How is COVID-19 diagnosed?
COVID-19 is a disease caused by the virus Sars-CoV-2. Clinicians use several things to determine whether someone has COVID-19, including symptoms, exposure, and testing. None of these pieces of information alone are enough to diagnose COVID, and no single piece of information is perfect. For example, someone with known exposure and classic symptoms may be presumed to have COVID-19 even with a negative test. Someone with no symptoms and no known exposure but a positive test might be diagnosed with COVID-19 anyway because transmission is high enough in that location to assume they have been exposed even without knowing it.

What tests are available for COVID-19?
The most widely used test to diagnose COVID-19 right now is a molecular test which detects genetic material (ribonucleic acid, or RNA) from the virus. These are sometimes called nucleic acid amplification (NAAT) tests or polymerase chain reaction (PCR) tests based on the method of testing. Sometimes people refer to these tests by the way they are collected, such as nasopharyngeal swab test, nasal swab test, or oropharyngeal swab test. Antigen tests are also being developed but are not yet available. These tests detect antigens, which are proteins on the surface of the virus that our immune system recognizes. Antibody tests are starting to become available. These tests are also called serology tests. Antibody tests look for the body’s response to an infection instead of looking for the virus itself. Antibodies are proteins that the body makes to fight off infections. They are one part of the immune system response to infection. Because it takes days to weeks for the body to create antibodies, these types of tests are not recommended for initial diagnosis of COVID-19.

Are all these tests approved by the Food and Drug Administration (FDA)?
No. None of the tests for COVID-19 are approved by the FDA, including the molecular tests. This is because FDA approval is a rigorous process which usually takes months to years. It requires a lot of testing to make sure tests work properly and to prove the quality and accuracy of the tests. However, during a public health emergency like the current pandemic, we cannot wait months for a test to receive approval. The FDA can grant an Emergency Use Authorization (EUA) which allows potentially life-saving products, medicines, and tests which meet certain criteria to be used. Many tests have been granted EUA. A list of tests with EUA is available at https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd
In addition to authorizing tests for emergency use, the FDA has allowed companies to make and sell tests which meet certain criteria even before an EUA is granted. As of 4/25/20, there are 7
manufacturers with an EUA for serology testing, and dozens of manufacturers who have notified the FDA that they will be making and selling serology tests.

**Why aren’t we testing everyone?**
There are many reasons that we don’t have enough tests for everyone. Sars-CoV-2 is a new virus which didn’t even exist before approximately November 2019. When the virus was recognized, scientists in China quickly sequenced the genome. That information was released in early January and scientists around the world began developing molecular tests for the virus. Some countries used the test provided by the World Health Organization, and others developed their own. In the US, the early tests were not accurate and were delayed. In addition, scientists had trouble getting samples of the virus and getting patient specimens which are used to create tests. When an accurate test was created in the US, there were only a few laboratories which were able to perform the tests. As more companies created tests, approval to use the tests was sometimes slow. When laboratory testing capacity was increased, a shortage of personal protective equipment (PPE) meant that too few health care workers could safely collect a specimen from patients. There are also shortages of nasopharyngeal swabs, viral transport media, and other specimen collection materials. This is in part because many of the factories which make these were shut down temporarily due to COVID, and in part because everyone around the world needs lots more of these than usual. There are shortages of the chemicals used to run the tests in laboratories for the same reason. Although there are more tests available now, we are still seeing shortages of PPE, specimen collection kits, and lab capacity to run tests. We are working very hard to try to increase the tests available in Chester County and Delaware County.

**Are all the antibody tests the same?**
No. There are many companies making these tests. Some of the tests are not performing as well as expected. The antibody test that CCHD is currently using has good test characteristics, but no test is perfect. CCHD continues to evaluate other tests as they become available to see if they will be useful for our community. CCHD is monitoring the early results of the current antibody test to make sure the results are reliable.

**What kinds of antibodies are there?**
The body makes different kinds of antibodies at different times in illness and recovery and in different parts of the body. The antibody test CCHD is using looks for two of these: IgM and IgG. IgM is often the first antibody made when a person is exposed to a germ. Your body usually starts to make IgM
during the first week of illness and stops making IgM antibodies after a couple weeks. IgG is usually made next. Your body usually starts to make antibodies after the first week of illness. IgG antibodies may stay in the body for weeks or longer. Antibodies are only one part of the immune system, which has lots of cells and processes for protecting us from infections.

**What are the possible results of the current antibody test offered by CCHD?**

The antibody test looks for IgM and IgG. If you have enough IgM or IgG in your blood for the test to detect, then the test will be positive for one or both. Usually this takes between 2 and 10 days after symptoms start. This test does not measure how many antibodies you have, only if antibodies are there or not. The test does not tell you how well your antibodies work. The test might pick up antibodies from a coronavirus that does not cause COVID-19.

