A social and medical examination of Long COVID as a “mass disabling event”: Part 2

Frank Gaglioti
4 April 2023

This is the second of a multi-part series on Long COVID. Part one can be read here, part three here, and part four here.

Possible causes of Long COVID

Four possible theories of the causes of Long COVID have emerged, but it must be emphasized that this work remains at an early stage.

Danny Altmann, an immunologist at the Imperial College London, told *Nature* last August, “If you look at long COVID at this moment in time, I’d paint a slightly ‘Wild West’ and desperate picture really.” He added that “we’ve now got little scattered bits of evidence. We’re all scuttling to try and put it together in some kind of consensus. We’re so far away from that. It’s very unsatisfying.”

Given that Long COVID has approximately 200 symptoms and is known to attack every system in the human body, some researchers think the condition may turn out to be a number of syndromes.

Jennifer Couzin-Frankel, a staff writer on biomedical and clinical research for the journal *Science*, explained the complex process of Long COVID research in an article last June:

> For each of these researchers—and many others exploring the causes of Long Covid—untangling the complex syndrome, with a still-evolving definition, is a laborious, step-wise process. First, they must show that a possible contributor—such as minuscule clots, lingering virus, or immune abnormalities—crops up disproportionately in people with Long Covid. Then comes the hard part: proving that each of these traits, alone or in combination, explains why the coronavirus has rendered millions of people shadows of their former selves.

Without an understanding of the cause of the condition, there is little chance of developing effective treatments. The current research so far is dealing with a moving target, but some insights have been gleaned.

There are four theories for the possible causes of Long COVID: microclots in blood, immune dysfunction, the persistence of the virus over a long period and dysbiosis of the gut microbiome (disruption to the gut’s normal micro-organisms). Studies are in their very early stages, and other factors will most likely emerge in the future after further research.

Speaking at an online forum last August hosted by *Knowable Magazine*, Akiko Iwasaki, a Long COVID advocate, immunologist and professor of immunobiology at Yale School of Medicine, explained that the four causes “are not mutually exclusive. People can have a combination of these things too.”

Persistent virus

Evidence is emerging that the SARS-CoV-2 virus persists and continues to replicate in the body long after the initial infection.

A study published last December by investigator Daniel S. Chertow and his team at the Critical Care Medicine Department of the University of California found virus in brain, muscle, gut and lung tissue. They found evidence that the virus was replicating.

A number of studies have shown that bits of the SARS-CoV-2 virus can persist in the gut. In an article published last May in *Nature*, oncologist and geneticist Ami Bhatt of Stanford Medicine referred to the persistent bits of virus as “ghosts.”

Between 11-18 percent of people hospitalized with COVID-19 have experienced gastrointestinal (GI) symptoms such as nausea, vomiting and diarrhea. A paper published last April by senior research scientist at the Department of Genetics at Stanford University Aravind Natarajan and his team reported that “gastrointestinal symptoms and fecal shedding suggests prolonged gastrointestinal infection” and that there was persistent evidence of SARS-CoV-2 RNA in the GI tract.

The paper stated:

> Furthermore, prolonged presence of SARS-CoV-2 in the GI tissue may also have an impact on the hitherto mysterious phenomenon of post-acute sequelae of SARS-CoV-2 infection (PASC) or “Long COVID,” where individuals suffer from an unusual constellation of symptoms even after recovery from the respiratory SARS-CoV-2 infection. Taken together, it is critical that we understand whether or not the GI tract is infected and the dynamics of the infection in this tissue, from the standpoint of both the acute infection and the long-term sequelae of COVID-19.

Research published last May by gastroenterologist Herbert Tilg and his team at the Medical University of Innsbruck examined 46 people who had a COVID-19 infection an average of 219 days prior to endoscopy, 21 of whom were experiencing at least one Long COVID symptom. They found that 70 percent of the patients had the presence of SARS-CoV-2 by polymerase chain reaction and 31 percent had detectable viral RNA in their biopsy specimen.

The authors stated:

> We provide evidence for SARS-CoV-2 antigen persistence in the gut as a basis for immune perturbation in postacute COVID-19. Whether viral antigen persistence (in and beyond the gut) underlies the pathophysiology of post-acute COVID-19 warrants further

clinical trials to tackle this rapidly emerging disorder across the globe.

"Our paper is a clinical observation and doesn't prove that lingering virus is harming people," Tilg commented to *Science.*

Microclots

The microclot theory has been led by Etheresia Pretorius, a physiologist at Stellenbosch University in South Africa, and Douglas Kell, a systems biologist at the University of Liverpool. Supporters of the microclot theory have promoted it through the #teamclots hashtag on Twitter.

