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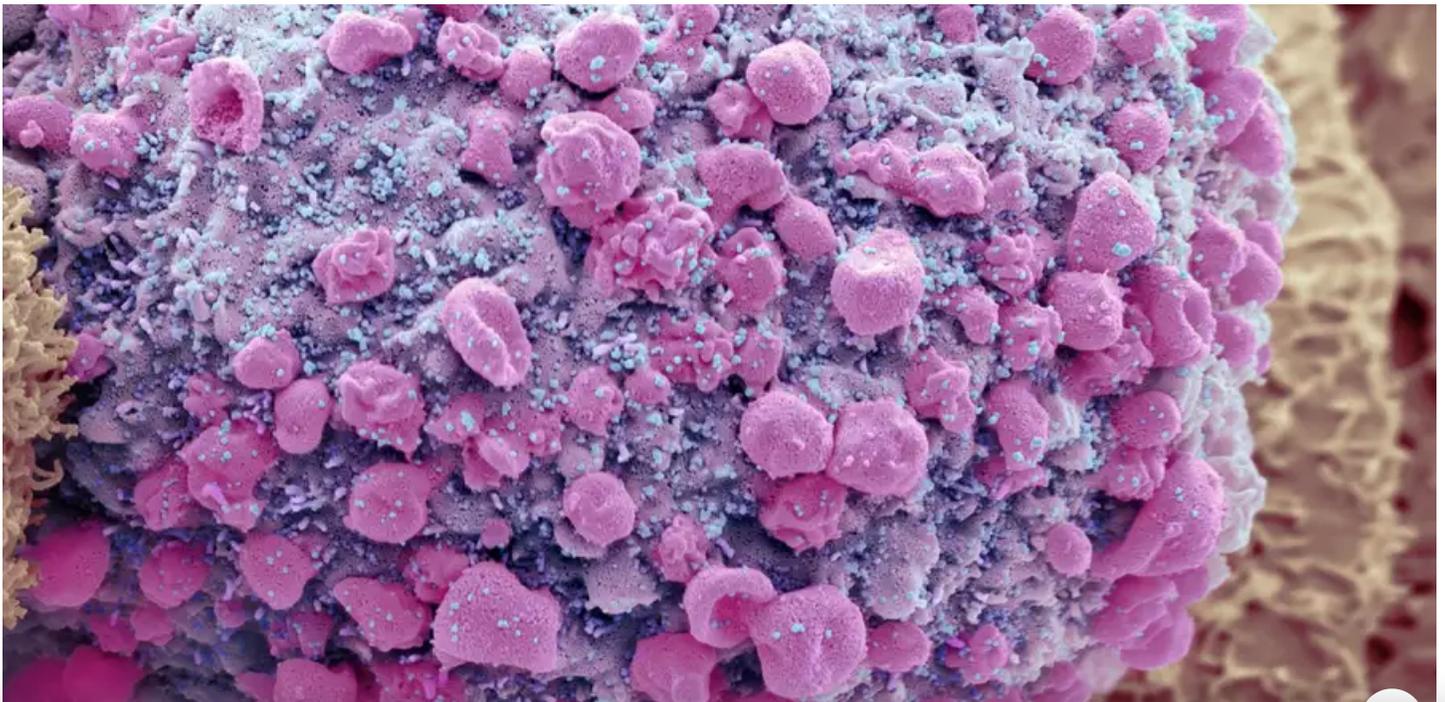
Health

The covid-19 virus affects our gut – but we still don't know how

The coronavirus commonly causes gastrointestinal symptoms, but whether this is due to inflammation, disruption to our microbiome or the virus affecting the permeability of our gut wall is unclear

By [Michael Marshall](#)

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▲ A scanning electron micrograph of the delta SARS-CoV-2 variant (blue dots) budding from a human gut cell

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As the first wave of cases of the coronavirus swept the world in early 2020, gastroenterologist [Siew Ng](#) at the Chinese University of Hong Kong was expecting the impact of the virus to extend beyond the body's airways. She and her colleagues vividly remembered the SARS coronavirus outbreak of 2003, giving them some notion of what to expect from SARS-CoV-2. In particular, they anticipated that many people would develop gut problems.

As these early cases emerged, Ng and her team started collecting stool samples. At the start of the outbreak, everyone in Hong Kong who tested positive for the [coronavirus](#) had to go to hospital, regardless of the severity of their symptoms, says Ng. As a result, the team's collection soon ran to hundreds of samples, providing some of the first evidence that the infection can disrupt [gut](#) function.

In some cases, this disruption was linked to an increased risk of [death](#) or chronic complications. However, despite an ever-growing mountain of evidence, it is unclear what the [virus](#) does to the gut, which makes developing effective treatments all the more difficult.

