



HEALTH

Could COVID-19 be prevented before it starts? Some researchers are looking for a way.

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Finding a way to protect against COVID-19 would transform the fight against the coronavirus that has spread across the world since late last year.

Pharmaceutical companies and doctors have been hunting for drugs to treat COVID-19 and launched a major effort to develop a vaccine against it, but they haven't focused as much on therapies for preventing infection before or after someone is exposed to the virus that causes the disease.

"The idea of having a way of preventing the infection and/or symptoms remains a critical need," said Dr. Susanna Naggie, vice dean for clinical research and an associate professor at the Duke University School of Medicine.

That's why there was so much excitement over the drug hydroxychloroquine, which President Donald Trump said he was taking for a while, to avoid infection with the virus. A study published last week found hydroxychloroquine failed to prevent infection. Other studies are ongoing, including some larger ones, that will confirm or contradict that finding.

Hydroxychloroquine has received the most scientific attention – undergoing more than 200 ongoing trials – both because it was one of the earliest drugs available to be considered and because Trump's support drove public interest.

Now that questions have been raised about its effectiveness, focus is slowly beginning to turn elsewhere, and trials of other approaches, from medications to mouthwashes, are beginning.

Even though some of those approaches already are well used, it will be months before scientists will know whether they can prevent COVID-19.

Turning focus elsewhere

The negative attention on hydroxychloroquine has made it much harder for researchers to get enough volunteers to complete trials of the drug, said Naggie, who is helping to lead one of the largest.

Naggie said her team had hoped to quickly get 15,000 health care workers to volunteer to take hydroxychloroquine and finish her study in five or six months. Instead, only about 800 have signed up, and she expects her study to take months longer.

Public opinion of the drug has suffered, she said, in response to the politics and observational studies such as one in *The Lancet*, which has since been retracted, that raised questions about its effectiveness and risks in patients very sick with COVID-19.

Her \$50 million study, called Healthcare Worker Exposure Response and Outcomes, or HERO, will be useful to definitively answer the question about hydroxychloroquine's effectiveness for pre-exposure prevention, she said.

Other prevention approaches are likely to be added to the study in the hopes that one or more will eventually prove useful against the virus.

"The level of enthusiasm for something that is not hydroxychloroquine will be much higher," Naggie predicted. "The politicization of hydroxychloroquine, as well as the data that has come out in the inpatient setting, made a murky picture for this drug in particular."

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A prevention approach differs from a vaccine, though it may be useful in combination, Naggie said. A vaccine hopefully provides long-term protection; a prophylaxis could help in the case of an exposure, or ongoing risk, such as to a health care worker.

For the flu, for example, an annual vaccine is not 100% effective, though it can reduce risk of serious infection. Many people exposed to the flu are prescribed the antiviral Tamiflu to help limit the infection. In HIV, for which researchers have tried for decades to develop a vaccine, people at high risk for the infection can be prescribed the same drug cocktail for prevention as is used for treatment.

There are no federally approved treatments for COVID-19, though the anti-viral drug remdesivir has shown some effectiveness against it and is routinely used in many places. For now, remdesivir is delivered only intravenously, so it is not a good option for people looking to prevent disease.

Researchers hope that whatever works as a treatment will also prevent initial infection and visa versa.

On the hunt for other preventives

In a gigantic global trial called Solidarity, the World Health Organization is testing four different approaches to treating COVID-19: hydroxychloroquine, remdesivir and two combinations of drugs used to combat HIV, Lopinavir and Ritonavir, and Lopinavir and Ritonavir plus the multiple sclerosis drug Interferon beta-1a. The two-drug combination was tested in China early in the outbreak and shown not to work as a treatment in very serious disease, but there is some hope that it might work in lesser infections.

Romark, a pharmaceutical company based in Tampa, Florida, is running two different trials of its candidate drug nitazoxanide, which has long been used to treat "traveler's diarrhea." For the past 15 years, the company has been studying whether it can be used to prevent a wide range of respiratory viruses.

Romark is testing the drug in 800 people in nursing homes and 800 health care workers and first responders to see whether it can prevent infection in people who have been exposed to the coronavirus. They hope to have results by the end of the summer, said Marc Ayers, Romark CEO.

Although it's too soon to know whether the drug will be successful, if it is, Romark will be prepared to produce as much as 200 million pills by the end of the year at its production facility in Puerto Rico, Ayers said.

For the trial, the pills will be given twice a day for six weeks. In nursing homes, once someone in the facility has COVID-19, Ayers said, he hopes nitazoxanide will stop the virus from spreading. Nursing homes are eligible to join the trial if they have an outbreak, he said, and the company pledged to enroll a nursing home within 72 hours of first contact with the company.

"We're working with a sense of urgency," he said.

Could simple iodine help?

Dr. Alexandra Kejner was in her third trimester of pregnancy and struggling with insomnia this spring when it struck her that the iodine she uses to sterilize the nose and throat of her patients might help clear COVID-19.

"That's what I wash my hands with before surgery," said Kejner, an assistant professor at the University of Kentucky, adding it's also used for wound packing and sinus disease, and is relatively safe and affordable.

Kejner, the mother of a 2-month-old girl, has since launched a major study examining a specific concentration of iodine to prevent COVID-19. The aim is to coat the inside of the nose and mouth to prevent the virus from getting a foothold.

She's started to enroll 300 patients in the trial, as have collaborators at George Washington University and Louisiana State University.

Eligible participants use the carefully dosed iodine nasal spray and gargle with it three times a day. Originally, they were going to be asked to use a nasal swab similar to the COVID-19 testing swabs, but Kejner's husband tried it and vetoed it.

"No one will do this three times a day," he warned. So she changed the protocol.

The trial will include two groups of participants: patients hospitalized for non-COVID-19 reasons and health care workers exposed to COVID-19 patients. To enroll, each participant will be tested to ensure he or she is not infected and screened for allergies to iodine.

For health care workers, Kejner said she sees iodine as a "second line of defense" in case they don't have enough personal protective equipment or it fails to keep them safe.

She hopes to have at least preliminary data within the next two to three months.

Dr. Michael Paasche-Orlow, a professor of medicine at Boston University School of Medicine and Boston Medical Center, said he wishes such trials had started sooner, so more results could arrive this summer.

The federal government, he said, focused too much on hydroxychloroquine instead of spreading the research into different prevention approaches.

"The early enthusiasm distorted the market," he said. "Why would we have 200 recent studies about hydroxychloroquine and not more diversity of projects? It feels that there was a missed opportunity."

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