Experts explain the ins and outs of different COVID-19 tests

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With kids returning to school and many adults heading back to the office or traveling, something as simple as a cough or runny nose might lead to panic—and the need for a COVID-19 test. But because of the wide availability of COVID-19 vaccines, the topic of testing—and which one to use—has fallen off our collective radar.

A lot has changed since the early days of the pandemic, when people lined up (on foot or in their cars) outside testing sites awaiting their turn at a nasal swab. Whether it's at a pharmacy, urgent care center, or testing site, it's now easier than ever to get a COVID-19 test. You can even buy a kit online or at a drugstore to test yourself—and get results—in your own home.

In fact, there are so many different options, it can be confusing. If you are traveling and need to show a negative COVID test, which is the best kind to get? Are they all equally accurate? Do some produce results faster than others? And do you still have to get a Q-tip in your nose?

Some of these questions are easy to answer, while others are more difficult—particularly when it comes to accuracy. That's because all of the tests—and there are hundreds of them, from a growing number of companies and laboratories—are offered through a Food and Drug Administration (FDA) emergency use authorization (EUA). Therefore, they have not been as rigorously tested or vetted as other medical tests with full FDA approval.

And since the virus is new, all the tests are also new, meaning we have neither a long track record of comparing results, nor a true gold-standard test yet.

Below, Yale Medicine experts fielded our COVID test questions.

What are the different types of tests to diagnose COVID-19?

Unlike antibody tests, which look for prior infection, COVID diagnostic tests look for current infection with SARS-CoV-2, the virus that causes COVID-19. They are broken into two categories: molecular and antigen (more below).

A summary of their differences

Because the samples are, for the most part, collected in the same way for both, the differences between the two kinds of tests are largely in how they're processed. Molecular tests are generally more accurate and mostly processed in a laboratory, which takes longer; antigen tests—which are sometimes referred to as 'rapid tests'—are processed pretty much anywhere, including in doctor's office, pharmacies, or even at home. You can get antigen test results in about 15 minutes, but they tend to be less accurate.

Health care providers typically rely on molecular tests, particularly when people have COVID-19 symptoms, whereas antigen testing is often used when quick results are needed or for general screening and surveillance.

Below, we take a closer look at the two categories.

Molecular COVID tests (also called nucleic acid amplification test, or NAAT)

The first test created to detect COVID—and still the most widely used—is a molecular test called PCR (polymerase chain reaction), says Sheldon Campbell, MD, Ph.D., a Yale Medicine pathologist and microbiologist. "PCR and similar tests look for the COVID virus's RNA," meaning genetic material that comes only from the virus, Dr. Campbell explains. "They tend to be quite sensitive, but even among these, they are on a continuum of sensitivity and vary a whole lot."

"Sensitivity" measures how often a test correctly delivers a positive result for people with the condition that's being tested. A test that's highly sensitive will catch almost anyone who has the disease and not generate a lot of false-negative results.

How does the test work? A molecular test looks for genetic material from the virus. The test uses sophisticated chemicals and equipment to reproduce millions to billions of copies of viral-related DNA from even the smallest sample. Because of that, the test is considered highly sensitive, leading to very few false negatives.

How is a sample obtained? Usually with a swab inserted into your nose. There are three different methods for nasal collection:

- Nasopharyngeal: A health care professional inserts a long swab deep into your nostril to collect fluid from the back of your nose.
- Mid-turbinate: This method, which someone can be coached to do themselves or is done by a professional, involves placing a soft swab straight back into the nostril (less than one inch) to collect a sample.
- Anterior nasal swab: This test, which can either be self-administered and supervised by a trained health care provider, or done by a health care professional, involves putting a swab three-quarters of an inch into the nostril and twirling it around at least four times to get a sample.

