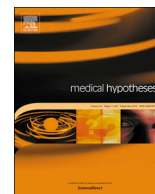




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## Letter to Editors

## Into the looking glass: Post-viral syndrome post COVID-19



## ARTICLE INFO

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## Letter to the Editor

We are writing to highlight the potential for a post-viral syndrome to manifest following COVID-19 infection as previously reported following Severe Acute Respiratory Syndrome (SARS) infection, also a coronavirus [1]. After the acute SARS episode some patients, many of whom were healthcare workers went on to develop a Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) – like illness which nearly 20 months on prevented them returning to work [2]. We propose that once an acute COVID-19 infection has been overcome, a subgroup of remitted patients are likely to experience long-term adverse effects resembling CFS/ME symptomatology such as persistent fatigue, diffuse myalgia, depressive symptoms, and non-restorative sleep.

Post-mortem SARS research indicated the virus had crossed the blood brain barrier into the hypothalamus via the olfactory pathway [2]. The pathway of the virus seemed to follow that previously suggested in CFS/ME patients, involving disturbance of lymphatic drainage from the microglia in the brain [3]. One of the main pathways of the lymphatic drainage of the brain is via the perivascular spaces along the olfactory nerves through the cribriform plate into the nasal mucosa [4]. If the pathogenesis of coronavirus affects a similar pathway, it could explain the anosmia observed in a proportion of COVID-19 patients.

This disturbance leads to a build-up of pro-inflammatory agents, especially post-infectious cytokines such as interferon gamma, and interleukin 7 [5], which have been hypothesized to affect the neurological control of the ‘Glymphatic System’ as observed in CFS/ME [3]. The build up of cytokines in the Central Nervous System (CNS) may lead to post viral symptoms due to pro-inflammatory cytokines passing through the blood brain barrier in circumventricular organs such as the hypothalamus, leading to autonomic dysfunction manifesting acutely as a high fever and in the longer term to dysregulation of the sleep/wake cycle, cognitive dysfunction and profound unremitting anergia, all characteristic of CFS/ME. As happened after the SARS outbreak, a proportion of COVID-19 affected patients may go on to develop a severe post viral syndrome we term ‘Post COVID-19 Syndrome’ – a long term state of chronic fatigue characterised by post-exertional neuroimmune exhaustion [6].

Clinically, one of the authors (RP) has already seen a patient with possible post COVID-19 syndrome. A 42 year old male, married with 5 children who was fit and healthy with no prior existing symptoms with the exception of mild anxiety 10 years previously and a month of

fatigue following a viral infection 4 years previously. He contracted the virus, showing symptoms from 3 to 15th April 2020, during which time he was virtually bed bound for about 2 weeks. At the end of April, he contacted the osteopathic clinic and scored 164/324 regarding the severity of symptoms on the validated rating scale Profile of Fatigue Related States (PFRS) [7]. The PFRS consists of 54 symptoms each with a score of 0–6 where 0 = no symptom, 3 = moderate and 6 = extreme. Twenty four of his symptoms initially scored high i.e. 4, 5 and 6 on the scale.

He was seen in clinic on 5th May, complaining of severe physical fatigue, insomnia, difficulty reading with brain fog, general myalgia, dry skin and increased anxiety. On physical examination he had a restricted and inflamed mid-thoracic spine, engorged varicose lymphatics in the chest with severe tenderness in the left breast lateral and superior to the left nipple. Marked tenderness was also felt in the coeliac plexus. These signs have utility in aiding the diagnosis of CFS/ME [3].

Manual treatment was provided to aid central lymphatic drainage, improve mechanics and reduce the inflammation of the spine and reduce the allostatic load by improving the sympathetic tone.

Three treatments were completed, once a week and the patient followed a self-massage routine to aid lymph drainage along with gentle exercises to improve thoracic spinal mobility. By the third treatment (27th May) his symptom severity had reduced significantly with a follow-up PFRS score of 75/324 with all but five of the very severe symptoms relating to physical and mental fatigue reducing from 4, 5 or 6 to only mild / moderate complaints i.e. 1–3 on the severity scale. He remains in active follow-up.

It may be that early intervention and supportive treatments at the end of the acute phase of COVID-19 can help overcome acute phase symptoms and prevent them in becoming longer-term consequences. Without this, in a contracted future economy (at least in the short to intermediate term), managing these likely Post COVID-19 syndrome cases, in addition to existing CFS/ME cases will place additional burden on our already hard pressed healthcare system.

In the light of this and similar cases and in the context of the available evidence for SARS, we suggest that priority should be given to examine the prevalence of fatigue related symptoms following COVID-19 infection and to explore pragmatic relatively low cost techniques to treat post-viral fatigue, to alleviate symptoms and improve the quality of life for those affected by the longer term sequelae of COVID-19.

Let's start the preparations now for what may come in due course.

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### Contributor statement

Dr. Raymond Perrin led on the writing of the article with contributions in terms of literature search and current perspective from Dr. Lisa Riste, Dr Andreas Walther and Dr. Adrian Heald. Mark Hann provided statistical advice regarding PFRS change scores. Dr. Annice Mukherjee provided further academic input and also senior review. All authors contributed to the final version of the manuscript and approved the final version.

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### Conflict of interest statement

RP developed the Perrin Technique which is described here. No other author has any competing interests.

### Ethical approval

No ethical approval was required for this piece of work.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2020.110055>.

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