Scientific Study

Clinical Markers Confirm Multiple Chemical Sensitivity and Validate Environmental Medicine Approach

"Epidemiological studies show that MCS is a stunningly common disease, even more common than diabetes."

Martin L. Pall, PhD, Professor Emeritus of Biochemistry and Basic Medical Sciences at Washington State University has uncovered an independent research group which has confirmed three clinical markers in people with multiple chemical sensitivity.

The Environmental Protection Agency defines multiple chemical sensitivity as "a diagnostic label for people who suffer multi-system illnesses as a result of contact with, or proximity to, a variety of airborne agents and other substances."

The three confirmed markers for multiple chemical sensitivity are elevated inflammatory cytokines, nitric oxide, and oxidative stress.

Inflammatory cytokines, when elevated, amplify the inflammatory response in the body in order to deal with a health threat. Elevated cytokines could lead to sepsis, renal failure, and other organ death in a potentially fatal immune reaction known as a cytokine storm. Inflammatory cytokines have also been found in chronic fatigue and fibromyalgia.

This finding confirms that MCS patients differ from normal controls in their responses to low level chemical exposure. Pall presented other changes in responses to low level chemical exposure in his recent MCS toxicology review. These replicated objective changes should serve as clinical diagnostic markers which may be used to identify patients with MCS.

FOR IMMEDIATE RELEASE

Predictions of Multiple Chemical Sensitivity Mechanism Confirmed by Roman Study

Portland, OR – July 5, 2010 - The physiological mechanism for Multiple Chemical Sensitivity proposed by biochemist Martin L. Pall has been confirmed with the recent findings of an independent research group in Rome.

Multiple chemical sensitivity (MCS), also known as chemical sensitivity and toxicant-induced loss of tolerance (TILT), is a disease initiated by toxic chemical exposure, leading to toxic brain injury that produces high level sensitivity to the same set of chemicals that are implicated in initiation of the disease. Sensitivity responses in other areas of the body are also often seen.

"Epidemiological studies show that MCS is a stunningly common disease, even more common than diabetes," said Pall, professor emeritus of biochemistry and basic medical sciences at Washington State University. "My review of the literature and other research I've conducted over the past eleven years shows the probable central mechanism of MCS is a biochemical vicious mechanism, known as the NO/ONOO- cycle."

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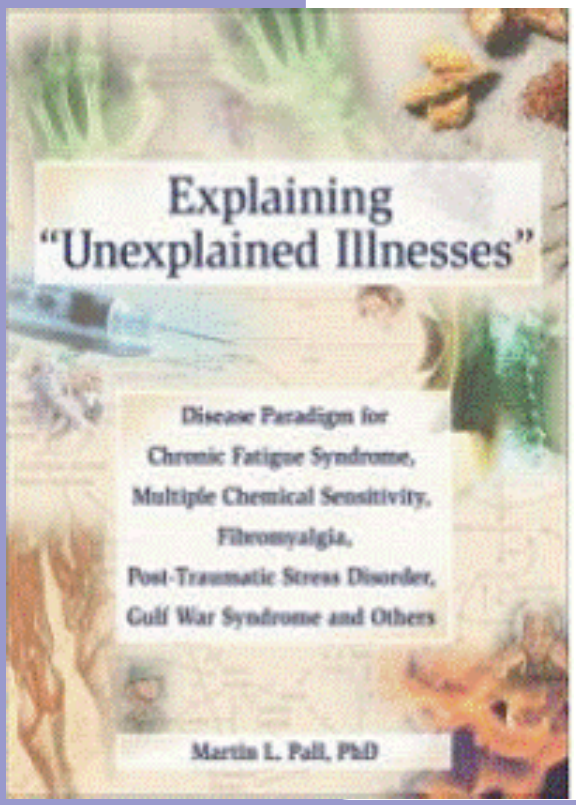
Pall's work is widely published in books and articles, the most recent of which is a chapter in the authoritative international reference manual for professional toxicologists, General and Applied Toxicology, 3rd Edition, 2009.

The NO/ONOO- Cycle

The NO/ONOO- cycle, pronounced no-oh-no, is named for the chemical structures of nitric oxide (NO) and peroxynitrite (ONOO-). This biochemical vicious cycle mechanism predicts that each of the elements linked together in the cycle are elevated in patients suffering from MCS and related diseases. Most of the elements of the cycle have been shown to be elevated in such related diseases as chronic fatigue syndrome and fibromyalgia and also in animal models of MCS. However, several cycle elements have never been measured in MCS patients.

