Review of: "LC, POTS, and ME/CFS: Lifting the Fog"

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This paper by Patrick Chambers describes a pathogenic pathway for long covid, POTS, and ME/CFS. He identifies plausible hypotheses regarding these condition, but provides little or no scientific backing. A case in point is the questionable scholarship around the MTHFR C677T common variant. There are hundreds of studies in which this variant has been analyzed in countless clinical conditions, with the results ranging from no association to modest association depending on the condition. In the case of connections to long covid, POTS, and ME/CFS, there is no robust data to support any association.

For example, he cites references 1 and 2 for the assertion that “Other research has revealed a close association between Covid-19 and a very common enzymatic polymorphism in the folate cycle involving methylenetetrahydrofolate reductase (MTHFR).” Reference 1 is from the journal Medical Hypotheses, which publishes any idea in the absence of data, and reference 2 is highly questionable. Those authors simply noticed that the frequency of the MTHFR polymorphism was higher in countries with a higher mortality from covid. Sorry – this is not evidence sufficient to back up the author’s claim. The connection to increased concentrations of homocysteine in the CSF in patients with fibromyalgia and chronic fatigue is also tenuous; it’s based on 12 cases. And, there is no evidence supporting the statement in the conclusion that …. “In summary LC reveals undiagnosed MTHFR 677TT present in 30-40% of the population. These patients comprise the majority of those with LC and POTS.” There are no studies in Pubmed showing associations between long covid and MTHFR other than PMID: 35056324, which is also a review that cites as its source of a connection between long covid to MTHFR the same low quality paper described above (ref 2, Ponti et al). And there are no publications showing associations to POTS.

The connection between shingles and long covid is also questionable. There seem to be epigenetic changes in PBMCs, a reasonable experimental finding, but that does not mean that MTHFR is involved. Neither ref 62 nor 63 mentions MTHFR. In addition..

In short, although the author presents plausible hypotheses, he seems to have cherry picked papers to satisfy that agenda.