

# Community Spotlight

## An Interview with Martin L. Pall, PhD



*Martin L. Pall, PhD works at Washington State Universities School of Molecular Biosciences. He has long-term interests in biological regulatory mechanisms. His current research is focused on a theory he has developed on the cause (etiology) of chronic fatigue syndrome and the overlapping and related conditions of multiple chemical sensitivity, fibromyalgia, and post-traumatic stress disorder.*

### **How did you become interested in MCS and the tenth disease paradigm?**

I became interested in this group of illnesses, mainly because I came down with chronic fatigue syndrome after a viral infection a bit over ten years ago. My interest in CFS became broadened to this group of illnesses, as I became aware of their many similarities, their comorbidity and the proposals from others that they may share a common etiology (causal mechanism).

### **What, in your opinion, is the most likely cause of MCS?**

MCS is caused by essentially the same vicious cycle mechanism that causes other illnesses in this group, but involving tissues in which three classes of pesticides and organic solvents can act to increase the activity of the NMDA receptors and as a consequence of that, you get increases in nitric oxide and peroxynitrite. The tissues involved include areas of the brain, particularly regions of the hippocampus and also peripheral areas of the body, often including the bronchi, upper respiratory tract, areas of the skin and often the gastro-intestinal tract. The mechanisms that lead to the extraordinary chemical sensitivity are all well-documented

mechanisms in the body, and the only thing that is new about my explanation, is the assumption that they fit together in ways that you might assume they fit together. My proposed mechanism includes neural sensitization mechanisms in the brain, as proposed earlier by Dr. Iris Bell, and the neurogenic inflammation mechanism proposed earlier by Dr. Meggs. Both of these are thought to be triggered by excessive nitric oxide and other aspects of what we call the NO/ONOO- cycle, such as the vanilloid receptors, the NMDA receptors and peroxynitrite, all likely to have important roles as well.

### **Would you define peroxynitrite, nitric oxide, and the effects of excess levels?**

Nitric oxide is a normal chemical produced in the body. It has important roles in controlling the nervous system, the immune system and the blood vessels. So it has important normal roles in the body. When produced in excess, a lot of it may be involved as a precursor of peroxynitrite and the high levels of peroxynitrite can have important negative (pathophysiological) effects on the body. These negative effects are important in many different chronic inflammatory diseases, not just in CFS, MCS, fibromyalgia and, I also argue, post-traumatic stress disorder.

**“The effectiveness of these protocols is strongly dependent on individuals avoiding stressors.”**

**Are there any agents that can reduce excess nitric oxide and peroxynitrite (NO/ONOO-) cycle?**

I think there are many agents (nutritional, pharmaceutical, and herbal) that can reduce the NO/ONOO- cycle. I think one has to look the entire cycle, not just the nitric oxide and peroxynitrite – it is the entire cycle that needs to be down-regulated, not just specific parts of it.

**Would you describe what to expect in terms of improvement and/or cure for someone who follows your supplement protocol to downregulate NO/ONOO-?**

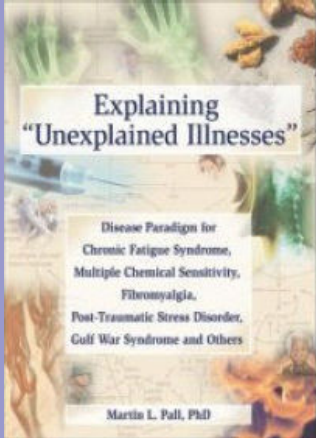
Let me say, that I am a PhD, not a MD and nothing I say or write should be viewed as medical advice. I discuss five treatment protocols in my book developed by five different physicians, each of which involve at least 14 agents or classes of agents predicted to down-regulate different aspects of the NO/ONOO- cycle. I think that each of these can produce substantial improvements over periods of three months or so. But we need many more studies on them to compare their relative effectiveness and to

compare them with other approaches and also with placebos. Because many of these agents are nutritional supplements, which in the US, at least, are still available over-the-counter, individuals in this country can access them on their own, if they so desire. I designed a protocol for the Allergy Research Group which is entirely over-the-counter. Having said that, the effectiveness of these protocols is strongly dependent on individuals avoiding stressors that will otherwise up-regulate the NO/ONOO-cycle. Which such stressors are important to avoid, will vary from one individual to another but will often include chemical exposure in MCS, food allergens in those who have developed food allergies, exercise in the case of CFS, psychological stress especially in the PTSD group and chronic infections, especially in the CFS and Gulf War syndrome groups.

**Most patients find practicing avoidance of chemical exposures and other stressors that wear on the adrenals and upregulate the NO/ONOO- Cycle near impossible. Is this a crucial part of recovery or is the supplement regime enough?**

Certainly for the most sensitive individuals, this is a key part of the recovery program. Those who are less sensitive may be able to get away with more exposure, although even for those, exposure should be avoided where possible. Yes, I know it is difficult, but is it very important.





**“We need to get past the view that we don’t have the foggiest idea of what is going on here.”**

**What do you suggest to patients in terms of gaining the support of friends, family, and co-workers in their recovery?**

You might give them a copy of my book to read, or possibly the copy of the relatively accessible paper that I wrote for the Townsend Letter for Doctors and Patients.

**Will avoidance and stressor reduction need to be practiced indefinitely, or is there a stage at which patients recuperate enough to tolerate life stressors?**

I think (as do many others) that MCS is the most difficult of this group of illnesses to treat. While there is a literature that about 10% of CFS and fibromyalgia patients have full recoveries, there is no such literature on MCS. I know of only one person who can make a very credible claim to have had a severe case of MCS, who has had a full recovery. So I think that for MCS, we are probably talking about years. Still, Dr. Ziem says that her chemically sensitive patients often show sufficient improvement over a period of a year or so, such that they can resume social interactions that were not possible previously. So, it is my hope that people will recover sufficiently to tolerate these stressors, but it may take a long time, especially in MCS.

**Where do we go as a community of researchers, physicians, advocates, and patients from here?**

I would hope that our future progress will be as follows:

A. We need to get past the view that we don’t have the foggiest idea of what is going on here and that we don’t have any idea how to treat this group of ill-

nesses. We also need to view this group of illnesses as a group because our understanding of one of these is often of great value in understanding others.

B. We need to develop specific biomarker tests for each of these illnesses and I suggest approaches in my book on how to do this for both CFS and MCS. This is a key need because it is what is needed in order to have objectively measurable approaches toward diagnosis.

C. We need much more study in terms of therapy. I think we know how to approach this but we need much more data on it.

D. The NO/ONOO- cycle mechanism as a model for these illnesses is bound to be oversimplified and therefore, incomplete. That is essentially also the case with other such models of complex diseases and it is, therefore, likely to be true with the cycle. I do think that the cycle model already makes useful predictions in terms of therapy. But we need (and I need) others to weigh in about how it may be oversimplified and how we may be able to make still better predictions in terms of therapy. This should not be a one person job. Interestingly, I learned some useful things at the meeting I spoke at two weeks ago in Sonoma County on CFS that suggest two important aspects that I had not previously given enough attention to. So I see this as a progressive process, which I hope will involve many other scientists.

**Editors Note**

Martin L. Pall recently published *Explaining 'Unexplained Illnesses': Disease Paradigm for Chronic Fatigue Syndrome, Multiple Chemical Sensitivity, Fibromyalgia, Post-Traumatic Stress Disorder, and Gulf War Syndrome.*