

Book Review

Explaining unexplained illnesses disease. *Paradigm for chronic fatigue syndrome, multiple chemical sensitivity, fibromyalgia, post-traumatic stress disorder, Gulf War syndrome and others*

Martin L. Pall. 446 pp. **Price:** US\$ 39.95 **Publisher:** The Haworth Press, Inc. **Date of Publication:** 2007. **Place of Publication:** United States of America. **ISBN:** 978-0-7890-2389-6.

Prof. Martin L. Pall is working in the Biochemistry and Basic Medical Sciences, Washington State University, USA. In this book, Prof. Pall proposed a theory of nitric oxide (NO) and its oxidant product peroxynitrite (ONOO⁻) as the causal mechanism for explaining “unexplained illnesses” such as chronic fatigue syndrome (CFS), fibromyalgia syndrome (FMS), multiple chemical sensitivity (MCS), post-traumatic stress disorder (PTSD), Gulf War syndrome, and other related syndromes. These multi system illnesses share overlapping symptoms and signs, the chronicity nature, difficult to explain their causes, diagnosis, or effectively treat them. Although these syndromes have much in common, yet they have symptoms that are specific for each. They can be triggered by over 12 diverse stressors including infectious diseases, chemical exposures, physical, psychological, and emotional traumas. He identified a well-crafted common molecular and biochemical pathway that can be triggered by many different factors (stressors), that results in a wide spectrum of symptoms that are shared by these syndromes. Stressors act by raising NO synthesis and consequent levels of its ONOO⁻. This initiation is converted into a chronic illness through the action of NO/ONOO⁻. The vicious circle clinical features of these syndromes are generated by elevated levels of NO/ONOO⁻ or inflammatory cytokines and an elevated neural transmitter system in the brain known as N-methyl-d-aspartate and vanilloid receptor activities. The author proposed the NO/ONOO⁻ cycle mechanism theory as the causal factor, based on evidence from animal models and from humans, but the studies specifically aimed at testing NO/ONOO⁻ cycle roles in these diseases are just starting. Observations on animal models of these illnesses provide substantial support for this theory and are proposed as a major new paradigm of human diseases. A mouse model of chronic fatigue syndrome injected with bacterial extract resulted in increased and prolonged NO/ONOO⁻ cycle with features of fatigue response. The NO/ONOO⁻ cycle mechanisms are quite striking albeit difficult to see how all of these could have important causal roles. He also noted that “we do have evidence that several short-term stressors may act to increase NO synthase activity, but studies on the mechanism of action of the short-term stressors are only beginning to be focused on the issue of their role in initiating the NO/ONOO⁻ cycle”. This theory is based on observation rather than explanation of the etiology of unexplained illnesses. The author also suggested the need for further experiments to confirm

or deny important predictions of the theory. He found that the long-term clinical observations and a placebo-controlled trial suggests that vitamin B-12 acts as a potent NO lowering agent, and is an effective treatment for CFS, FM, MCS, PTSD, and other syndromes. Paroxetine is also reported to decrease NO synthesis. These observations support the role of NO in the etiology of these syndromes.

This excellent book has 446 pages with 16 chapters. Chapter 16 (Overview, p. 317-325) should be read first. It presents a summary of the aim of the book, the observation rather than the explanation of the theory of etiology, the proposal of a major new paradigm of human disease, and comparison with another paradigm. The author is aware of the test for proof of scientific theories. However, this does not always work in the areas of genetics, cancer, and others with incomprehensible complexity and are based on observations, however they are difficult to test. Scientific observations with new disease paradigm are not easily accepted. An example of that is the new paradigm for gastric ulcer as an infectious disease, this took 10 years to be accepted despite strong evidence of the cause and its response to effective treatment. Therefore, financial and logistic supports for such diseases research are scarce, and further delay the progress and advances to achieve the explanation to the unexplained, particularly when alternative methods are not available. Other chapters dwell with the NO/ONOO⁻ cycle as a cause of these syndromes, the localized nature of NO/ONOO⁻ cycle. Each of the syndromes was discussed separately in one chapter, and is well written. Chapter 6 deals with treatments of the clinical observation on the use of vitamin B-12 and paroxetine as NO lowering agents, and were found to be effective. Chapter 15 (Therapy, p. 265-316) discusses approximately 18 agents or classes of agents predicted to lower the cycle biochemistry. References for each chapter are placed at the end of the book. Subject index follows and the references are from pages 439-446, and are very helpful to the reader. This superb book is a tour-de-force in the field on non-traditional scientific exposé on the thesis of the etiology of the unexplained illnesses. The main purpose of this book is the introduction of the NO/ONOO⁻ cycle mechanism theory as the etiological factor for these unexplained syndromes.

I enjoyed reading this excellent book from cover to cover. It is essential reading for those interested in research and those who finance research. It should be in every medical library of universities and research institutes.

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