In general, the deeper you go for a specimen, the greater the sensitivity, says Richard Martinello, MD, a Yale Medicine infectious diseases specialist. "But, we've found it's much more comfortable to do mid-turbinate or anterior nasal swabs, and they provide a reasonable degree of sensitivity," he adds. "It's a compromise of sorts, but it does allow us to simplify the collection process."

Other collection methods include:

- Oropharangeal (throat) swab: A trained health care provider collects a sample using a swab to the back of the throat.
- Saliva: You spit into a sterile, leak-proof cap container. For now, this type of testing is only offered at select locations.

How is the test processed? Most specimens are sent to laboratories. Part of the reason COVID NAAT/PCR tests took so long early in the pandemic was due to inadequate supply plus incredible volume. Though COVID is very much still with us, supply is increased and testing volume is not as high as it was.

Where can you get one? Molecular tests are offered at pharmacies, doctor offices, and designated testing locations, such as health clinics, as well as locations set up by private or state and local public health systems.

How quickly can you get results? Because the tests are sent to a lab, it depends on lab capacity. Results are typically available within a range of one to seven days, depending on your location.

"Usually it's a day or sometimes even less now," says Dr. Martinello. "The Yale New Haven Health System is turning around results within 24 hours for 99.5% of specimens."

How accurate are they? According to the Centers for Disease Control and Prevention (CDC), laboratory-based tests, such as PCR, have a "generally high" test sensitivity.

"PCR tests are considered the most accurate available," Dr. Martinello says. "But because these tests are highly sensitive and specific, there is still a

risk for a false positive."

But limiting false negatives might be extremely important, especially with the rise of more transmissible variants, like Delta. "It's actually true for those who have—and who don't have—symptoms, but if you do have symptoms, a PCR test is more likely than an antigen test to pick up an infection accurately," says Dr. Campbell.

Antigen COVID tests

Whereas molecular tests require specialized equipment for processing samples, an antigen test is simpler, because it requires smaller devices that are easy to transport. Their design is similar to, say, a pregnancy test.

How does the test work?

Antigen tests search for pieces of protein from the SARS-CoV-2 virus. The sample you provide is treated with a reagent and analyzed on the spot by a health care professional. Unlike molecular tests, these require a higher level of virus in the test sample before the test will turn positive. This means that an antigen test may sometimes lead to a false negative.

How is a sample obtained?

As with molecular tests, a sterile swab is inserted into your nose or throat to obtain a specimen (see details above)—although throat swabs may be less common these days.

How is the test processed?

The sample is self-applied to a test strip or cartridge. Similar to a home pregnancy test, results show a colored line to signify positive or negative.

Where can you get one?

Antigen tests are offered in pharmacies, doctor's offices, and can be purchased to use at home.

How quickly can you get results?

Results are typically available in 10 to 15 minutes.

How accurate are they? According to the CDC, antigen test sensitivity varies depending on the time in the course of one's infection, but is considered to have "moderate to high" sensitivity during peak viral load. Compared to molecular tests, antigen tests are more likely to generate false negative results, especially when performed on people who don't have symptoms.

To offset the decreased sensitivity, the FDA recommends doing serial testing—or taking multiple tests—over several days to improve the chance of catching asymptomatic infections.

ID NOW COVID Test

Complicating things a bit is the availability of ID NOW, a rapid molecular test used by some testing locations, such as pharmacies, that can read results on-site—in about 15 minutes.

According to the CDC, point-of-care tests (such as those administered at a drug store, including ID NOW), have a "moderate to high" test sensitivity.

But where does it fit in the molecular vs antigen test result accuracy spectrum?

"ID NOW is not a completely different thing than PCR, it's just on the lower sensitivity end of the spectrum," Dr. Campbell says. "So, more accurate than an antigen test."

Should I take a home test?

The home tests that give instant results are all antigen. However, there are home kits that require mailing a sample to a lab that use molecular technology. Whereas testing at pharmacies and doctor's offices is typically free or covered by insurance, your insurance company may not cover the cost of a home test, which may cost anywhere from $24 for a set of two to $38 for one.

