

of severe acute respiratory syndrome (SARS) and Ebola – but US researchers are hoping to increase the value of the treatment by selecting donor blood that is packed with antibodies and giving it to people most likely to benefit.

A key advantage of convalescent plasma is that it's available immediately, whereas drugs and vaccines take months or years to develop. Infusing blood in this way seems to be relatively safe, as long as it is screened for viruses and other infectious agents. Scientists who have led the charge to use plasma want to deploy it now as a stopgap measure, to keep serious infections at bay and hospitals afloat as a tsunami of cases comes crashing their way. "Every patient that we can keep out of the ICU is a huge logistical victory because there are traffic jams in hospitals," says Michael Joyner, an anaesthesiologist and physiologist at Mayo Clinic in Rochester, Minnesota.

Thanks to the researchers' efforts, the US Food and Drug Administration announced last week that it will permit the emergency use of plasma for patients in need. As early as this week, at least two hospitals in New York City – Mount Sinai and Albert Einstein College of Medicine – hope to start using survivor plasma to treat people with the disease, Joyner says.

After this first roll-out, researchers hope the use will be extended to people at a high risk of developing COVID-19, such as nurses and physicians. For them, it could prevent illness so that they can remain in the hospital workforce, which can't afford to be depleted.

Hard evidence

At the same time, US academic hospitals are planning to launch placebo-controlled clinical trials to collect hard evidence on how well the treatment works.

Liise-anne Pirofski, an infectious-disease specialist at Albert Einstein College of Medicine, says that, in one proposed trial, researchers plan to infuse patients at an early stage of the disease and see how often they advance to critical care. Another trial would enrol people with severe infections. A third would explore plasma's use as a preventive measure for people in close contact with those confirmed to have COVID-19, and would evaluate how often such people fall ill after an infusion, compared with others who were similarly exposed but not treated. These outcomes can be measured within a month, she says. "Efficacy data could be obtained very, very quickly."

Even if it works well enough, convalescent serum might be replaced by modern therapies later this year. Research groups and biotechnology companies are identifying antibodies against the coronavirus, with plans to develop these into precise formulas. "The biotech cavalry will come on board with isolating antibodies, testing them, and developing drugs and vaccines, but that takes time," says Joyner.

Q&A



Should we infect healthy people with coronavirus?

With no end to the coronavirus pandemic in sight, researchers are discussing a dramatic approach that could help to end it: infecting a handful of healthy volunteers with the virus to speed up vaccine testing.

Many scientists see a vaccine as the only solution to the pandemic. At least one candidate is in safety trials, but a major hurdle is showing that a vaccine works. This typically requires large studies in which thousands of people receive a vaccine or a placebo, and researchers track who becomes infected naturally.

It would be quicker to do a 'human challenge' study, argue scientists in a March preprint (N. Eyal *et al.* Preprint at DASH <http://go.nature.com/33y1hey>; 2020). This would involve exposing healthy people to the virus and seeing whether those who are vaccinated escape infection.

Nir Eyal, the director of the Center for Population-Level Bioethics at Rutgers University in New Brunswick, New Jersey, and co-author of the preprint, tells *Nature* how the study could be done.

Why should we consider human-challenge studies of coronavirus vaccines?

They could greatly accelerate the time to approval and potential use. Testing vaccines

"There are some historical precedents for exposure to very deadly viruses."

in phase III trials takes a long time. That's done on many people, some of whom get the vaccine and some of whom get placebos or competing vaccine candidates. Researchers then look for differences between these groups in infection rates.

But many people will try to be careful in this outbreak – by self-isolating, say – and it will take a very long time until interpretable results emerge. If, instead, one exposes all study participants to the pathogen, one can not only rely on far fewer volunteers but, more importantly, take a much shorter period to get results.

Are there any precedents for infecting healthy people with a pathogen?

We do human-challenge studies for less deadly diseases quite frequently – for example, for influenza, typhoid, cholera and malaria. There are some historical precedents for exposure to very deadly viruses. The thing that demarcates the design that we propose from some of these historical instances is that we feel there is a way to make these trials surprisingly safe.

How could you conduct such a study?

You would start only after some preliminary testing to ensure that a vaccine candidate is safe and that it raises an immune response in humans. You then gather a group of people at low risk from any exposure – young and healthy individuals – and ensure that they are not already infected. You give them either the vaccine candidate or a placebo and wait for an immune response. Then you expose them to the virus.

You follow all the participants closely to catch any signs of infection as early as possible. You are trying to check whether the vaccine group is doing better than the placebo group. That might be in terms of viral levels, the time until symptoms emerge or whether they're infected or not.

Is this ethical?

It might seem that anybody volunteering to participate in such a study lacks capacity for rational decision-making. But humans do many important things out of altruism. And although the study introduces risks, it also removes them. And the net risks, although unclear, are not clearly extremely high. So, it is potentially rational – even from a selfish point of view – to participate in such a study.

We also let humans volunteer to do risky things all the time; for example, to be in the emergency medical services during this period. That elevates their risk of getting infected but it's very important. In this case, vaccines could be our societies' only way out of the bind between economic stagnation and widespread mortality.

Interview by Ewen Callaway

This interview has been edited for length and clarity.