Oxford researchers plan a COVID-19 reinfection human challenge trial

Written by Robby Berman on April 22, 2021 — Fact checked by Rita Ponce, Ph.D.

Scientists are planning a trial that will determine whether or not people who have had COVID-19 are now immune to the virus that causes it. STEVE PARSONS/Getty Images

- **Experts still have a lot to learn about the likelihood that people who have had COVID-19 can contract SARS-CoV-2 again.**
- **Scientists at the University of Oxford in the United Kingdom have announced a human challenge trial to gather hard, precise data that will provide a better understanding of how reinfection works.**
- **Under carefully controlled conditions and for research purposes, scientists will reinfect the participants in the study with the original SARS-CoV-2 variant.**

exposure to the SARS-CoV-2 virus again.

Scientists at the University of Oxford have announced a human challenge trial that will investigate the response of the human immune system to a second SARS-CoV-2 infection.

According to Shobana Balasingam, the vaccines senior research advisor at the Wellcome Trust — which is the organization funding the trial — "There are still many unknowns surrounding this virus, and human infections studies can enable us to learn a lot about COVID-19."

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"This study has the potential to transform our understanding by providing high quality data on how our immune system responds to a second infection with this virus."

The trial has two phases, the first of which begins this month. The second phase is expected to begin this summer.

The value of challenge studies

Helen McShane, a professor of vaccinology at the Department of Paediatrics at the University of Oxford, is the study's chief investigator. She explains the value of challenge studies, saying, "Challenge studies tell us things that other studies cannot because, unlike natural infection, they are tightly controlled."

"When we reinfect these participants, we will know exactly how their immune system has reacted to the first COVID infection, exactly when the second infection occurs, and exactly how much virus they got."

"As well as enhancing our basic understanding, this may help us to design tests that can accurately predict whether people are protected."

Prof. Johnathan Stoye, who is not involved in the investigation, is a virologist from the Francis Crick Institute in London, U.K. He also commented on the importance of such research, telling *Medical News Today*, "This is an extremely interesting and important area."

"Well-documented cases of reinfection can have different consequences. There are clearly many open questions that probably can only be answered by approaches along these lines of this study."

Prof. Stoye went on to commend the "bravery of the volunteers and medical professionals involved."

Phase 1

The investigation's first phase will determine the minimum dose of SARS-CoV-2 that causes reinfection. The researchers will be using the original variant of SARS-CoV-2 from Wuhan, China.

Up to 64 healthy volunteers, all aged 18–30 years, who had previously contracted SARS-CoV-2 will participate in this phase of the trial. Before reinfecting them, the investigators will ensure that the participants are completely fit and have completely recovered from their first SARS-CoV-2 infection to minimize their risk.

The scientists will divide the phase 1 participants into two groups. The first group, of 24 individuals, will have exposure to increasing amounts of the SARS-CoV-2 virus to establish the dosing threshold at which reinfection occurs. The researchers will then administer this optimal dose to the second group.

The study participants will isolate in a specially designed hospital suite for at least 17 days.

The research team will be responsible for their care and will administer a range of medical tests, including CT lung imaging and MRI heart scans. The individuals will only be able to leave the hospital suite when they no longer have the infection and are no longer infectious.

If anyone develops any symptoms of COVID-19, they will receive monoclonal antibodies.

The participants will take part in a minimum of eight follow-up examinations over the course of 12 months.

Speaking to *MNT*, Prof. Stoye noted some important questions that might come up during this phase of the challenge, particularly regarding determining the "optimum dose" for the challenge.

"Would [this dose] be different in different people depending on their

initial infection?" he asked. "If [it] is, what impact will it have on the proposed phase 2 studies?"

Phase 2

"In phase 2," says Prof. McShane, "we will explore two different things. First, we will define very carefully the baseline immune response in the volunteers before we infect them."

With this information in mind, Prof. McShane goes on to add that, "We will then infect them with the dose of virus chosen from the first study and measure how much virus we can detect after infection."

> "We will then be able to understand what kind of immune responses protect against reinfection. Second, we will measure the immune response at several time points after infection so we can understand what immune response is generated by the virus."

What the researchers hope to learn

Because they provide precise information about the infection timeline, the data that come from a challenge study such as this can be invaluable.

Christopher Coleman, who is not involved in the investigation, is an assistant professor of infection immunology at the University of Nottingham in the U.K. He told *MNT*, "The second phase will really tell us what is happening upon reinfection in the immune system."

"We can tell if the immune system is acting as though the infection is still the first one or is responding to a virus it already recognizes (and that can be good or bad, depending on the exact nature of the response)."

"Medically, this could also help us understand which parts of the immune response are critical for protection against the virus — either to test a vaccine or for drugs that may help that specific response."

Balasingam, from the Wellcome Trust, concludes that, "The findings could have important implications for how we handle COVID-19 in the future and inform not just vaccine development but also research into the range of effective treatments that are also urgently needed."

> "Keeping up the pace of scientific research and development through crucial studies such as this remain the only way we will truly get ahead of this pandemic and bring it under control."