Here is a summary of the possible results of this antibody test:

<table>
<thead>
<tr>
<th>IgM</th>
<th>IgG</th>
<th>Control</th>
<th>What we think this means:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Negative</td>
<td>Visible</td>
<td>You probably have COVID-19 and you are probably contagious.</td>
</tr>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>Visible</td>
<td>You probably have COVID-19 and may be starting to recover, but you might still be contagious.</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive</td>
<td>Visible</td>
<td>You are probably at the end of a COVID-19 infection, or you had it in the past.</td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>Visible</td>
<td>You have no antibodies to COVID-19 yet. You are presumed susceptible. Or, you could have an early infection before your body has had time to make antibodies.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not Visible</td>
<td>The test did not work properly and there is no result. A repeat test is needed.</td>
</tr>
</tbody>
</table>

**What does it mean if I have a positive IgM?**

Based on information we have learned from around the world, we believe that people with a positive IgM may still be contagious (even if you also have positive IgG). Even if you don’t have symptoms, we recommend that you stay at home until 7 days after you were tested. If you develop symptoms, stay home until 7 days from the start of your symptoms.
What does it mean if I have a positive IgG and negative IgM?

We believe that people with positive IgG have likely had COVID-19 and are in recovery, or have recovered. People with IgG may have immunity to COVID-19. We do not know for sure if the IgG antibodies are the kind of antibodies which block the virus from infecting our cells (neutralizing antibodies) or whether they might be antibodies which just flag the immune system that a germ is there (binding antibodies). When people have immunity to a disease, sometimes it means they cannot get infected again. Sometimes it means they can get infected again, but the disease is usually milder. We do not know if people who had COVID-19 in the past can get infected again. In many parts of the world, doctors and nurses who got COVID and recovered went back to work caring for patients with COVID, and they do not seem to be getting sick again. We do not know how long immunity might last. Based on information about other coronaviruses and new information about COVID-19, we think immunity might last for at least a few months. We do not know how other parts of the immune system, such as T-cells, are involved in protecting us from COVID-19. Much more research is needed to know for sure, but early information is hopeful.

If I have IgG, can I donate my plasma?

Some places are doing research on using convalescent plasma, which is taking antibodies from someone who has recovered from a disease and giving them to someone else who is fighting off the disease. This treatment has been used for other infections, such as Ebola, and might help with COVID-19. Potential donors are screened to make sure they have antibodies that would help and no other infections which could be spread to the recipient. For more information, or to find a place you might be able to donate, visit https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/donate-covid-19-plasma.

If I have IgG, can I stop physical distancing or stop wearing a mask?

No. We do not know if people who are immune might still be able to give the virus to other people who are not immune, even if they don’t get sick again themselves. As mentioned before, we do not know if having IgG means you are immune, how strong immunity might be, and how long immunity might last. It is essential that everyone in our community follow all our public health guidance to protect everyone else in the community.

How do you know how good a test is? Can I believe these results?

Tests have several characteristics. Stay with me: we are going to talk about some science. Sensitivity is how likely a test can detect a disease that is there. If a test is very sensitive, you will not have a lot of
false negatives. False negatives are when the disease is really there but your test doesn’t pick it up. The molecular tests have up to a 30% false negative rate. That is why if a clinician thinks someone has COVID-19, a negative test does **not** mean the person does not have COVID-19. There are lots of reasons that a molecular test might have a false negative: the specimen collection wasn’t good enough, there is not a high enough amount of virus in the body (viral load) to detect, etc.

**Specificity** is how likely a test will correctly tell when a disease is not there. If a test is very specific, it will only be positive when the disease is present. You will not have a lot of false positives, which is when the test says you have a disease but you really don’t. The molecular tests generally have a high specificity, so when a COVID-19 test is positive, it almost always means the patient has COVID-19. But remember: molecular tests only detect virus genetic material. Late in the disease, a person might have dead virus in their body, and might not be contagious anymore, but could still have a positive molecular test.

The antibody test we are using has been studied to evaluate how it works. Overall sensitivity was reported as 97% and specificity 98%. In general, serology tests have a lower sensitivity because of the timing of the tests. Your body makes antibodies between a few days and a few weeks after the start of the illness, so when you test for antibodies early, the tests will be negative. With serology tests, if you have a false negative (low or moderate sensitivity), that is not very harmful for people or for the community. It means you believe you can still catch the disease and should still be careful, which we all should be doing anyway! But with serology tests, if you have a false positive (low or moderate specificity) that can be a problem. A false positive IgM might mean that you are sent home from work, or put in isolation, because we thought you are contagious. That can be inconvenient, but is not dangerous. But a false positive IgG would mean that you think you are immune and you are not. With the test we have chosen, there were no false positive IgGs in the two studies (reported specificity for IgG 100%).

