A Glimpse of Current Research in ME/CFS/SEID

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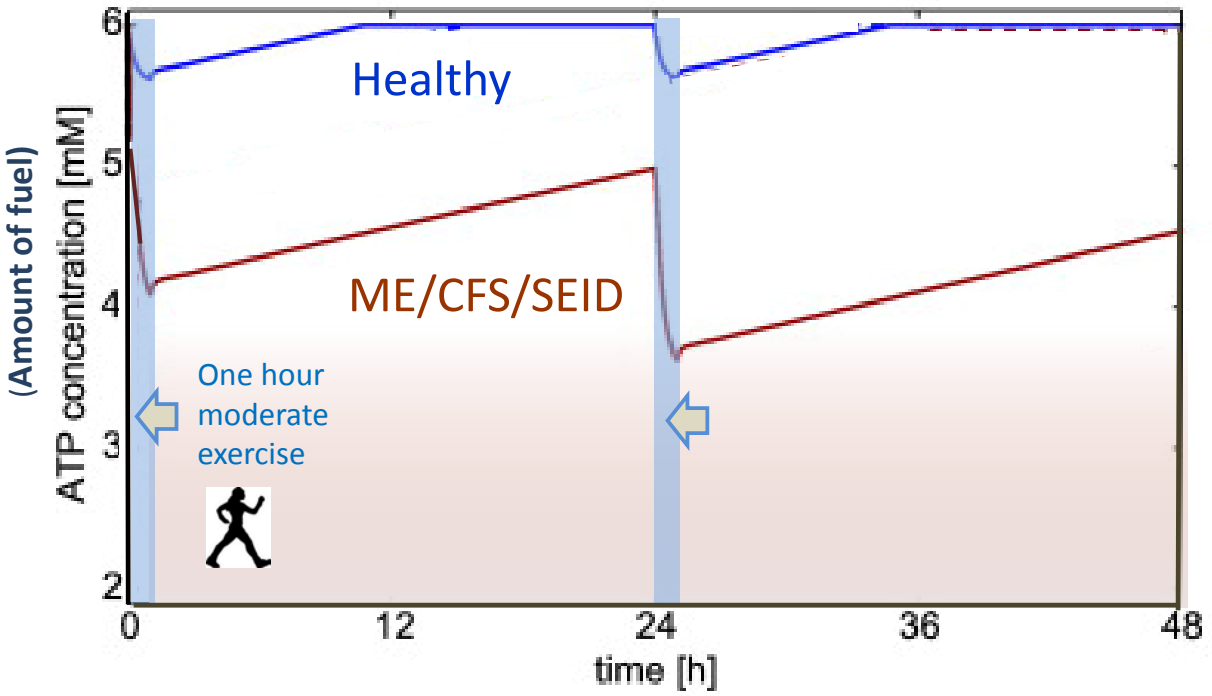
The disease has been with us for many years - decades, hundreds of years, longer, under different names. The disease, whatever it is called, is awful, because it robs people of their health, function, and enjoyment of life. Why has it been so difficult to understand and to treat? Why does it take so long to find a cure?

My wife Cathleen developed ME, CFS, or 'Systemic Exertional Intolerance Disease' fifteen years ago. She is but one of an estimated 2500 patients with the disease in Chittenden County alone.

As a medical researcher at the University of Vermont, I am struck how complicated the disease is – involving so many systems of the body. There is so much more we have to learn. I am not surprised it has taken us so long to get to even our current level of limited understanding, given the complexity. But I am hopeful - even encouraged - that we're making important progress.

Although there are many exciting research projects that I could tell you about had I the time, there *is* one very exciting report that I would like to mention here. It was just published in the Journal of Biophysical Chemistry, by two Germans, Nicor Lengert and Barbara Drossel, from Darmstadt, and when I read it last week I was astonished because they had reduced one aspect of the complexity – the part that fuels our cells – into mathematical equations that reproduce many features of the disease. I will try to give you a thumb-nail sketch of what they report.

The following figure is adapted from their paper. The graph *simulates* (i.e. represents) what happens to our energy reserve, i.e. our fuel supply, when we exercise. The amount of fuel in our muscle cells that is simulated is the concentration of ATP (the fuel molecule) that is available to power our muscles; that is plotted along the vertical axis. Time is plotted along the horizontal axis. This simulation is based on data from published studies. The authors plugged the data into equations that describe a multitude of biochemical reactions that fuel muscle contraction.



Lengert & Drossel, Biophys. Chem., 202, 2015, Fig. 2

The blue line in the graph tells us what happens to me, a healthy person, when I take, for example, a one-hour walk in our neighborhood. The red line tells us what happens to Cathleen, who has ME/CFS/SEID, when she takes the walk. At the beginning of the walk, the fuel level, or concentration of ATP, in Cathleen's and my leg muscle is ~6 (mM, a measure of concentration).

When I walk for an hour the concentration of ATP falls slightly because I'm using ATP to fuel my walk faster than it is being replenished. Note, however, Cathleen's fuel level falls much more, from 6 to about 4¼ mM, not because she's using more ATP to fuel her walk, but because she is has a serious impairment in her ability to replenish the fuel during the walk. This is called a 'metabolic defect'. The level of ATP drops dangerously near the threshold where muscle function gives out because of a diminished fuel supply (gradient shown in pink).

Even more striking is the fact that *it takes much more time to replenish Cathleen's depleted fuel supply after the walk that it does to replenish mine.*

Even for the healthy adult, it takes about 12 hours* to restore the ATP level by breathing oxygen and using it to produce ATP inside tiny organelles inside our cells, called mitochondria. This is because the biochemical reactions that regenerate ATP take a long time. For the patient with ME/CFS/SEID, it takes *more than 36 hours* to restore the level of ATP!

The situation is even worse if Cathleen takes another walk a day later. A one hour walk produces an even greater drop in ATP than the walk a day earlier. In the interim Cathleen's ATP has been only partially restored. My ATP level, on the other hand, has been completely restored before the second walk, whereas Cathleen's has not.

This figure vividly shows a hallmark of the disorder: post-exercise malaise (prolonged fatigue). It is this feature - the inability to recover rapidly from a drop in ATP - which I am currently investigating. I have helped assemble a research team at the University of Vermont to study the immunological basis of this disorder. I am also proposing to do research at the University of Washington to investigate the ATP replenishment problem in more detail. This effort requires time and money, which are in short supply, but we are making progress setting up the research programs.

If it is frustrating for me, as a researcher, to grapple with the ambiguities of the disease, it is obviously much more frustrating and painful for the patient - who suffers with the disease - to wait for a cure, or even an effective treatment. However, rest assured, there are many, many people working hard to solve ME, and that progress is being made.

*Other studies indicate that, in healthy adults, [ATP] is likely maintained near resting levels, and in single muscle contractions, this appears to be the case during fatiguing contractions lasting several minutes. Thus [ATP] may recover in seconds/minutes instead of hours.