U.S.

Doctors Begin to Crack Covid's Mysterious Long-Term Effects

Severe fatigue, memory lapses, heart problems affect patients who weren't that badly hit initially; 'It's been so long'

By Sarah Toy, Sumathi Reddy and Daniela Hernandez
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Nearly a year into the global coronavirus pandemic, scientists, doctors and patients are beginning to unlock a puzzling phenomenon: For many patients, including young ones who never required hospitalization, Covid-19 has a devastating second act.

Many are dealing with symptoms weeks or months after they were expected to recover, often with puzzling new complications that can affect the entire body—severe fatigue, cognitive issues and memory lapses, digestive problems, erratic heart rates, headaches, dizziness, fluctuating blood pressure, even hair loss.

What is surprising to doctors is that many such cases involve people whose original cases weren't the most serious, undermining the assumption that patients with mild Covid-19 recover within two weeks. Doctors call the condition "post-acute Covid" or "chronic Covid," and sufferers often refer to themselves as "long haulers" or "long-Covid" patients.

"Usually, the patients with bad disease are most likely to have persistent symptoms, but Covid doesn't work like that," said Trisha Greenhalgh, professor of primary care at the University of Oxford and the lead author of an August BMJ study that was among the first to define chronic Covid patients as those with symptoms lasting more than 12 weeks and spanning multiple organ systems.

For many such patients, she said, “the disease itself is not that bad,” but symptoms like memory lapses and rapid heart rate sometimes persist for months.

In October, the National Institutes of Health added a description of such cases to its Covid-19 treatment guidelines, saying doctors were reporting Covid-19-related long-term symptoms and disabilities in people with milder illness.

“You don’t realize how lucky you are with your health until you don’t have it,” said Elizabeth Moore, a 43-year-old lawyer and mother of three in Valparaiso, Ind. Pre-Covid-19 she was an avid skier and did boot-camp workouts several times a week. Since falling ill in March, she has been struggling with symptoms including memory problems and gastrointestinal issues. She has lost nearly 30 pounds.

Estimates about the percentage of Covid-19 patients who experience long-haul symptoms range widely. A recent survey of more than 4,000 Covid-19 patients found that about 10% of those age 18 to 49 still struggled with symptoms four weeks after becoming sick, that 4.5% of all ages had symptoms for more than eight weeks, and 2.3% had them for more than 12 weeks. The study, which hasn’t yet been peer reviewed, was performed using an app created by the health-science company Zoe in cooperation with King’s College London and Massachusetts General Hospital.

Another preliminary study looking mostly at nonhospitalized Covid patients found that about 25% still had at least one symptom after 90 days. A European study found about one-third of 1,837 nonhospitalized patients reported being dependent on a caregiver about three months after symptoms started.

With more than 46 million cases world-wide, even the lower estimates would translate into millions living with long-term, sometimes disabling conditions, increasing the urgency to study this patient population, researchers said. What they find could have implications for how clinicians define recovery and what therapies they prescribe, doctors said.

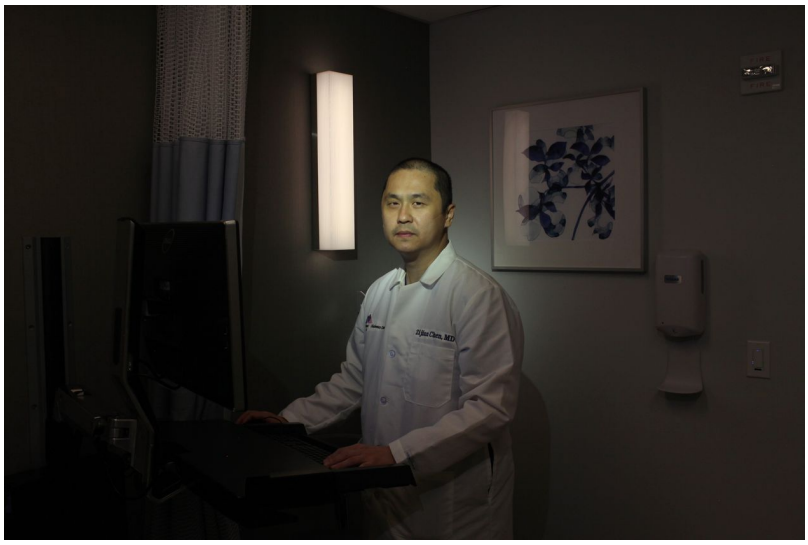
Doctors say anxiety caused by social isolation and uncertainty surrounding the pandemic may exacerbate symptoms, though that isn’t likely the primary cause.

