

Long-term effects of COVID-19 and support to cope

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A dying cell from a COVID-19 patient (in green) releases SARS-CoV-2 virus particles (in yellow) as it succumbs to the infection. While the novel coronavirus shares some common features with other respiratory diseases, there are also important differences in how it affects the body, both in the short- and long-term. Credit: National Institute of Allergy and Infectious Diseases, National Institutes of Health

In the early days of the COVID-19 pandemic, much of the public health

messaging concerned flattening the curve, helping to prevent disease and lighten the load on hospitals caring for the sickest patients.

But what happens next, after the acute infection is over? Doctors are only beginning to understand how it can lead to maladies that persist long after the virus has been quelled.

"In our [local community](#), we only started seeing these patients in March," says Joseph Berger, a neurologist at the Perelman School of Medicine. "That's only five or six months of experience with the disease, too early to comment meaningfully on how this is going to affect patients long-term."

Yet Berger and others are seeing patients whom they suspect will have lasting effects from a bout with COVID-19, whether those are the result of serious complications such as strokes, a consequence of time on a ventilator or receiving other [intensive care](#), or by a subtle and as-yet poorly understood mechanism.

In addition to providing acute care for very [sick patients](#), Penn Medicine is also following up with patients who struggle to return to full health through the Post-COVID Recovery Clinic, which offers a coordinated approach aimed at addressing the multitude of ways that COVID-19 can wreak havoc on the body.

"We're all on a steep learning curve," says Robert Kotloff of Penn's Harron Lung Center. "There have already been quite a few publications coming out about how to handle acute care of the COVID patient. We're much better equipped to understand and treat the immediate complications of the infection. But we're still learning about the patients who are beyond the [acute infection](#) and what lingering issues they're going to have to deal with."

A moving target

Clinicians at Penn are well-positioned to identify the potential longer term effects of infection as they follow up with patients they've treated. And they've seen slow-to-recover patients fall into a few different categories.

Kotloff says that some patients they've seen coming to the Post-COVID Recovery Clinic survived a critical illness. "These are patients who have been in the ICU on mechanical ventilation, those patients who have had a prolonged course of critical illness," he says. Their needs are similar to those of patients who have gone through an intense illness other than COVID, like a severe bout with flu or sepsis. Some may have needs that parallel those cases, like difficulty swallowing, profound weakness, a slow recovery of lung function, or even psychological issues. "We call this post-intensive care syndrome," Kotloff says.

Other patients may have had a serious form of COVID-19, including pneumonia, and may have been hospitalized or managed at home, but were never critically ill. "A number of these patients are coming to the clinic with shortness of breath and persistent shadows on chest X-rays," Kotloff says. "The question in my mind is, do we watch and wait or would some of these patients benefit from corticosteroids."

Kotloff and others suspect that these patients may be experiencing continuing lung inflammation as a response to coronavirus infection, even if they're no longer battling the virus itself. Steroids like prednisone can expedite healing in other such cases, but come with side effects, especially with prolonged use, so treatment remains a balancing act.

A third category of patients coming in with unresolved conditions compose the majority of Post-COVID Recovery Clinic patients. "These cases are more curious," Kotloff says. "These are patients who had

relatively mild infections, not even pneumonia, but come to us later with shortness of breath, and often with profound fatigue, but we can't find anything physiological to account for these symptoms."

What makes treating these patients so complicated at this early stage, says Kotloff, is that it's unclear just yet if these symptoms are truly long-lasting, or if they will eventually resolve on their own. Stress and anxiety about the disease can contribute to recovery as well, especially given that much remains unknown about COVID-19. "I think that fear can feed into people seeking medical attention to make sure that they're OK," Kotloff says.

One early clue linking some patients who are slow to recover from a bout of coronavirus deemed "mild" may lie in their inflammatory response. Kotloff has seen measures of the inflammatory marker C-reactive protein persistently elevated in a subset of patients, a finding he doesn't quite know what to make of yet. "This is something we should pursue," he says.

An interesting observation is that lengthier-than-expected recoveries have been seen in a wide range of patients. "A [Centers for Disease Control] publication concluded that older patients and patients with comorbidities are more likely to have a protracted recovery course," Kotloff says, "and that's panned out from what I've seen. But I have also seen some young patients who are taking a while to get back on their feet."