Pretorius and Kell brought forward their prior work on clotting disorders after the COVID-19 pandemic hit in 2020. "We thought to look at clotting in COVID, because that is what we do," Pretorius told *Nature*.

Pretorius and Kell examined fibrin, a protein associated with clotting, comparing people recently infected with COVID-19, Long COVID sufferers, and a non-infected cohort as a control. They found that there was more clotting than they had previously discovered in other inflammatory diseases such as diabetes.

Another study led by Pretorius published last August in the journal *Cardiovascular Diabetology* examined blood from 80 patients on a Long COVID register in South Africa. The study found evidence of microclotting in all the blood samples, along with extremely high levels of activation of platelets (blood components that control clotting).

The study noted, "Together with platelet pathology and the presence of microclots in the circulation, endothelial damage may be key drivers of persistent Long COVID/PASC symptoms."

A comment by Pretorius published in *The Guardian* in January 2022 stated:

> The presence of persistent microclots and hyperactivated platelets (also involved in clotting) perpetuates coagulation and vascular pathology, resulting in cells not getting enough oxygen in the tissues to sustain bodily functions (known as cellular hypoxia). Widespread hypoxia may be central to the numerous reported debilitating symptoms.

It is not clear what activates the formation of microclots. Pretorius and Kell think that the spike protein, used by the virus to gain access to the host cell, may stimulate the formation of microclots. A study conducted by Pretorius and Kell demonstrated that the addition of the SARS-CoV-2 spike protein to blood induced clotting.

A paper published in *Bioscience Reports* by researcher Lize M. Grobbelaar at the Department of Physiological Sciences at Stellenbosch University stated:

> [We] provide evidence that spike protein does indeed play a major role in hypercoagulability (hyperclotting) seen in COVID-19 patients. It causes anomalous clotting in both purified fluorescent fibrinogen (blood plasma protein) and in PPP (platelet-poor plasma) from healthy individuals, where the nature of the clots were shown to be amyloid (aggregate of proteins associated with various diseases).

Researchers have pointed to possible treatments. Pretorius and Kell report the treatment of Long COVID patients with a combination of two antiplatelet therapies and an anticoagulant can provide relief from symptoms for some patients. These treatments must be accompanied with careful monitoring, as they can cause excessive bleeding. Apheresis, a process similar to dialysis, has been used to filter the blood, with some promising results.

The microclot theory has drawn criticism, as it is based on relatively small studies. Other researchers have failed to detect microclots following COVID-19 infection.

Alex Spyropoulos, a haematologist at the Feinstein Institutes for Medical Research in New York, told *Nature* that the microclot hypothesis presents "a very elegant mechanism" but that much more work is needed to tie the lab markers to clinical symptoms. "What's a little bit disturbing is that these authors and others make huge leaps of faith," Spyropoulos said.

Immune system gone haywire

Another leading theory on Long COVID is that the immune system is overactivated, attacking healthy proteins, due to the persistence of SARS-CoV-2 RNA lingering in the body.

In a comment in the *Los Angeles Times* last August, Eric Topol noted the following immunological processes that could explain Long COVID:

> Antibodies attacking the body's own proteins; persistent antibodies to the virus' spike protein, indicating a reservoir of infection triggering a response; exhausted T-cells (immune system cells that attack foreign particles); and markers of reactivation of prior virus infections in the herpes virus family (Epstein-Barr (Herpes virus) and varicella-zoster (chicken pox virus)).

Early in the pandemic, scientists noted that harmful inflammation—the so-called cytokine storm—was likely attributable to an agitated immune system that could result in tissue damage and death.

Last August, immunologist Matthew Woodruff and his team at Emory University published a research paper in the journal *Nature* which found that some patients developed antibodies to fight their COVID-19 infection which in turn also attacked body tissues and organs.

Woodruff stated, "We also show that self-directed antibodies can persist for months or even years in those suffering from Long COVID-19."

The process through which the immune system turns on its own body's tissues is very complex. Under normal circumstances, when a pathogen enters the body, B cells are produced that are known as naïve. These cells have to undergo a program where they learn to identify and attack a specific invader, a process that can take up to a fortnight. In the case of severe infection, this process can break down so that the antibodies attack the body itself. The work of Woodruff and others shows that these aberrant antibodies can persist for months.

Woodruff commented, "What's more, in work currently under development and not yet peer-reviewed, we find that these responses are not restricted to those recovering from severe illness and are readily identifiable in a large subset of Long COVID-19 patients who had recovered from more mild illness as well."

One of the first and most consistent scientists to sound the alarm about COVID-19 causing damage to the immune system is T-cell immunologist Dr. Anthony Leonardi, who conducted two extensive interviews with the

WSWS on these and other topics related to the pandemic in November and December 2021.