Other viral outbreaks, including the original SARS, MERS, Ebola, H1N1 and the Spanish flu, have been associated with long-term symptoms. Scientists reported that some patients experienced fatigue, sleep problems and joint and muscle pain long after their

bodies cleared a virus, according to a recent review chronicling the long-term effects of viral infections.

What differentiates Covid-19 is the far-reaching nature of its effects. While it starts in the lungs, it often affects many other parts of the body, including the heart, kidneys and the digestive and nervous systems, doctors said.

“I haven’t really seen any other illness that affects so many different organ systems in as many different ways as Covid does,” said Zijian Chen, medical director for Mount Sinai Health System’s Center for Post-Covid Care.



Zijian Chen, director of Mount Sinai’s Center for Post-Covid Care, described colleagues who were energetic, but after getting sick, had trouble getting through the day.

PHOTO: JEHAD NGA FOR THE WALL STREET JOURNAL

He described colleagues who were energetic, but after getting sick, had trouble getting through the day. He said he has seen up close how Covid-19 still affects their ability to do the things they love.

“We thought it was a virus that, once it does what it does, you recover and you go back to normal,” he said. Sometimes that isn’t the case, and that “is really scary,” he said.

A leading explanation for long-Covid symptoms is that immune-system activity and ensuing inflammation continue to affect organs or the nervous system even after the virus is gone, researchers said.

Some of the most compelling evidence for the inflammation theory comes from Covid-19 patients with signs of heart inflammation and injury months after illness. One study looking at 100 Covid-19 patients two months after getting sick found that 78 had

abnormal findings on cardiac magnetic resonance imaging, while 60 had cardiac MRIs indicating heart-muscle inflammation. The study included hospitalized, nonhospitalized and asymptomatic patients.

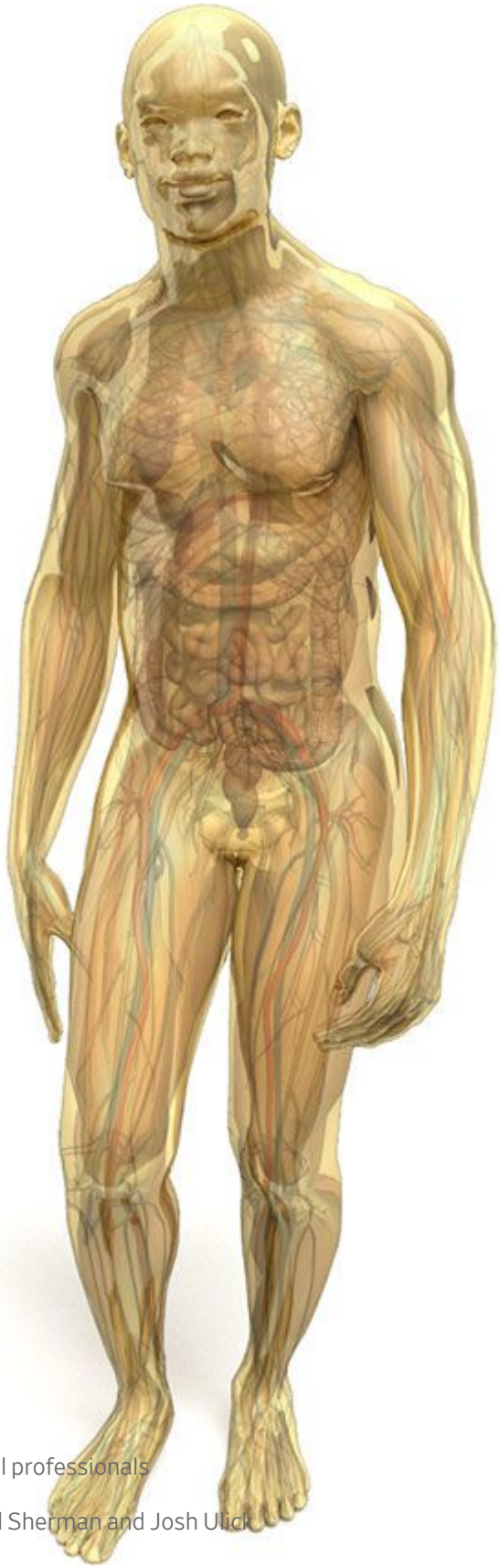
“Even those who had no symptoms and were young and fit…even in those patients we saw abnormalities,” said Eike Nagel, one of the lead authors and director of the Institute for Experimental and Translational Cardiovascular Imaging at the University Hospital Frankfurt in Germany.

Some patients had scarring on their heart imaging, he said, which worried him. The scarring wasn’t too serious, he said, but “we know from other studies that this is related to worse outcomes.”