Many manifestations

Pulmonary difficulties like shortness of breath are not unexpected from a respiratory disease like COVID-19, but what has set this infection apart is its penchant for disparate organs and body systems.

In a small number of patients, strokes and other blood clots, kidney failure, and cardiac inflammation are among a group of rare but worrisome consequences of the acute phase of the illness.

Berger himself has seen individuals with what he calls "strange phenomena" who report neurological symptoms after a COVID infection, such as confusion and behavioral changes, which may also accompany headaches and dizziness. "It may be some sort of structural damage to the brain we're not able to see," he says. "We haven't seen anything major on imaging studies and even spinal fluid examinations have not been terribly revealing."

Berger believes only a "vanishingly small" number of patients' brains actually get infected by the virus, likely because the ACE2 receptor the virus uses to enter cells is not widely expressed in the brain.

However in a small number of patients—Berger estimates 2 to 5% of those hospitalized for COVID-19—he and colleagues have noticed on brain MRIs indications of a "global process due to hypoxic injury, or a combination of hypoxia and small vessel disease," a consequence of a lack of oxygen to the brain. Berger says hypoxia can injure the brain akin to how a heart attack affects the body, leading to an incomplete recovery.

Another very rare subset of COVID patients has been found to sustain a Guillain-Barré-like autoimmune disease affecting the nervous system. "Even though [the [coronavirus](#) infection is] an acute insult that doesn't continue," Berger explains, "the response to it can leave patients with weakness and other neurological manifestation. But fortunately these are small numbers, very small numbers, of patients." It remains uncertain whether these autoimmune diseases occurring in association with COVID-19 occur more frequently with this viral disease than with others, such as influenza, he says.

Serious illness can do strange things, though, he points out, such as cause stress that leads to the unmasking of a psychiatric illness. Patient data collected to date suggest that neurological complications will likely continue to be rare.

"I think that individuals who are otherwise neurological healthy, upon recovery from COVID, are very unlikely to develop something thereafter," Berger says.

"Although I'm not anticipating that we're going to see unusual effects from this virus moving forward," he adds, "I've been practicing medicine almost 46 years and I can tell you that I have been surprised in those 46 years. So I think we're just going to have to be vigilant."

Support system

When it became clear that some patients were not bouncing back after leaving the hospital, Penn Medicine's Benjamin Abramoff and Franklin Caldera, together with colleagues, spearheaded the creation of the Post-COVID Recovery Clinic.

"We had been seeing people in inpatient rehab—pretty much the sickest patients, those with long ICU stays, multi-organ system failure—who had a lot of multidisciplinary needs," says Abramoff. "At the same time, on the outpatient side, our specialists had seen patients who had a residual cough or residual shortness of breath, or other symptoms like weakness, loss of endurance, or pain."

The doctors recognized that their patients would be better served by a more structured, integrated care approach. Now the Post-COVID Recovery Clinic brings together experts in pulmonology, cardiology, [physical therapy](#), psychiatry, and case managers, and other fields to coordinate care and develop a tailored plan for every patient. "It's one of

the big uses of my time, trying to figure out ways we can build and offer more to these patients," Abramoff says.

The clinic—a conceptual arrangement rather than a physical space—brings patients in with a thorough telemedicine appointment to get the scope of their needs. Physical therapist John Barry of Good Shepherd Penn Partners helped craft guidelines specifically for COVID patients to address their symptoms, personalizing the approach.

"Let's say you have someone with pulmonary difficulties like shortness of breath," says Abramoff. "Rehab could involve different breathing techniques or postural positioning techniques."

For patients with other issues, such as dizziness when standing up, Abramoff explains, it could be using something like a tilt table or going all the way up to more aggressive cardiac or cardiopulmonary exercise programs. "The good thing about therapy is it is in a monitored environment," he notes. "We can check their heart rate, pulse, blood pressure. Our patients get comfort from that."

As the pandemic stretches on, clinicians are continuing to learn, while closely observing and caring for their patients. "It's a moving target," Abramoff says. "We're understanding more as we go and hopefully some of these patients will see these lingering symptoms improve."

For some questions, though, time and experience with the disease are what's needed to understand the full picture of its capacity to harm, and our bodies' capacities to heal.

"I'm afraid that, because we do not have a huge experience and the time frame has been so limited," Berger says, "there are unknown unknowns with respect to this particular virus."

Provided by University of Pennsylvania

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