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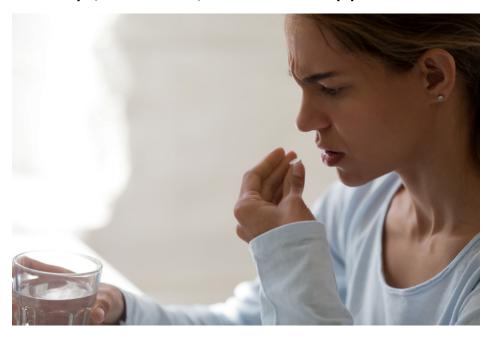
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Treatments for COVID-19

What helps, what doesn't, and what's in the pipeline



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Most people who become ill with COVID-19 will be able to recover at home. No specific treatments for COVID-19 exist right now. But some of the same things you do to feel better if you have the flu — getting enough rest, staying well hydrated, and taking medications to relieve fever and aches and pains — also help with COVID-19.

In the meantime, scientists are working hard to develop effective treatments. Therapies that are under investigation include drugs that have been used to treat malaria and autoimmune diseases; antiviral drugs that were developed for other viruses, and antibodies from people who have recovered from COVID-19.

What is convalescent plasma? How could it help people with COVID-19?

When people recover from COVID-19, their blood contains antibodies that their bodies produced to fight the coronavirus and help them get well. Antibodies are found in plasma, a component of blood.

Convalescent plasma — literally plasma from recovered patients — has been used for more than 100 years to treat a variety of illnesses from measles to polio, chickenpox, and SARS. In the current situation, antibody-containing plasma from a recovered patient is given by transfusion to a patient who is suffering from COVID-19. The donor antibodies help the patient fight the illness, possibly shortening the length or reducing the severity of the disease.

Though convalescent plasma has been used for many years, and with varying success, not much is known about how effective it is for treating COVID-19. There have been reports of success from China, but no randomized, controlled studies (the gold standard for research studies) have been done. Experts also don't yet know the best time during the course of the illness to give plasma.

On March 24th, the FDA began allowing convalescent plasma to be used in patients with serious or immediately life-threatening COVID-19 infections. This treatment is still considered experimental.

Who can donate plasma for COVID-19?

In order to donate plasma, a person must meet several criteria. They have to have tested positive for COVID-19, recovered, have no symptoms for 14 days, currently test negative for COVID-19, and have high enough antibody levels in their plasma. A donor and patient must also have compatible blood types. Once plasma is donated, it is screened for other infectious diseases, such as HIV.

Each donor produces enough plasma to treat one to three patients. Donating plasma should not weaken the donor's immune system nor make the donor more susceptible to getting reinfected with the virus.

Is there an antiviral treatment for COVID-19?

Currently there is no specific antiviral treatment for COVID-19.

However, drugs previously developed to treat other viral infections are being tested to see if they might also be effective against the virus that causes COVID-19.

Why is it so difficult to develop treatments for viral illnesses?

An antiviral drug must be able to target the specific part of a virus's life cycle that is necessary for it to reproduce. In addition, an antiviral drug must be able to kill a virus without killing the human cell it occupies. And viruses are highly adaptive. Because they reproduce so rapidly, they have plenty of opportunity to mutate (change their genetic information) with each new generation, potentially developing resistance to whatever drugs or vaccines we develop.

What treatments are available to treat coronavirus?

Currently there is no specific antiviral treatment for COVID-19. However, similar to treatment of any viral infection, these measures can help:

- · While you don't need to stay in bed, you should get plenty of rest.
- Stay well hydrated.
- To reduce fever and ease aches and pains, take acetaminophen. Be sure to follow directions. If you are taking any combination cold
 or flu medicine, keep track of all the ingredients and the doses. For acetaminophen, the total daily dose from all products should not
 exceed 3,000 milligrams.

Is it safe to take ibuprofen to treat symptoms of COVID-19?

Some French doctors advise against using ibuprofen (Motrin, Advil, many generic versions) for COVID-19 symptoms based on reports of otherwise healthy people with confirmed COVID-19 who were taking an NSAID for symptom relief and developed a severe illness, especially pneumonia. These are only observations and not based on scientific studies.

