Long Covid: Are pockets of Covid in the gut causing long-term symptoms?

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Scientists are investigating whether reservoirs of virus 'hiding' in the body are contributing to long Covid

Since the early days of the pandemic it has been clear some people shed genetic material from the virus in their stools for months after catching Covid-19. The findings were initially regarded as a curiosity, but there is mounting evidence to support the idea that persistent pockets of coronavirus – in the gut, or elsewhere – may be contributing to long Covid.

Earlier this month, Prof David R Walt and colleagues at Harvard Medical School announced that they had detected Sars-CoV-2 proteins – most commonly the viral spike protein – in the blood of 65% of the long Covid patients they tested, up to 12 months after they were first diagnosed.

Though small and preliminary, the study provides some of the most compelling evidence yet for the idea that reservoirs of the virus could be contributing to people's long-term ill health. "The half-life of spike protein in the body is pretty short, so its presence indicates that there must be some kind of active viral reservoir," Walt said.

Spike protein wasn't detected in the blood of Covid patients who didn't have ongoing symptoms.

Walt was motivated to carry out the study after earlier research by his colleagues detected genetic material from the Covid virus (viral RNA) in stool samples from children with multisystem inflammatory syndrome (a rare but serious condition that often strikes around four weeks after catching Covid) as well as spike protein and a marker of gut leakiness in their blood. Treating them with a drug that reduced intestinal permeability led to rapid clearance of the spike protein and an improvement in their symptoms. Walt's working hypothesis is that something similar may be happening in people with long Covid.

If other groups could replicate Walt's findings, it would be "pretty much game over" for the idea that pockets of the virus were not still present in at least some long Covid patients, said Dr Amy Proal, a microbiologist at the PolyBio Research Foundation, a US nonprofit that supports research into complex chronic inflammatory conditions: "I don't personally see a mechanism by which the spike protein would be able to persist over long periods of time without the virus [being present]."

Other groups have also found evidence of the virus continuing to be present – called "viral persistence" – in patients who have recovered from Covid. In April, Ami Bhatt, of Stanford University in California, and colleagues reported that about 13% of individuals were still shedding viral RNA in their stools four months after catching Covid, and nearly 4% continued to do so at seven months. These people also often reported ongoing gastrointestinal symptoms such as nausea, vomiting and abdominal pain.

"The question is whether or not continued presence of the virus in the gut or elsewhere may kind of

tickle the immune system, and cause there to be persistent symptoms," Bhatt said.

Separate research, which analysed gut tissue from 46 people with inflammatory bowel disease who had recovered from mild Covid, found that viral RNA or proteins could still be detected in 70% of them seven months later. Roughly two-thirds of these individuals reported continuing symptoms such as fatigue or memory issues – whereas none of those without detectable virus did.

Yet other preliminary research has recovered virus – in some cases replicating virus – from other anatomical sites including the eyes, brain and heart many months after people became infected.

Viral persistence is also seen in other illnesses, such as Ebola, where the virus hides out in "anatomical sanctuaries" such as the eyeball or testicles that are less accessible to the immune system – and which are thought to contribute to ongoing symptoms such as joint and muscle pain, or fatigue, in many survivors.

Even so, definitive proof that viral reservoirs contribute to long Covid is still lacking, and Bhatt would like to see further studies done before reaching this conclusion.

Some of these are already taking place. For instance, the US National Institutes of Health's Recover study is searching for signs of coronavirus in stool samples and intestinal tissue from people with long Covid. "These types of studies will be critical for starting to tease apart what the relationship between long-term viral reservoirs and long Covid might be," Bhatt said.

If viral persistence really is driving at least a subset of people's symptoms, it could also spur the investigation into antiviral drugs as a treatment for long Covid. Although this may sound like a no-brainer, some virologists are concerned about the implications of doing so.

"The idea of giving people long-term antiviral monotherapy to try and clear the virus is a pretty contentious issue because, given how much adaptation of the virus we see even in short periods of time, the possibility of the virus escaping is extremely high," said Dr Deepti Gurdasani, a clinical epidemiologist at Queen Mary University, London. "I think we really need to start thinking about dual or triple therapies, and trialling them, because we can't really afford to create more escape mutants at this point in time."

Whether it's scrutiny of tissue samples, or trials of antivirals, for those who have been living with long Covid, some for upwards of two years, such studies can't come fast enough.

Linda Geddes Science correspondent

P.S.

• The Guardian. Tue 28 Jun 2022 18.09 BST:
https://www.theguardian.com/society/2022/jun/28/are-pockets-of-covid-in-the-gut-causing-long-term-symptoms

• *Linda Geddes's articles in The Guardian:*
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