For COVID-19, home tests can be useful if you need an immediate answer, Dr. Campbell says. "But the tricky part is that the cost can pile up and people don't always do the test correctly, either," he says. "I would think it's better to have the test done by someone whose job it is to do it, especially if

there are free testing locations available."

Dr. Martinello agrees. "I think it's a good assumption that home tests are not as accurate as NAAT tests you can get at a drive-through or walk-in testing site, but they do improve access to testing," he says.

What type of test should I get?

If you are exhibiting a fever, cough, trouble breathing, or other COVID-19 symptoms, you should get tested, regardless of vaccination status, health experts advise. You should also get tested if you have no symptoms, but know you were recently exposed to the virus.

Deciding which type of test to get can be a little more complicated.

"A lot of this depends on access and what is readily available to you. We are thankful to have rapid antigen tests that are easy to find, but if you don't have symptoms, their sensitivity is limited and we know that 40% of people who are contagious with COVID are asymptomatic," Dr. Martinello says. "A NAAT test is more sensitive, but a lot still depends on the quality of the specimen."

Still, for the diagnosis of people seriously ill (with a presumed case of COVID-19), doctors will generally use a PCR test, because false-negative tests might result in inadequate treatment.

Travel

If you are traveling, you might be required to get tested, too. The location you are visiting might require a certain type of test and approved testing locations as well.

Dr. Campbell says a PCR test probably makes the most sense for travel. "You want to detect the virus early, and the PCR test is the most sensitive for that to make sure you are not infectious for your trip," he says, acknowledging that many places require a negative COVID-19 test 72 hours before boarding a plane.

School and workplaces

For surveillance, such as at schools or workplaces, antigen tests work well, Dr. Campbell says.

"Say you are testing kids in a school twice a week in perpetuity. You can do it much more quickly and easily and for less cost if you use antigen tests," he says. "You want to answer the question of if kids are infectious now or not. Would PCR be better in that setting? Yes, but you won't get the answer back in a day necessarily, and you would spend a lot of money to find a few positives."

General peace of mind

Some people might like to do regular COVID tests for peace of mind. Say you are vaccinated but recently attended a crowded event and you are planning to visit an immuno-compromised relative. Preparing for this by ensuring you have a negative COVID test might not be a bad idea, but the timing is important, Dr. Campbell says.

"If you went to a crowded concert and are worried about COVID, you don't want to take any COVID test—molecular or antigen—the next day. You should wait three to five days after potential exposure," he says. "It's quite complicated. We think that you have to have a fair amount of virus present to be infectious to others, and we know that in the course of infection, the viral load goes up and down."

Will any of the tests tell me which variant I have?

None of the COVID-19 tests you take, either at home or at a pharmacy, will tell you if you have a variant, such as Delta. Detecting variants requires genetic testing done in a lab. Across the country, a selection of positive COVID-19 samples are sent to specialized labs, where they are anonymously sequenced to identify variants so that public health officials can monitor COVID-19 trends.

And not all positive specimens are tested; only sample amounts are taken. So, if you hear that 75% of cases in an area are a particular variant, for example, that reflects a computation based on the number of samples tested—and it is just an estimate.

Are there tests that look for COVID-19 and the flu?

Since the symptoms of COVID-19 and the flu are similar, it's helpful to know there are molecular tests you can have that detect each virus using a single sample. In fact, there are even tests that diagnose COVID-19, flu, and RSV (respiratory syncytial virus), a virus that causes common cold symptoms, at once.

Such tests are offered at doctor's offices and clinics and need to be sent to a lab, and should come back in a day or less. These tests will become available closer to flu season, in October.

Even for physicians, COVID-19 testing can be complicated and confusing.

In the end, it's best to remember the basics: get your vaccine, when in doubt wear a mask and social distance, and stay home and away from others if you feel sick, Dr. Campbell says.

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