A Persistent Multifront Attack

How chronic Covid-19 affects the body

Doctors also are reporting cases of long-Covid patients with gastrointestinal issues. Recent work has found the new coronavirus, known as SARS-CoV-2, in fecal matter and intestinal lining of some Covid-19 patients, suggesting the virus can infect and damage the cells of the gut. The intestines have a high density of ACE2 receptors, a type of protein on the surface of cells, which SARS-CoV-2 uses to infiltrate cells.



Nervous System

Many patients report issues with concentration and memory, sometimes referred to as “brain fog.” Some say they forget what they’re trying to say or do. Neurologists seeing such patients say cognitive problems are among the most common symptoms.

Some neurologists say they are seeing patients with signs of dysautonomia, or dysregulation of the autonomic nervous system. The autonomic nervous system regulates involuntary functions such as breathing, digestion and heart rate.

Source: medical professionals

Graphic: Merrill Sherman and Josh Ulick

Taste and Smell

Patients say it can take weeks or months to regain their senses of smell and taste. They say the loss of these senses affects not just their diet but their mental health.

Lungs

Some patients report persistent shortness of breath. Doctors often prescribe asthma inhalers and breathing exercises to help improve lung function. The exact cause is unknown. It could be related to aberrant nervous system function, lung injury or a compromised cardiovascular system.

Cardiovascular System

Many patients experience a racing heartbeat, or tachycardia, as well as extreme blood pressure changes. Some physicians think this could be related to an issue with the nervous system, particularly the autonomic arm, which deals with involuntary functions like heart rate and blood pressure.

Some patients have signs of heart-muscle inflammation weeks or months after infection, doctors and researchers say. In some cases, they don't report any symptoms, while others say they have shortness of breath and chest pain.

Digestive System

Patients report issues with abdominal pain and diarrhea weeks or months after coming down with Covid-19. Some physicians are recommending avoiding certain foods, such as dairy and gluten.

Musculoskeletal System

Some patients report mild muscle and joint aches. Others have more severe pain.

Many patients also report persistent fatigue weeks or months after coming down with Covid-19, even when they had a mild or moderate course of illness and didn't require hospitalization. The fatigue can be debilitating and get in the way of regular daily activities, like work and spending time with family.

The virus also might cause changes in gut bacteria, said Brennan Spiegel, a gastroenterologist and director of health services research at Cedars-Sinai Health System, who has had patients come in with abdominal pain and diarrhea weeks or months after coming down with Covid-19.

Ms. Moore, the Indiana lawyer, got Covid-19 in March and initially felt better by the end of April. "I thought I beat this thing. I was ecstatic," said Ms. Moore, who tested positive for coronavirus antibodies in May.

That month, her health took a sharp turn for the worse. She struggled with tachycardia, or a racing heartbeat, and blood-pressure fluctuations. Those symptoms improved, but she still has gastrointestinal problems. A recent test found stomach-lining inflammation. Pepcid, antihistamines and avoiding dairy products have provided some relief, but other symptoms such as memory deficits persist.

"I feel like there has to be some sort of next step," she said, "because I'm not ready to accept this as my new reality."

Ms. Moore, 43, pictured with her son, also has struggled with gastrointestinal problems. She has lost nearly 30 pounds.

PHOTO: TAYLOR GLASCOCK FOR THE WALL STREET JOURNAL

Ms. Moore tests her blood pressure many times a day while working from home in Valparaiso, Ind.

PHOTO: TAYLOR GLASCOCK FOR THE WALL STREET JOURNAL

She enrolled in a research study at the Neuro Covid-19 Clinic at Northwestern Medicine in Chicago, one of several clinics across the country aiming to find solutions for patients.

Some symptoms could be collateral damage from the body's immune response during the acute infection, researchers said. Some patients might harbor an undetectable reservoir of infectious virus or have bits of noninfectious virus in some cells that trigger an immune response, they said.

Another possibility is that the virus causes some people's immune systems to attack and damage their own organs and tissues, researchers said. A June study found roughly half of 29 hospitalized ICU patients with Covid-19 had one or more types of autoantibodies—antibodies that mistakenly target and attack a patient's own tissues or organs.

Doctors say some patients appear to be developing dysautonomia, or dysregulation of the autonomic nervous system, the part of the nervous system that regulates involuntary functions like breathing, digestion and heart rate, some researchers and doctors said.