The recent study conducted by the research group in Rome is significant in regard to the NO/ONOO- cycle theory because it shows that three elements of the cycle are elevated in MCS patients (De Luca et al, Toxicology and Applied Pharmacology, 2010, April 27 Epub ahead of print). Those elements are the inflammatory cytokines, nitric oxide, and oxidative stress. Each of these measurements provides important confirmation of the disease mechanism proposed by Pall.



The inflammatory cytokines and nitric oxide elevation have never before been measured in MCS patients, although they have been shown to be elevated in animal models of MCS. Oxidative stress has been reported in two earlier studies of MCS patients, but the data provided in the De Luca et al study are much more extensive than are the earlier data. Consequently, these new data all provide important confirmation of the NO/ONOO- cycle as the central disease mechanism in MCS.

The NO/ONOO- cycle also is useful in understanding the role of toxic chemicals in MCS and the role of treatment. Each of the seven classes of chemicals implicated in MCS are thought to act indirectly to increase the activity of the NMDA receptors, which are glutamate receptors for controlling synaptic plasticity and memory function. This activity, in turn, leads to rapid increases in intracellular calcium (Ca2+), nitric oxide and peroxynitrite (ONOO-), acting to greatly stimulate the NO/ONOO- cycle.

"Many of the agents used by environmental medicine physicians to treat MCS patients can be viewed as lowering different parts of the cycle, and thus are validated in part by this mechanism," Pall said. "Consequently, the NO/ONOO- cycle mechanism can be viewed as validating therapeutic approaches used in environmental medicine in the U.S., in Germany and some other areas of Europe and in some other countries."

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"Altered redox and cytokine patterns suggest inhibition of expression / activity of metabolizing and antioxidant enzymes in MCS."

Following is the actual abstract of the scientific study to which Pall refers:

Biological definition of multiple chemical sensitivity from redox state and cytokine profiling and not from polymorphisms of xenobiotic-metabolizing enzymes

Chiara De Lucaa, Maria G. Scordob, Eleonora Cesareoa, Saveria Pastorea, Serena Mariania, Gianluca Maiania, Andrea Stancatoa, Beatrice Loretic, Giuseppe Valacchid, e, Carla Lubranoc, Desanka Raskovicf, Luigia De Padovac, Giuseppe Genovesic and Liudmila G. Korkinaa, *Toxicol Appl Pharmacol. 2010 Apr 27. [Epub ahead of print]*

Abstract

Background

Multiple chemical sensitivity (MCS) is a poorly clinically and biologically defined environment-associated syndrome. Although dysfunctions of phase I/phase II metabolizing enzymes and redox imbalance have been hypothesized, corresponding genetic and metabolic parameters in MCS have not been systematically examined.

Objectives

We sought for genetic, immunological, and metabolic markers in MCS.

Methods

We genotyped patients with diagnosis of MCS, suspected MCS and Italian healthy controls for allelic variants of cytochrome P450 isoforms (CYP2C9, CYP2C19, CYP2D6, and CYP3A5), UDP-glucuronosyl transferase (UGT1A1), and glutathione S-transferases (GSTP1, GSTM1, and GSTT1). Erythrocyte membrane fatty acids, antioxidant (catalase, superoxide dismutase (SOD)) and glutathione metabolizing (GST, glutathione peroxidase (Gpx)) enzymes, whole blood chemiluminescence, total antioxidant capacity, levels of nitrites/nitrates, glutathione, HNE-protein adducts, and a wide spectrum of cytokines in the plasma were determined.

Results

Allele and genotype frequencies of CYPs, UGT, GSTM, GSTT, and GSTP were similar in the Italian MCS patients and in the control populations. The activities of erythrocyte catalase and GST were lower, whereas Gpx was higher than normal. Both reduced and oxidised glutathione were decreased, whereas nitrites/nitrates were increased in the MCS groups. The MCS fatty acid profile was shifted to saturated compartment and IFNgamma, IL-8, IL-10, MCP-1, PDGFbb, and VEGF were increased.

Conclusions

Altered redox and cytokine patterns suggest inhibition of expression/activity of metabolizing and antioxidant enzymes in MCS. Metabolic parameters indicating accelerated lipid oxidation, increased nitric oxide production and glutathione depletion in combination with increased plasma inflammatory cytokines should be considered in biological definition and diagnosis of MCS.

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