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OPINION

Long-lasting damage and more illnesses: COVID-19 survivors face daunting, unknown aftermath

By **Rosie DiManno** Star Columnist

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A short time coming, a long time going.

And uniquely invasive.

COVID-19: We hardly know you, still.

Crucially, what's still virgin terrain is the lingering hereafter of the coronavirus — how recovery is complicated and compromised in those who've been severely afflicted by the illness.

Overwhelmingly, patients who contract the virus will grope their way back to health without medical intervention, the median time for recovery being about 14 days. However, even in mild cases, those who've emerged from sickness are reporting symptoms many weeks after contracting the disease: Persistent dry cough, headaches, fatigue, loss of taste and sense of smell.

A professor of infectious diseases at the Liverpool School of Tropical Medicine posted a blog for the British Medical Journal documenting his experience. "Health professionals, employers, partners, and people with the disease need to know that this illness can last for weeks and the long tail is not some 'post-viral fatigue syndrome' — it is the disease," wrote Paul Garner, who fell ill in mid-March.

"The symptoms changed, it was like an advent calendar, every day there was a surprise, something new. A muggy head; acutely painful calf, upset stomach, tinnitus; pins and needles, aching all over; breathlessness, dizziness, arthritis in my hands; weird sensation in the skin ..."

After 44 days of feeling intensely lousy, Garner decided he was well enough to try a little exercise, participating in an online cycling class. The effort drove him back to bed for a week.

Many veterans of the COVID wars will empathize.

The coronavirus is deeply attached to its human host, petrifying the lungs, infiltrating other organs with stealth, often triggering cytokine storms from a hyperactive immune system desperately trying to fend off the invader. In critical cases, they end up on ventilators, with a poor prognosis for restoration to their former selves, or even for survival. Convalescence is protracted and stuttering. Wellness feels a distant horizon.

"Probably the long-term impact of COVID-19 will not be clear until you get data over a long period of time," says Dr. Margaret Herridge, respirologist, critical-care physician and senior research scientist at University Health Network. "Those data will start to emerge in the next one to two years."

Herridge and her colleague, Dr. Angela Cheung, both professors of medicine and senior scientists at University Health Network/University of Toronto, have recently been appointed co-leads of the Canadian COVID-19 Prospective Cohort Study, funded by the Canadian Institutes of Health Research. The study isn't expected to report its findings for at least 18 months, but Herridge and Cheung bring decades of research knowledge to the project. Together, they produced a five-year tracking study of Acute Respiratory Distress Syndrome in 2011 in the New England Journal of Medicine. Herridge was also the senior author of a one-year evaluation paper on patients with Severe Acute Respiratory Syndrome. (In the 2003 SARS outbreak — another coronavirus illness — 375 people were stricken by the disease in Canada; 44 died.)

In severe COVID-19 cases, patients can develop ARDS, requiring mechanical intervention. One early Chinese study found that 50 of 54 patients who died of COVID-19 had ARDS; only nine of 137 survivors had it.

"COVID seems a little different than conventional ARDS ... However, I suspect these folks will have some similar challenges to our ARDS patients," says Herridge.

Herridge emphasizes that ARDS patients typically don't have long-term lung complications. They do, however, suffer from the consequences — similar to COVID patients, presumptively — of being sick and in intensive care for a long time.

"They have problems related to muscle wasting and weakness and typically also peripheral nerve injury. These problems will create functional disabilities and functional dependencies. The weakness in these patients, which has been termed intensive care acquired weakness, will affect the strength in the shoulder and hip girdle. Washing, bathing, climbing stairs, getting in and out of a car, these things can become very difficult."

Lengthy ICU isolation, particularly when patients haven't been exposed to rehab therapy, can result in contraction of the joints, says Herridge. "Some of the joints can get a little bit frozen or they may have mobility issues. Some patients have (breakdowns) in skin and develop complex wound infections. That's got nothing to do with ARDS."

The other challenge, Herridge continues, is brain function, including declines "in things like attention, concentration, memory and processing speed. This isn't related to an overt brain injury, like if they've had a stroke," though some COVID patients do have strokes, usually related to blood clots. "The patient's been so sick with this severe inflammatory total-body response. The other problem with the brain function is that patients may develop severe mood disorders."

So, there's all of that possibly lurking for COVID-19 survivors. But it's too soon to draw any conclusions, Herridge stresses.

"Outcome researchers around the world fully expect that COVID patients will have these problems. But other specific issues related to COVID-19? Hard to know."

There's scant reliable literature on the coronavirus as yet and even less that's been peer-reviewed. Mostly it's been front-line doctors talking to each other on social media, trying to grasp the mysteries of what they've seen in their patients.

"Anecdote is not really what you want to hang your hat on," Herridge warns.

"What we really need to study are hundreds of patients, at least a thousand patients and their caregivers, across a spectrum of illness. People who are positive in their community and they get better. People who are in the hospital on the ward but they never come to the ICU. And then people who get critically ill.