Specificity of 98% or 99% sounds very high. However, the chance that your positive result is really a true positive also depends on how much disease is in the community (the prevalence). The chance that your negative result is a really a true negative also depends on prevalence. An example: we use a test with 99% specificity for IgG. We test 100 people (Group A) who have stayed at home, never leaving the house, for the last 6 weeks. All food and household goods have been delivered, and they wash their hands after touching all packages. We also test 100 people (Group B) who went on vacation 6 weeks ago. They flew to Florida, and then went on a cruise for two weeks. For the 4 weeks since they came back, they have worked in a nursing home where there is a known outbreak of COVID-19. In each group, 1 person tests positive for IgG. How likely is the result a true positive? In Group A, it is very likely a false positive! In Group B, there is a much greater chance this is a true
positive. Right now in our community, even though lots of people have come down with COVID-19, the prevalence is low. That means even tests with pretty high sensitivity and specificity have a higher risk of inaccurate results.

If the reported specificity is 100%, then doesn’t that mean the test is perfect?
No test is perfect. The studies to get these tests EUA were done in small numbers of people. When we perform these tests in thousands or millions of people across the country, we learn much more about these tests. Also, in studies, tests are performed the exact same way by a small number of trained scientists or clinicians. In the real world, with thousands of people in hospitals, labs, and offices performing these tests, there is much variation in the way the tests are done.

What is herd immunity?
Herd immunity means enough people in a population have immunity so that even people without immunity can be somewhat protected. This happens because if the people who are immune do not give the infection to others, the infection will not spread as quickly, or at all. If the infection is not spreading, then the people who are not immune have a smaller chance of getting the infection. Herd immunity depends on how well an infection spreads and how many people are immune. COVID-19 is a new disease, but it is estimated that around 60% to 80% of a population would need immunity to have “herd immunity.” Right now, we estimate that less than 5% of our population, and maybe only 1% or 2%, has immunity.

I heard that 25% to 50% of people have no symptoms of COVID-19. Doesn’t that mean up to half of us have been exposed, and we can go back to normal soon?
No. We estimate that 25 to 50% of people who have COVID-19 do not have symptoms at the time of diagnosis. Many of them later develop symptoms, but some people never have any symptoms at all. However, only a small number of people have even been exposed to COVID-19. In some areas, we estimate that 1 to 4% of people have been exposed. We believe Chester County and Delaware County will be in this range, but we will not know until more antibody testing is done. In some areas where there was much more transmission, up to 10% or 15% of the people have been exposed. No area anywhere in the world has enough people who were exposed to COVID-19 to be even close to herd immunity.

Should we just stop all the stay-at-home orders so that we can get to herd immunity faster? If the young and healthy get exposed won’t that help the people who are more at risk?
No. If you try to get just enough people infected to reach herd immunity, the virus is impossible to stop and many more vulnerable will be exposed than you intended. Also, when many people are exposed, we cannot care for them all at once. Not everyone gets sick enough to be in a hospital or in an intensive care unit (ICU). But when more people are sick at one time, we do not have enough of everything (room in the hospital or ICU, ventilators, medicines, health care workers, PPE, etc.) to care for everyone. Also, when hospitals are full of patients with COVID-19, we do not have ability to care for everyone else with heart attacks, strokes, broken bones, and everything else. This is why we try to “flatten the curve.” For more information, see:

If we cannot get to herd immunity quickly, how can we ever get back to normal?
Several things are needed to get back to normal. We will not get completely back to normal immediately, but gradually. We will likely need to have public health measures ramp up and back down depending on how much the virus is spreading.

1. The spread of the virus must be slower. We do this through physical distancing, wearing masks, and other public health measures.
2. We must have lots of rapid tests. Right now, some results take days. We need to figure out who has COVID-19 quickly, to try to stop them from spreading germs to others.
3. We need to be able to isolate people with COVID-19 quickly and safely.
4. We need to track all the contacts of people with COVID-19 quickly. We will need lots of trained contact tracers to do this.
5. We need to quarantine contacts of people with COVID-19 quickly and safely.
6. We need treatments and vaccines, so that the way we handle COVID-19 is more like the way we handle influenza.

Getting fully back to normal may not happen for months to years, with tighter and looser restrictions in several steps along the way. Americans have overcome difficult challenges before and we will succeed again.