative samples during the test validation process. None of the tests under the EUA have been approved to give quantitative (Ct value) results, only qualitative (positive/negative) results. Additionally, some PCR tests do not use Ct values, but rather relative light units (RLUs) or cycle numbers (CN). The fact is that at this time, the clinical utility of the Ct value is not known, and there are numerous factors that can influence the Ct value: instrument used, type of specimen collected, how much specimen was collected on the swab, and transport conditions are just some of the variables.

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