"In the short-term, COVID patients will definitely have some of the same problems as ARDS patients, for sure. Whether they'll have other additional problems ... we think they will. But it's hard to know ... because not every patient will have these various complications from COVID-19. That much seems clear."

Their foe spreads in invisible droplets in a puff of a cough, and in barbed microbes penetrating outlier organs, from kidney to liver to heart to brain.

Medical experts worry about the subset of patients who will suffer long-term damage from their encounters with the coronavirus. Physicians have reported hospitalized patients experiencing a high rate of blood clots that cause strokes, heart attacks, lung blockage and other complications, even among younger individuals. Pulmonary embolisms that occur when clots block circulation in the lungs; clots in the kidneys causing renal failure, which means dialysis for a considerable number of patients, whether temporary or not. And loss of muscle mass.

A Wuhan study published in January, two months before the World Health Organization declared a pandemic, found that 12 per cent of COVID patients showed signs of cardiovascular damage. Other studies have revealed evidence of myocarditis — inflammation of the heart muscles that can cause scarring and heart failure.

It's too early to determine whether COVID-19 causes permanent lung damage. Naturally, survivors want to know how long symptoms will linger — weeks? months? years? Questions impossible for experts to answer about a novel disease that's only been

present in humans for some six months. A whole lot of "we don't know," particularly regarding those who've been gravely ill and hospitalized.

"They've been lying in bed, heavily sedated, having their breathing assisted and often paralyzed to facilitate the use of ventilators," explains Dr. John Granton, respirologist and critical-care doctor at UHN. "COVID-19 is unique in some respects in that the level sedation, the intensity of sedation, the duration of sedation and the length of time that we use medication to paralyze them is much greater. So we're seeing a lot of very weak de-conditioned people. Severe weakness but also alteration in their level of consciousness; confusion, delirium as well.

"That fog of war is going to take a long time to wear off."

Longer hospital stays means cascading effects, like susceptibility to skin breakdown and other infections.

"In general with people who've been critically ill, the recovery is limited not by their lung function but by their overall strength and the disability related to being in bed for a long time," Granton continues. "So the direct cost of COVID will extend beyond the hospitalization, the acute phase, to the chronic phase. It might not take weeks or months but a year to recover many of the functions, physical as well as cognitive. Many don't get it back. Uniquely to COVID, we don't know."

While hospitals are seeing fewer COVID patients admitted in Toronto, it should not be forgotten that many are still in ICU and the step-down process is prolonged.

Granton points to possible unknown effects on clotting and asks, "How does that affect the brain? Direct effects of the virus on blood cells, how is that going to affect lung function, heart function, brain function? What are the problems these people are going to experience further on in their lives because of the battlefield that the infection left behind?

"Will they be more susceptible to heart disease, with breathing difficulties? We also recognize that COVID-19 may actually lead to more direct lung damage, like fibrosis or scarring. All these things will come out within, I would say, the next year."

It's not just the physiological quandary. There's psychological healing as well. Dr. Ishrat Husain notes that weeks in intensive care, "with quite invasive procedures like ventilation, (can) have quite a traumatic impact on one's emotional well-being."

Husain, a clinician scientist and staff psychiatrist at the Centre for Addiction and Mental Health, assistant professor (brain and therapeutics) at the University of Toronto, has expertise in the field of biological psychiatry — understanding mental disorders in terms of the biological function of the nervous system. It's an evolving area of research which looks the associations between the body's inflammatory and immune responses and mental health — called immunopsychiatry.

"We know that with people who go through chronic or severe illnesses that effect their immune system, as COVID-19 does, there's a higher chance of having a mood disorder, specifically depression."

It's thought to be caused by a link between body and brain and how the immune system — so profoundly affected by COVID-19, the overwrought essence of the disease — interacts with chemicals in the brain. These patients might not respond to antidepressants.

"There's a two-way relationship between mood and the inflammatory response system," says Husain. "COVID-19 poses a unique opportunity to try and study in people who are recovering."

Fundamentally, the recovering COVID patient requires multi-dimensional support, from medical professionals and families. Yet, Husain says, "They've been isolated in the hospital. When they come out they have to be quarantined as well for a couple of weeks. If they don't have the support of family and friends within the home, that in itself can be quite isolating. And social isolation we know does contribute to depression and anxiety."

Add to that the spectre of future medical unknowns — unimagined health complications that might yet emerge; the lack of assurance that, having survived COVID-19, you're forever done with it and consequences. Husain says that uncertainty "alone would be quite anxiety-provoking. Especially when they are surrounded by reminders of their traumatic experience. COVID-19 is on the news every day."

As Dr. Herridge puts it: "Critical illness is a traumatic life event. Period."

COVID-19 casts a long shadow. How long and how pernicious? The future is obscure.

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