**COVID**

How “long covid” is shedding light on postviral syndromes

The global burden of long covid has put a spotlight on the long neglected mystery of postviral syndromes. Brian Owens asks what’s changing

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Long covid really shouldn’t have been a surprise, says Vett Lloyd, a biologist at Mount Allison University in Sackville, Canada. “When the pandemic started, the general assumption was that there were two possible outcomes to an infection—you’d either get better or die,” she says.

But there’s a possible third outcome. It’s long been known that a number of disease causing pathogens—some viral and some bacterial—are associated with ongoing post-infection symptoms in a significant minority of patients.

“There was no real reason to think SARS-CoV-2 should be any different than the original SARS, which also caused post-infection syndromes,” says Lloyd. She is one of many researchers who hope that the attention and funding directed towards long covid will help to shed light on how and why other infections can lead to persistent and sometimes debilitating symptoms.

**Common symptoms**

The list of infectious diseases linked to long term symptoms includes Ebola, West Nile virus, polio, and Lyme disease. Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is also thought to be a postviral syndrome.

While these diseases all have different acute symptoms, the symptoms associated with their post-infection syndromes tend to be remarkably similar: fatigue, neurological impairments, muscle and joint pain, sleep disturbances, and irritability are all common, says Andrew Lloyd, an infectious disease physician at the University of New South Wales mostly dismisses those ideas. “The lessons we’ve learned from other post-infection syndromes is that it is not a persistent infection, not immunological, not a simple psychological disorder,” he says.

Among researchers who study these illnesses, including long covid, the smart money is now on some kind of disorder of the central nervous system, he explains. And since there’s no clear evidence of any major structural problems in the brain, this suggests that the disorder lies at the cellular and protein level.

“Somebody is going to have to do studies to show this is real,” she says. “It went from this is all in your head, to this is real, to dedicated clinics, the fastest I’ve seen for any post-infection syndrome.”

That was due at least partly to the huge numbers of people affected, with some studies suggesting that as many as half of all covid-19 infections can lead to lingering symptoms. Andrew Lloyd expects the actual prevalence of long covid to be more like 10-15%.

**Unanswered questions**

Finding a common cause of the various syndromes would be a breakthrough in postviral syndrome research. Several hypotheses have been put forward, including persistent but undetected infections, autoimmune responses, dysregulation of the microbiome, and tissue damage. But Andrew Lloyd of the University of New South Wales mostly dismisses those ideas. “The lessons we’ve learned from other post-infection syndromes is that it is not a persistent infection, not immunological, not a simple psychological disorder,” he says.

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“Somebody is going to have to do studies to show this is real,” he says. “But nothing concrete yet.”

**Treatments**

Alba Azola, co-director of the Post-Acute Covid-19 Team at Johns Hopkins University School of Medicine in Baltimore, USA, has been treating patients with lingering covid-19 symptoms since April 2020.

At first, the patients with long covid seemed to have a lot in common with people with postural orthostatic tachycardia syndrome (POTS), a blood circulation disorder characterised by elevated heart rate and other symptoms brought on by standing up, as fatigue and brain fog are also common symptoms of that condition. So Azola, a physical and rehabilitation physician, along with a team of physiotherapists, started treating these patients using the same protocols as for POTS, focusing on things such as diet and exercise.
But after about three months it was clear that this exercise focused treatment regimen was not working. The team realised that long covid was more like ME/CFS, says Azola, and began drawing on ideas from that area instead. This meant focusing on managing and conserving energy levels and understanding which triggers can bring on fatigue, to get off what she calls the “corona-coaster,” where patients start to feel better, become more active, and then crash.

She says that, in the absence of a reliable treatment or cure, patients need to learn to live with the condition by being selective with their energy and what they invest it in, which can be as simple as using a chair in the shower to avoid unnecessary exertion. “I learned all of this from the ME/CFS community,” she says.

**Long covid sparks investment—at last**

Because post-acute conditions have been neglected for years the medical field is lagging far behind when it comes to finding effective treatments, but Azola is hopeful that the focus on long covid will help to shed light on other related illnesses.

In some places this is already starting to happen. The Canadian province of Quebec recently announced that it was providing C$20.5m (£13.5m; €15.6m; US$15.6m) to open 15 clinics focused on both long covid and Lyme disease. The clinics, which are slated to open in autumn 2022, will bring together different specialists to help coordinate treatments for these complicated conditions, in the kind of multidisciplinary teams Azola is advocating for. The American Academy of Physical Medicine and Rehabilitation has also launched a multidisciplinary team to develop clinical guidelines and educational resources for physicians.

Vett Lloyd also sees the Quebec clinics as an important step in getting to the bottom of the whole suite of post-infection syndromes. “It’s horrible that it’s taken the suffering of so many people with long covid to make it happen, but integrated clinics like these will help people with many post-infection syndromes,” she says.

Andrew Lloyd agrees. “Billions of dollars have been thrown at long covid research,” he says. “With a bit of luck we will find something relevant not only to long covid but to other post-infection syndromes too.”

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