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Long-Haul COVID

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Modern medicine has faced its biggest challenge from the smallest of organisms. It is becoming increasingly apparent that many patients who recovered from the acute phase of the SARS-CoV-2 infection have persistent symptoms. This includes clouding of mentation, sleep disturbances, exercise intolerance and autonomic symptoms (Table 1). Some also complain of persistent low grade fever and lymphadenopathy. Although there are no peer reviewed papers at the moment on these patients, many news articles have been written about this phenomenon¹⁻⁴ and there are Facebook groups with several thousand patients describing these symptoms. They call the illness, “Long-Haul-COVID” or “Long-tail COVID”. Many of these patients are health care workers who had massive exposure to the virus early in the pandemic and describe having symptoms for “100+ days”⁵.

A 26 year-old high school teacher from Georgia described the symptoms as such:

My chest hurts and head pounds

The body aches and heart races

I can hardly move, it's extreme fatigue

Brain's in a fog, can't remember the name of my dog

Lost my sleep and my appetite

Feet are tingling and ears are ringing

It's the Long-Haul COVID

Most of these patients were in excellent health prior to getting infected with SARS-CoV-2. They all had a myriad of symptoms during the acute phase. However as the fever and respiratory symptoms improved, they are left with persistent systemic symptoms some of which are gradually improving but not all are following that course. Still others feel they had nearly recovered from the acute illness and then a few days later, developed a plethora of symptoms

that are now persisting. Some describe a cyclical nature to their symptoms where they improve and then worsen every few days. While some were admitted to the hospital due to pulmonary symptoms, the majority were isolated at home. Access to testing and medical care has been limited and most appointments with physicians are being done via telemedicine which has its limitations. Some patients have had extensive testing by internists, infectious disease specialists, cardiologists and pulmonary medicine experts but nothing has been found to explain the symptoms⁵. These patients, some of whom are physicians themselves are concerned that they could be stigmatized as being “functional”. Many of these symptoms overlap with those of patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)^{6,7}. However one needs to be careful not jump to the conclusion that they have ME/CFS unless other possible causes of their symptoms have been investigated (Table 2).

The cause of ME/CFS remains unknown despite decades of research on the syndrome. Many patients with ME/CFS similarly report a viral infection as a trigger but since they come to our attention often years after symptom onset, it is impossible to know what may have triggered the symptoms⁸. Long-Haul COVID thus represents an excellent opportunity to study the pathophysiology of ME/CFS and in doing so may have broader implications.

Even at this early stage, it might be important to determine what the potential pathophysiological mechanisms might be. So far there is no convincing evidence for wide spread infection of the brain with the virus. Virus has been detected in CSF and brain of very rare cases⁹ however, there is evidence for wide spread glial cell activation which may be related to metabolic dysfunction or to the massive immune activation in the periphery. Other possibilities include specific immune responses targeted against specific regions of the brain and autonomic nervous system. Depending on the predominant underlying pathophysiological mechanism at play, targeted treatment might be possible.

Unfortunately, it looks like the pandemic has gotten out of control. It is spreading rapidly across the globe and even if we have an effective vaccine, we might never have enough dosages to vaccinate the eight billion inhabitants on this planet. And we also have a population that is opposed to any kind of vaccination. So COVID-19 is here for the long haul and neurologists are going to play a critical role in the management of these Long-Haulers! Many of their symptoms are neurological in nature. It is important for us to carefully document the clinical manifestations, to investigate them and treat them. As necessary, we need to conduct research to determine the biological basis of this illness. We discovered the biological basis of diseases such as epilepsy and dystonia, to name a few, which had been called “hysteria” for centuries. Long-Haul COVID is our calling and we should take the lead. In fact, several efforts are underway to prospectively follow these patients with persistent symptoms, including studies at the intramural program at the National Institutes of Health in Bethesda. As we put these efforts in place, it is equally important for us to remember that we should study and treat not the disease that affects patient but rather the patient that is affected by the disease. Only then can we hope to find solace for these patients in a timely manner.

Table 1: Autonomic symptoms in Long-Haul COVID

1. Tachycardia upon mild exercise or standing
2. Night sweats
3. Temperature dysregulation
4. Gastroparesis
5. Constipation/ loose stools
6. Peripheral vasoconstriction

Table 2: Possible etiopathogenesis of Long-Haul COVID

1. Unmasking of underlying co-morbidities
2. Residual damage from acute infection
- 3.
4. Persistent or restricted viral replication
5. Persistent immune activation
6. Unknown cause

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