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More than 100 coronavirus vaccines are in development, but will any of them work?

Michael Le Page

JUST months after the coronavirus pandemic began, 10 vaccines designed to prevent covid-19 are already being tested in people, and another 114 are in development.

A vaccine that provides effective, long-lasting protection against the coronavirus would be a game-changer, far better than any treatment. “Do we need a vaccine? Absolutely we do. It’s really better to prevent,” says Peter Horby, who is leading a UK trial evaluating several covid-19 treatments.

However, we don’t yet know whether it is possible to induce long-lasting coronavirus immunity with a vaccine. When people are infected by other kinds of coronaviruses, their immunity seems to fade rapidly – although subsequent infections are milder. There are concerns this could mean that any protection from a vaccine would fade too. “It may be that we don’t get a one-dose vaccine that lasts for a lifetime,” says Martin Hibberd at the London School of Hygiene & Tropical Medicine.

A vaccine that ensures people only become mildly ill would still be good, says Hibberd. “We would be pretty happy with that.”

Vaccines work by teaching your immune system to recognise part of a pathogen. There are a variety of ways to do this and just about every approach is being tried for the coronavirus.

Four of the 10 already being tested in people are inactivated vaccines, which administer the coronavirus in a chemically inactivated form that is unable to replicate. Another of the front runners is a subunit vaccine, consisting of the spike protein on the outside of the coronavirus, which the virus uses as a key to gain entry to our cells.

Inactivated and subunit vaccines tend not to provoke a big immune response, so chemicals often have to be added to boost their effects. Many vaccines we use today are one of these two types, including many flu vaccines.

The other five front runners use various methods – such as fatty droplets or the shell of another virus – to deliver genetic code for a viral protein, such as the spike protein, to human cells. This RNA or DNA code is then used by the cells to make the protein. Using DNA or RNA for vaccines in this way is a relatively new idea, and none has yet been approved for any disease.

None of the coronavirus vaccines currently in trials are live attenuated vaccines. This kind of vaccine uses a mutated version of the virus that is only capable of causing very mild disease, if any symptoms at all, and is the method used for many of the most effective vaccines we have, including the measles, mumps and rubella vaccines that are usually given together. Two groups in India are working on live attenuated coronavirus vaccines, but experimental vaccines of this kind have a higher risk of giving people covid-19, so it will be a while before human trials are ready to begin.

So far, the 10 experimental coronavirus vaccines that have been tested in people appear safe, based on the preliminary announcements from several teams, the fact that none of the trials have been stopped by regulators yet and one published peer-reviewed study (The Lancet, doi.org/dwj).
Volunteers, to speed up the trial process. Such “human challenge” trials would be controversial because we have no effective treatments for covid-19 yet. If the experimental vaccine doesn’t work, volunteers could die.

Advocates of the idea, such as bioethicist Nir Eyal at Rutgers University in New Jersey, argue that such trials are acceptable if they involve young volunteers with no known health conditions who have a high risk of getting coronavirus. For the average person in their twenties, the risk of dying from covid-19 is less than 1 in 3000. The idea seems to be gaining momentum, with more than 26,000 people worldwide volunteering via the website 1daysooner.org, but it remains to be seen if any country will allow such trials. “At this point, I would put it only a bit over 50-50 in favour of challenge trials,” says Eyal.

Such trials wouldn’t reveal whether an experimental vaccine protects the most vulnerable, however. And if you want to know whether immunity lasts for, say, a year, a trial would have to take at least that long.

Even if trials do find effective vaccines, the immense challenge of making enough doses for up to 7 billion people will be a big bottleneck. This is true even for those vaccines for which manufacturing capacity is already being created before it is even clear if they work.

No one can predict how quickly a vaccine could be made. Some kinds are much harder to manufacture than others, says Altmann, and there can be unexpected hiccups that hold up production. For instance, there is currently a global shortage of the glass vials used to store vaccine doses.

When the coronavirus pandemic began, the UK scrambled to get more ventilators for use in intensive care. But now some doctors are trying to keep people off ventilators, as they believe it makes some people with covid-19 worse – although we don’t have the results of studies to assess this yet.

Ventilators are used to treat people with covid-19 who have difficulty breathing on their own, but the procedure is invasive and can even be traumatic. Doctors have other, less invasive, options, including giving patients oxygen by face masks or nasal cannulas, two tubes that sit just inside the nostrils.

Those with severe infection may need to be put on a ventilator, which usually requires a patient to be unconscious so a tube can be put down their throat. But this carries risks, and recovery can take weeks or even months.

Initially, people taken to hospital with breathing difficulties due to covid-19 were quickly being put on ventilators. This was partly because of anecdotal reports from China that people given face masks and nasal cannulas often deteriorate and need ventilation anyway, says Stephen Brett at Imperial College London.

As doctors have gained more experience with covid-19, some now argue against being too quick to ventilate. One factor has been the high death rate in covid-19 patients put on ventilators, which has been more than 50 per cent in the UK.

“There’s a belief among some that some people can be supported non-invasively”

“The success rate reported from Italy and New York was very low,” says Michael O’Connor, who heads critical care at the University of Chicago Medicine. He believes, based on the patients he has treated, that the high air pressures used in ventilation could be worsening lung damage.

Concerns are also lessening that face masks and nasal cannulas spread infections. It had been thought that they blow more virus into the air than ventilators. “People are now feeling that the cross-infection risk is manageable,” says Brett. “There’s a belief among some that there’s a population of people who can be supported non-invasively, but there are some institutions that remain sceptical.”

There are no figures on which approach is being used the most, but ongoing trials should answer the question, says Matt Morgan at the University Hospital of Wales in Cardiff.

“Should we use [ventilation] only at the very end, when the patient is about to stop breathing, or intervene earlier? You don’t want to do it in the heat of the moment. Until we have trial results we do not know what the best thing to do is.”

Earlier this year, there was concern over how the UK could source more ventilators. The UK had about seven intensive care beds per 100,000 people, compared with 12 for Italy and France, and 30 in Germany.

The UK government told ventilator manufacturers to increase production and placed a provisional order for 10,000 machines from the firm Dyson. This has since been shelved as demand for ventilators has been less than initially predicted.

Hospitals in the UK raised their intensive care capacity by cancelling non-urgent surgery and using ventilators from operating theatres, and some extra machines have been bought from abroad.

Brett says some of the manufacturers’ new, simpler designs may be useful for low-income countries. “There has been some very useful engineering done,” he says.

Part of a ventilator at a site focused on increasing production.