Dysbiosis of microbiome or disruption of gut micro-organisms

Trillions of microbes live in the human gut and are responsible for contributing to overall health. The gut is known to harbor bacteria, virus, fungi and archaea (organisms roughly similar to bacteria).

Under normal conditions, the microbiome lives in harmony with its human host. According to a June 2021 article published in *Frontiers in Microbiology* by microbiologist Amy D. Proal of the PolyBio Research Foundation, "Under conditions of health, these host microbiome/virome communities are kept 'in check' by a robust host immune response, and persist in a state of balance or homeostasis."

It has been postulated that a SARS-CoV-2 infection can disrupt the microbiome, causing dormant pathogens to reactivate.

"It's also possible that there are latent viruses that are reactivated to cause some of these symptoms such as the Epstein-Barr virus," Ikiko Iwasaki told *Knowable Magazine*. Epstein-Barr is a herpes virus thought to cause chronic fatigue syndrome.

An opinion piece by researchers Kai Hilpert and Ralf Mikut published in September 2021 in *Frontiers in Microbiology* reviewed the current literature demonstrating the impact of SARS-CoV-2 on the gut microbiome.

The authors stated, "These changes can be caused by an infection directly in the gut, as a response to increased inflammation and crosstalk between the oral, lung, and gut microbiome." They went on to observe that "some of the symptoms described in chronic COVID-19 syndrome (CCS), like fatigue, sleep disturbance, joint pain, anxiety/depression, headache, and diarrhea, have also been correlated with a dysbiosis of the gut microbiome."

Importantly, they show that the gastrointestinal tract is central in achieving an immune system homeostasis and that dysbiosis drives inflammation and fuels long-term symptoms.

Cures and treatments

Given that scientists do not fully understand the cause of Long COVID, no cure yet exists for the condition. However, a number of treatments have been developed, which so far are not scientifically proven and can be considered an ad hoc approach based on treating the myriad of Long COVID symptoms.

A review of treatments by researcher Ho Cheng Koc and her team at the Centre of Reproduction, Development and Aging of the University of Macau stated, "Although several guidelines on Long COVID management have been released, there remains a large practical gap. … In general, current clinical practice adopted a symptom-based approach in managing Long COVID."

Scientists have suggested a number of possible treatments which require further study. For persistent virus, the use of antivirals such as Paxlovid or Molnupiravir could effectively target the virus. If Long COVID is an autoimmune disorder, then immunosuppressives could potentially be used. Dysbiosis of the microbiome could possibly be treated by diet or probiotics.

Antihistamines have been used to treat the inflammatory effects of Long COVID, and dietary supplements such as vitamins and minerals have been used as anti-inflammatories. Antibody treatments have been studied, including Infliximab, Tocilizumab, Siltuximab, Anakinra and Leronlimab, with mixed results.

With future research, the understanding may emerge that Long COVID is an umbrella term covering several conditions. Physician and heart disease researcher Chahinda Ghossein of Maastricht University commented that "the biggest obstacle that we are facing is we gave it one name, we gave it the name of Long Covid, which implies that it is one disease. … All the studies being performed show us that it is not."

The research is at a very early stage and other issues may emerge in a longer time frame, but clearly further research is crucial in order to clarify the causes of Long COVID. While paying lip service to the necessity for such research, the capitalist ruling elites internationally have limited or denied the funding necessary for this work to proceed.

The Brookings Institute report cited above noted that the US government has allocated just $1.15 billion to study the disease, concluding "overall, the government's record on supporting such work is poor." It added, "as of 2021, the NIH had budgeted less than $20 million annually for research on ME/CFS, another post-viral illness."

The $1.15 billion allotted to the NIH (National Institutes of Health) in December 2020 to study Long COVID is just 2.5 percent of the agency's $45 billion annual budget and just 0.1 percent of the Biden administration's unprecedented $1 trillion military budget request for the coming year. Furthermore, the Long COVID funding was a one-time, not annually recurring allocation.

In February, the British government set aside just £18.5 million for further funding into Long COVID, a miniscule amount considering the size and complexity of the problem.

In Australia, in the Albanese Labor government's first budget, nothing was allocated for research into Long COVID. This is despite the fact that in the past year alone tens if not hundreds of thousands of Australians have become afflicted with the condition after the government lifted all mitigation measures that slowed the spread of the virus.

The lack of research funding for Long COVID is part of the ruling elites' overall contempt for human life which has been on display continuously for the past three years of the pandemic. While allocating unlimited resources to their military machines, no resources are to be provided to alleviate the suffering of tens of millions of people globally.

The failure of governments to allocate the necessary funding for Long COVID research is bound up with their reckless program of simply covering up and ignoring the existence of the ongoing pandemic.

To be continued