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The primary challenge with understanding the impact that SARS-CoV-2 can have on the gut is that multiple systems interact in our gastrointestinal tract. For instance, the walls

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Nevertheless, it is clear that gastrointestinal problems can be a big part of the coronavirus's symptoms. [Up to 1 in 5 people present with gut-related symptoms](#), the most common being diarrhoea, abdominal [pain](#), loss of appetite and nausea, sometimes with vomiting. For some, these symptoms last months. [A 2021 study found that 16 per cent of people reported at least one gastrointestinal symptom more than 100 days after being hospitalised for covid-19, the condition caused by SARS-CoV-2.](#)

What this means for a person's prognosis isn't entirely clear. [A 2022 review pulled together 53 studies](#) covering more than 55,000 people with the coronavirus and found that gastrointestinal symptoms weren't associated with a higher risk of [death](#).

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However, a different picture emerges from studies that focused specifically on disruption to the gut [microbiome, suggesting that this may be linked to an increased risk of death from covid-19](#). The stool samples that Ng and her team examined revealed that [many helpful "commensal" bacteria can become depleted](#) when people are infected with the coronavirus, while harmful ones become more populous. The fungi in the gut – the mycobiome – [have shown similar disruptions](#). Crucially, [those with more severe illness tended to have more disrupted microbiomes](#), mimicking the results of [other studies](#).

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[We're starting to understand how viruses trigger chronic conditions](#)

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This helps explain why SARS-CoV-2 is so good at disrupting the gut, where its impact is “bigger than what we see in influenza and malaria”, says Ng.

But picking out what is happening in the guts of people with the coronavirus remains tricky. “When you look at the evidence, there are a lot of knowledge gaps,” says [Laure-Alix Clerbaux](#) at the European Commission’s Joint Research Centre in Ispra, Italy. She is one of the coordinators of the [CIAO project](#), which is attempting to trace the sequences of mechanisms that take place in people with covid-19 and [has revealed some peculiarities](#).

“There’s a lot of receptors for the virus in the gut and there’s disorder in the gut,” says Clerbaux. At first glance, this implies that the virus is infecting gut cells and replicating, but that may not be the case. “We could not find a body of evidence, or the body of evidence was weak, that there is this active replication of the virus,” she says. Nor is there much evidence that SARS-CoV-2 can infect the [bacteria](#) in the gut.

“We propose a different pathway,” says Clerbaux. If the virus is binding to the ACE2 receptor, that could disrupt nutrient uptake by the gut because ACE2 has a role in the uptake of tryptophan, an essential amino acid. “Clearly this could be a really interesting mechanism, because we could have also a therapeutic target there,” says Clerbaux.

Other lines of evidence suggest that gut microbiota are crucial to SARS-CoV-2’s potential gastrointestinal impact, even if the microbes aren’t being infected themselves. [In a small study published in 2022](#), Ng and her colleagues gave 25 people with a non-critical SARS-CoV-2 infection a mix of helpful gut bacteria and carbohydrates, which they took every day for 28 days alongside other treatments. Compared with 30 infected people who didn’t get the mixture, those who did were quicker to develop antibodies against the virus.

Inflammatory markers in their blood also fell sooner and any disruption to their gut microbiome resolved faster. This suggests that treating the harms caused to the gut microbiota can help to resolve the infection, says Ng.

Unfortunately, gastrointestinal disturbances can persist for many weeks or longer. Gastric distress of some form can be a symptom that affects people with [long covid](#), a post-infection condition that sometimes lasts years.

Mexico in Mexico City. In 2021, he and his colleagues [published a study](#) pushing for gastroenterologists to manage the “inevitable surge of post-covid-19 functional gastrointestinal disorders”.

Again, direct viral infection may not be to blame. [A 2022 study](#) found viral genetic material in the guts of people with long covid, but the researchers couldn't grow viruses from the samples. “There are these viral particles that are non-viable but are still in there,” says Schmulson. “What are they doing there? Are they producing some kind of inflammation? Are they stimulating the nervous endings? Are they impacting in the flora in the microbiota? Are they having some impact on the permeability [of the gut wall]? We don't know.”

This difficulty in elucidating the mechanisms of lasting gastrointestinal symptoms makes it harder to design treatments. Some researchers have proposed giving people probiotics to restore their gut flora. “There are many studies coming out with probiotics, but they don't have great evidence,” says Schmulson.

Another suggestion that has been mooted is faecal transplantation – transferring bacteria via a processed stool from a healthy donor to another person's intestine, with the aim of restoring their potentially disrupted microbiome. There is evidence that it treats certain gastrointestinal symptoms and it is already approved in many countries for recurrent *Clostridium difficile* infection. However, Schmulson says there isn't evidence yet that this helps people with long covid.

Ng and her colleagues are experimenting with probiotics and faecal transplants in clinical trials, but the going is slow – partly because treatments that work for some people don't work for others and it isn't clear why.

All this means that when it comes to the impact SARS-CoV-2 can have on the gut, and how best to treat it, “the evidence is still in [its] infancy”, says Ng. “There just aren't enough clinical trials.”

Article amended on 3 May 2023

The picture caption in this article has been changed to correct which colours in the micrograph represent SARS-CoV-2

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