Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

COMMENTARY

THE AMERICAN JOURNAL of MEDICINE®

Long COVID: Does It Exist? What Is It? We Can We Do For Sufferers?

As we gradually work our way out of the coronavirus disease 2019 (COVID-19) pandemic in the United States thanks to vaccinations, we will hopefully see many fewer desperately ill patients on ventilators and fewer deaths. Looming over the profession is the large and growing numbers of people with what has been termed long COVID: patients who have recovered from their acute illness who present with many persistent complaints. There is still considerable confusion about this entity. There is vigorous debate over whether this is a real entity with a biologic basis or whether it is psychosomatic. The National Institutes of Health (NIH) has announced plans to support research into long COVID, but patients are presenting to their physicians now and seeking help.

There are two relatively distinct forms that "long COVID" can take: persisting symptoms in those who were seriously ill and new symptoms in those, often younger people, who had only mild or even no symptoms with their acute infection.

It is not surprising that very sick COVID-19 survivors have symptoms that persist long after they are discharged from hospital. In recent years increased attention has been paid to the post-intensive care unit (ICU) syndrome.[1,2] A prolonged ICU stay is often followed by persistent cognitive dysfunction, muscle weakness, and intrusive memories similar to those seen with post-traumatic stress disorder.

Hospitalized COVID-19 patients with critical or severe illness were studied at discharge: 77% were below the 2.5th percentile in functional capacity assessed by the 1-minute sit-to-stand test and 15 of 48 had oxygen desaturation. After 3 months only 2 patient had a result above the 50th percentile.[3] Swedish investigators found that more than half of ICU-treated COVID-19 survivors had impaired carbon monoxide diffusing capacity at 4 months after discharge.[4] In France, 478 patients discharged from hospital were interviewed by telephone at 4 months after discharge.[5] A total of 51% reported at least 1 symptom that had not existed before their illness. The most common were fatigue in 31%, cognitive impairment in 21%, and dyspnea in 16%. Lung computed tomography was done in 171 patients and 63% had abnormalities, mostly subtle ground-glass opacities. In Italy, 143 previously hospitalized patients were assessed at a mean of 60.3 days after onset of symptoms. Only 18 (12.6%) were asymptomatic. The most commonly reported symptoms were fatigue (53%), dyspnea (43.4%), joint pain (27.3%), and chest pain (21.7%).[6]

These patients can often be assured that their symptoms should improve with time and seem to be helped by an active rehab program.[3]

Much more challenging are the patients whose initial infection was mild or even asymptomatic. Swedish investigators compared a group of health care professionals who were seropositive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) at enrollment and who reported no or mild antecedent symptoms with seronegative patients at 8 months after testing.[7] Most symptoms were mild, but 26% of seropositive subjects reported at least 1 moderate to severe symptom for at least 2 months compared to 9% of seronegative subjects. Mexican investigators studied 115 patients with mostly mild to moderate polymerase chain reaction (PCR)-confirmed COVID-19 at least 30 days after symptom onset. Four were sick enough to require ICU care. There was a severe decrease in quality of life in 56%.[8]

The University of Washington followed 177 patients with documented COVID-19, of whom 16 were admitted to hospital and 150 were treated as outpatients; 64% of the latter group sought no care after diagnosis. Of the outpatients contacted a mean of 169 days after symptom onset, 31% had 1 or more persisting symptoms.[9]

Patients' symptoms after mild COVID-19 include anosmia, fatigue, palpitations, insomnia, hyperhidrosis, dysgeusia, brain fog, and dyspnea.[6-10]

It is easy for physicians to attribute symptoms to anxiety, but this is neither helpful to our patients nor necessarily true. Hard neurologic illnesses, including ischemic strokes and intracranial hemorrhage, have been found to be more common in patients recovered from even mild COVID-19.[11]

Funding: None.

Conflicts of Interest: None.

Authorship: The author is solely responsible for the content of this manuscript.

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https://doi.org/10.1016/j.amjmed.2021.05.023

Certainly the two leading hypotheses as to the cause of long-COVID are psychosomatic and immune-mediated, but persisting small vessel thrombi have also been postulated.

Pending the results of larger controlled studies, what can we offer our patients? Although anecdotal at this point, many patients with persisting symptoms after a mild/asymptomatic infection have reported improvement in symptoms after vaccination. Because these patients are still at risk for reinfection, advising vaccination is appropriate whether or not it helps their symptoms. Critically, we should not dismiss their complaints as being all in their head. This may not be true and, even if correct, is not helpful. It is appropriate to acknowledge their distress, get those with fatigue or dyspnea in a structured exercise program, and work with all on symptomatic relief.

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References

1. Myers EA, Smith DA, Allen SR, Kaplan LJ. Post-ICU syndrome: rescuing the undiagnosed. *JAAPA* 2016;29(4):34–7.
2. Svenningsen H, Langhorn L, Agard AS, Dreyer P. Post-ICU symptoms, consequences and follow-up: an integrative review. *Nurs Crit Care* 2017;22(4):212–20.
3. Martin I, Braem F, Baudet L, et al. Follow-up of functional exercise capacity in patients with COVID-19: it is improved by telerehabilitation. *Resp Med* 2021;183:106438. https://doi.org/10.1016/j.rmed2021.106438.
4. Ekbom E, Frithiof R, Emilsson OI, et al. Impaired diffusing capacity for carbon monoxide is common in critically ill COVID-19 patients at four months post-discharge. *Resp Med* 2021;182:106394. https://doi.org/10.1016/j.rmed.2021.106394.
5. The Writing Committee for the COMEBAC Study Group. Four-month clinical status of a cohort of patients after hospitalization for COVID-19. *JAMA* 2021;325(15):1525–34.
6. Carfi A, Bernabei R, Landi F, et al. Persistent symptoms in patients after acute COVID-19. *JAMA* 2020;324(6):603–5.
7. Havervall S, Rosell A, Phillipson M, et al. Symptoms and functional impairment assess 8 months after mild COVID-19 among health care workers. *JAMA* 2021;325(19):2015–6. https://doi.org/10.1001/jama.2021.5612.
8. Ordinola Navarro AO, Cervantes-Bojalil J, Quevedo O deJ C, et al. Decreased quality of life and spirometric alterations even after mild-moderate COVID-19. *Respir Med* 2021;181:106391. https://doi.org/10.1016/j.rmed.2021.106391.
9. Logue JK, Franko NM, McCulloch DJ, et al. Sequelae in adults at 6 months after COVID-19 infection. *JAMA Netw Open* 2021;4(2):e210830.
10. Huang Y, Pinto MD, Borelli JL, et al. COVID symptoms, symptom clusters and predictors for becoming a long-hauler [preprint]. *medRxiv* 2021. https://doi.org/10.1101/2021.03.03.21252086.
11. Taquet M, Geddes JR, Husain M, et al. 6-month neurologic and psychiatric outcomes in 236,379 survivors of COVID-19: a retrospective cohort study using electronic health records. *Lancet Psychiatry* 2021;8(5):416–27.