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Beating severe covid-19

We are beginning to understand how the virus kills - and how to stop it

Clare Wilson

DEXAMETHASONE has become the first drug shown to lower the death rate from covid-19. The discovery of the benefits of this widely available steroid, which damps down an overactive immune system, was seen as a much-needed piece of good news. But we will need lots of other treatments to help us turn the tide of severe covid-19.

Many of the coronavirus drug trials so far have looked at antiviral medicines that may stop the virus from replicating. While some of these appear to shorten the length of time that an infected person is ill, none has yet been shown to reduce mortality. To save the lives of those who are seriously ill, we need treatments that tackle the effects of severe covid-19, which occur after the virus has already replicated within the body.

Evidence suggests that the virus kills through a two-pronged attack that perturbs both our immune defences and our blood-clotting system. Covid-19 was initially seen as a respiratory illness, but some of those who die from it experience not only lung failure but also heart attacks, strokes, kidney damage and other conditions caused by blood clots.

The good news is that several existing and novel treatments to fight both of those impacts are being investigated and some are already in use. “We think we know the mechanisms for how it [kills],” says Chris Meadows, an intensive care doctor at Guy’s and St Thomas’ hospitals trust in London. “Treatment is now directed against those mechanisms, largely towards reducing inflammation and clots. I think we are pretty close to working it all out.”

The coronavirus enters our body through cells lining the nose or mouth by latching on to a molecule on their surface called the ACE2 receptor. In some people, the virus spreads down into the lungs, where cells also bear the ACE2 receptor. Here it causes inflammation and leakage of fluid into the lung’s air sacs, interfering with breathing. This can lead a person’s oxygen levels to fall and mean they require treatment with supplementary oxygen or a ventilator. But even with intensive support, death rates for covid-19 patients receiving ventilation have been relatively high.

From early in the outbreak, doctors suspected that part of the problem was in how the immune system reacts to the virus. Normally, our immune cells fight off viruses or bacteria, but in some cases they overreact, pumping out too many cytokines – chemicals that recruit yet more immune cells in a vicious circle known as a cytokine storm. “There is fluid and inflammatory cells flooding into where air should be,” says Meadows. “This is like having a raging fire within the lungs.”

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Clotting in the body is normally tightly controlled to ensure that blood flows freely through our blood vessels, yet the slightest injury triggers a cascade of chemical reactions that turns this fluid into a plug. Cytokine storms were already known to predispose people to clots somewhat, but with covid-19, this was taken to a new level. Doctors saw clots in people’s lungs on scans and could even see clots forming as they tried to put tubes into people’s veins. “People were saying something odd is going on,” says Danny Jonigk at Hannover Medical School in Germany.

As well as these visible clots, autopsies have found small blood vessels in the lungs suffused with smaller clots. These were 10 times as common in seven people who died from covid-19 as in seven who died from bird flu, according to a study published last month (NEJM, doi.org/ggwtrb). “This is a disease that targets blood vessels,” says Jonigk, who worked on the study.

The finding is good news, but isn’t enough on its own. Other groups are looking for ways to tackle the way covid-19 leads to unwanted blood clotting – and there is hope that existing blood-thinning medicines could help.

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Dexamethasone and heparin are being tested for treating covid-19
Should I get an antibody test?

Antibody testing can reveal if you have had covid-19. Michael Le Page asks if it is worth paying for a test

TESTS for coronavirus antibodies vary in accuracy and may not be useful for everyone. Here’s what you need to know.

What can a coronavirus test tell me?
There are two main kinds of tests. One looks for the virus in nose or throat swabs, which can reveal if you are currently infected. In many countries, tests for active infections are free, so there is no need to pay.

The other type looks in your blood for the antibodies your immune system makes to attack the coronavirus. This can reveal if you were infected but have since recovered. It can take several weeks to produce antibodies, so there is little point in doing antibody tests during or soon after an illness you suspect could be covid-19.

Can an antibody test tell me if I’m immune to the coronavirus?
No. “A positive result may not mean a person is immune,” says the UK’s Medicines and Healthcare products Regulatory Agency (MHRA). People who have recovered should be immune for a while, but we don’t know how long immunity lasts yet. With other coronaviruses, studies show people can be reinfected as soon as six months after the initial infection.

What use are antibody tests?
For policy-makers, it is useful to know what percentage of people have been infected. But until we find out more about immunity to coronavirus, antibody tests are less useful for individuals.

You shouldn’t alter your behaviour based on a positive antibody test. You risk getting infected again, or infecting others. Plus, your test results might not be correct.

How do I get an antibody test?
In the UK, your only option is to have a blood sample taken by a qualified healthcare worker and then sent off for testing. Some private doctors and clinics will send someone to your home to take the sample.

Aren’t there home testing kits?
The antibody tests designed to be done at home haven’t proved reliable so far. In the UK, it is illegal to sell them but some companies still do. “We strongly discourage organisations and individuals from purchasing unvalidated antibody tests,” says a UK Department of Health and Social Care spokesperson.

Can I take a blood sample myself?
Some companies were sending out self-testing kits that use a drop of blood from a finger prick. However, on 29 May, the MHRA ordered companies to stop until it has been shown that antibody tests work with blood samples taken this way.

Which antibody test is best?
So far, 219 antibody tests have been evaluated in the UK and the rest of Europe. But that doesn’t mean there has been independent validation of these tests. “There’s no scrutiny,” says Jon Deeks at the University of Birmingham, UK. What’s more, he says many clinics offering antibody tests don’t reveal which specific test they use. Many countries, including the US and Australia, have stricter regulations.

Do we know how accurate any of the tests are?
Public Health England has evaluated five tests developed by Roche, Abbott, Euroimmun, DiaSorin and Ortho Clinical. These tests have a sensitivity of around 70 per cent or higher after about 14 days of infection, meaning 30 per cent or fewer results are false negatives and wrongly identified as not having the virus. The tests have a specificity of about 98 per cent or more – so less than 2 per cent of results are false positives.

If I get a positive test result, how sure can I be that it is correct?
This depends on your likelihood of having been infected, says Babak Javid at Tsinghua University in China. If you live in London and recently had a severe respiratory infection, a positive result is likely to be correct. But if you have been shielding in Cornwall with no symptoms, it could well be wrong, says Javid.