The WHO initially recommended using acetaminophen instead of ibuprofen to help reduce fever and aches and pains related to this coronavirus infection, but now states that either acetaminophen or ibuprofen can be used. Rapid changes in recommendations create uncertainty. Since some doctors remain concerned about NSAIDs, it still seems prudent to choose acetaminophen first, with a total dose not exceeding 3,000 milligrams per day.

However, if you suspect or know you have COVID-19 and cannot take acetaminophen, or have taken the maximum dose and still need symptom relief, taking over-the-counter ibuprofen does not need to be specifically avoided.

Are chloroquine and hydroxychloroquine effective for treating COVID-19?

Recently, there has been considerable discussion of whether two related drugs — chloroquine and hydroxychloroquine — that have been available for decades to treat other illnesses might also be effective in treating COVID-19.

The drugs are primarily used to treat malaria and several inflammatory diseases, including systemic lupus erythematosus (lupus) and rheumatoid arthritis. No drug is perfectly safe, but these drugs are quite safe when used for just the several days they might be needed to treat COVID-19. They are also cheap, already available at our local drug stores, and relatively free of side effects.

The question, of course, is whether they are effective against the coronavirus that causes COVID-19. Are they effective in killing the virus in a laboratory dish? And are they effective in killing the virus in people? If the answer to the first question is "no," there's no point in getting an answer to the second question.

There is strong evidence that both drugs kill the COVID-19 virus in the laboratory dish. The drugs appear to work through two mechanisms. First, they make it harder for the virus to attach itself to the cell, inhibiting the virus from entering the cell and multiplying within it. Second, if the virus does manage to get inside the cell, the drugs kill it before it can multiply.

But do the drugs work in people with COVID-19? Many studies are underway to get an answer to this question, but as of March 24, 2020, only two have issued preliminary results.

One report, published in February 2020, claimed that chloroquine had been used in more than 100 patients in China who had COVID-19. The scientists stated that their results demonstrated that chloroquine is superior to the control treatment in inhibiting the worsening of pneumonia, improving lung imaging findings, eliminating the virus from the body, and shortening the duration of the disease.

These claims are exciting. However, the report provided virtually no evidence in support of the claims. First of all, this was not a randomized, double-blind controlled trial, the gold standard for research studies. Second, no evidence was presented as to how severe the pneumonia was, nor whether findings on lung x-rays or CT scans really improved. Third, although they claim the drug made the virus disappear, they didn't report what the levels of the virus were before versus after the treatment. In short, not much evidence.

Another small study was conducted by a group of scientists in southern France, a region hard hit by COVID-19. This, also, was not a randomized trial. Instead, the scientists compared 26 patients who received hydroxychloroquine to 16 who did not: after six days, the virus was gone from the body in 70% of those given the treatment, compared to only 12.5% of those who weren't. The drug appeared to be as effective in the sickest patients as in the least sick, but the study was too small to be sure about that. The study also was too small to say that people who received the treatment were protected against a prolonged illness or death.

There are many studies underway, and we should have more solid answers within a few months.

Is the antiviral drug remdesivir effective for treating COVID-19?

Scientists all over the world are testing whether drugs previously developed to treat other viral infections might also be effective against the new coronavirus that causes COVID-19.

One drug that has received a lot of attention is the antiviral drug remdesivir. That's because the coronavirus that causes COVID-19 is similar to the coronaviruses that caused the diseases SARS and MERS — and evidence from laboratory and animal studies suggests that remdesivir may help limit the reproduction and spread of these viruses in the body. In particular, there is a critical part of all three viruses that can be targeted by drugs. That critical part, which makes an important enzyme that the virus needs to reproduce, is virtually identical in all three coronaviruses; drugs like remdesivir that successfully hit that target in the viruses that cause SARS and MERS are likely to work against the COVID-19 virus.

Remdesivir was developed to treat several other severe viral diseases, including the disease caused by Ebola virus (not a coronavirus). It works by inhibiting the ability of the coronavirus to reproduce and make copies of itself: if it can't reproduce, it can't make copies that spread and infect other cells and other parts of the body.

Remdesivir inhibited the ability of the coronaviruses that cause SARS and MERS to infect cells in a laboratory dish. The drug also was effective in treating these coronaviruses in animals: there was a reduction in the amount of virus in the body, and also an improvement in lung disease caused by the virus.