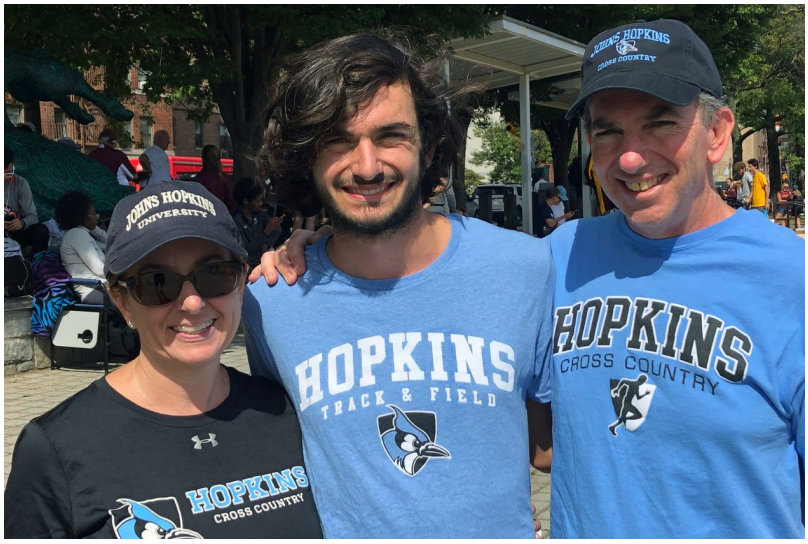
SHARE YOUR THOUGHTS

Have you suffered long-term Covid-19 effects? What are your symptoms? Join the discussion below.

David Putrino, director of rehabilitation innovation at Mount Sinai Health System in New York City, said the majority of the more than 300 long-Covid patients being seen at its Center for Post-Covid Care appear to have developed a dysautonomia-like condition. About 90% of such patients report having symptoms of exercise intolerance, fatigue and elevated heartbeats. About 40% to 50% also report symptoms such as gastrointestinal issues, headaches and shortness of breath.

Dr. Putrino said inflammation from the virus might be disrupting the normal functioning of the vagus nerve—the body's longest cranial nerve—which relays messages to the lungs, gut and heart.

As a member of the Johns Hopkins University varsity cross-country team, 19-year-old Christopher Wilhelm used to run 10 miles a day. Now, there are days he can't even walk a quarter mile with his mom around their Maitland, Fla., neighborhood without feeling wiped out.



Christopher Wilhelm, pictured with his parents, used to run 10 miles a day as a member of the John Hopkins varsity cross-country team. Now, short walks fatigue him.

PHOTO: WILHELM FAMILY

Mr. Wilhelm, who tested positive for Covid-19 in June, said his heart rate shoots up during those walks, ranging from 130 to 170 beats a minute. He was diagnosed recently with a form of dysautonomia characterized by fluctuations in blood pressure and heart rate when patients sit or stand up, a condition known as postural orthostatic tachycardia syndrome, or POTS. His doctors also are evaluating him for cardiac issues. Medications he has tried haven't yet helped his heart-rate spikes.

"After I tested positive, I was just expecting it to be two weeks of flulike symptoms, and then I'd pretty much be back to normal," he said. "It's been so long already, it's kind of daunting."

Six months after getting sick with Covid-19, Jennica Harris, 33, said she has persistent fatigue and problems with memory and concentration. She struggles to find simple words during conversations, often loses her train of thought and has developed a stutter.

Jennica Harris, shown with her children, has persistent fatigue and problems with memory and concentration.

PHOTO: HARRIS FAMILY

“I usually know what I want to say when I want to say it, and I usually don’t hold back,” she said. “When I try to get my point across and I can’t, that hurts my confidence, my sense of self.”

The constellation of such neurological symptoms, along with persistent fatigue, joint pain and headaches, resembles myalgic encephalomyelitis, also known as chronic fatigue syndrome, said Anthony Komaroff, a Harvard Medical School professor of medicine who has studied the syndrome for decades. The condition can follow certain viral and bacterial infections, he said. He thinks the condition likely follows Covid-19, too, at least in a portion of patients. A 2009 study of 233 SARS survivors found 27% met criteria for chronic fatigue syndrome four years after getting sick.

It still isn't known whether the new coronavirus gets into the brain itself, or if Covid-19's neurological symptoms stem from a body-wide inflammatory response, scientists say.

In autopsies of some Covid-19 patients, doctors have observed encephalitis, or inflammation of the brain. Small autopsy studies also have found preliminary evidence of coronavirus particles in regions of the brain important for smell. With other infections, viral particles have been found in the brains of patients with encephalitis, though it is rare, said Walter Royal, a neurovirologist and director of Morehouse School of Medicine's Neuroscience Institute. What is more common is that the virus infects the lining of the blood vessels, causing damage and inflammation that in turn affects the brain.

How long it will take long-Covid patients to recover remains unknown. Dr. Putrino said most of them won't get better on their own, and will need at least six months of structured rehabilitation.

"What tends to happen to people who don't get treatment and don't get the recognition they need is they slump down to a new normal of function," he said.

'I'm not ready to accept this as my new reality,' said Ms. Moore, pictured at home with her husband and daughter.

PHOTO: TAYLOR GLASCOCK FOR THE WALL STREET JOURNAL

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