The drug appears to be effective in the laboratory dish, in protecting cells against infection by the COVID virus (as is true of the SARS and MERS coronaviruses), but more studies are underway to confirm that this is true.

Remdesivir was used in the first case of COVID-19 that occurred in Washington state, in January 2020. The patient was severely ill, but survived. Of course, experience in one patient does not prove the drug is effective.

Two large randomized clinical trials are underway in China. The two trials will enroll over 700 patients, and are likely to definitively answer the question of whether the drug is effective in treating COVID-19. The results of those studies are expected in April or May 2020. Studies also are underway in the United States, including at several Harvard-affiliated hospitals. It is hard to predict when the drug could be approved for use and produced in large amounts, assuming the clinical trials indicate that it is effective and safe.

I've heard that high-dose vitamin C is being used to treat patients with COVID-19. Does it work? And should I take vitamin C to prevent infection with the COVID-19 virus?

Some critically ill patients with COVID-19 have been treated with high doses of intravenous (IV) vitamin C in the hope that it will hasten recovery. However, there is no clear or convincing scientific evidence that it works for COVID-19 infections, and it is not a standard part of treatment for this new infection. A study is underway in China to determine if this treatment is useful for patients with severe COVID-19; results are expected in the fall.

The idea that high-dose IV vitamin C might help in overwhelming infections is not new. A <u>2017 study</u> found that high-dose IV vitamin C treatment (along with thiamine and corticosteroids) appeared to prevent deaths among people with sepsis, a form of overwhelming infection causing dangerously low blood pressure and organ failure. Another <u>study published last year</u> assessed the effect of high-dose vitamin C infusions among patients with severe infections who had sepsis and acute respiratory distress syndrome (ARDS), in which the lungs fill with fluid. While the study's main measures of improvement did not improve within the first four days of vitamin C therapy, there was a lower death rate at 28 days among treated patients. Though neither of these studies looked at vitamin C use in patients with COVID-19, the vitamin therapy was specifically given for sepsis and ARDS, and these are the most common conditions leading to intensive care unit admission, ventilator support, or death among those with severe COVID-19 infections.

Regarding prevention, there is no evidence that taking vitamin C will help prevent infection with the coronavirus that causes COVID-19. While standard doses of vitamin C are generally harmless, high doses can cause a number of side effects, including nausea, cramps, and an increased risk of kidney stones.

What is serologic (antibody) testing for COVID-19? What can it be used for?

A serologic test is a blood test that looks for antibodies created by your immune system. There are many reasons you might make antibodies, the most important of which is to help fight infections. The serologic test for COVID-19 specifically looks for antibodies against the COVID-19 virus.

Your body takes at least five to 10 days after you have acquired the infection to develop antibodies to this virus. For this reason, serologic tests are not sensitive enough to accurately diagnose an active COVID-19 infection, even in people with symptoms.

However, serologic tests can help identify anyone who has recovered from coronavirus. This may include people who were not initially identified as having COVID-19 because they had no symptoms, had mild symptoms, chose not to get tested, had a false-negative test, or could not get tested for any reason. Serologic tests will provide a more accurate picture of how many people have been infected with, and recovered from, coronavirus, as well as the true fatality rate.

Serologic tests may also provide information about whether people become immune to coronavirus once they've recovered and, if so, how long that immunity lasts. In time, these tests may be used to determine who can safely go back out into the community.

Scientists can also study coronavirus antibodies to learn which parts of the coronavirus the immune system responds to, in turn giving them clues about which part of the virus to target in vaccines they are developing.

Serological tests are starting to become available and are being developed by many private companies worldwide. However, the accuracy of these tests needs to be validated before widespread use in the US.

Podcasts

COVID-19 therapies update: There are three potential pathways forming a bridge to a vaccine (recorded 4/13/20)

You've probably heard the anti-malarial drug <u>hydroxychloroqine</u> is getting a hard look as a potential therapeutic agent in the fight against COVID-19. However, as <u>Harvard Health Publishing</u> senior faculty editor <u>Dr. Rob Shmerling</u> points out, evidence remains weak. On the brighter side, he points to three potential avenues in COVID-19 research where therapies may be put to use while a vaccine remains in development.



For more information on coronavirus and COVID-19, see the Harvard Health Publishing <u>Coronavirus Resource</u> <u>Center</u>.

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