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Summary

Mast cell activation in Multiple Chemical Sensitivity (MCS)
Haris Theoharides, **MD, PhD**
Professor and Vice Chair of Clinical Immunology and Director, Institute for Neuro-Immune Medicine-Clearwater, Nova Southeastern University.

Dr. Haris Theoharides' presentation explored the significant role of mast cells in the pathophysiology of Multiple Chemical Sensitivity (MCS), presenting a compelling case that mast cell activation may serve as a central mechanism underlying the condition. Drawing on decades of pioneering research, Dr. Theoharides emphasized that mast cells—immune cells distributed throughout the body, particularly at interfaces with the external environment such as the skin, respiratory tract, and gut—respond not only to allergens but also to a broad array of environmental triggers including pollutants, formaldehyde, toxins from fungi, and even psychological stress.

He explained that mast cells are unique in their ability to release over 100 different molecules, including histamine, cytokines, chemokines, and nerve-sensitizing substances, which act as molecular signals and can lead to inflammation, pain, and systemic symptoms commonly reported by MCS patients. Importantly, he noted that activation of mast cells does not always involve classical degranulation or histamine release, which occurs in allergies. Instead, non-degranulating activation pathways may still result in the release of pro-inflammatory mediators that are capable of disrupting neurological and immune function. This suggests that MCS can be attributed to a mechanism that is completely independent of allergies.

Dr. Theoharides clarified that many diagnostic terms involving mast cells are often used interchangeably and inaccurately, contributing to confusion in both clinical and research contexts. He distinguished between mast cell disorders like mastocytosis, allergies, and idiopathic mast cell activation syndromes—arguing that much of what is labelled "unspecified" may, in fact, overlap with MCS. He acknowledged the current lack of diagnostic codes for MCS in countries like the

United States and underscored the need for better-defined clinical criteria and objective biomarkers.

He provided evidence through various studies, which demonstrate that mast cells are activated by bacteria, fungi, pesticides, herbicides, and a plethora of chemicals. Due to their distribution in various body systems, mast cell activation syndrome has far-reaching effects on one's respiratory, olfactory, immune, neural, and dermatological systems. The causes and symptomatic profile of mast cell activation syndrome overlaps that of MCS, which has been incorrectly labelled "allergies, unspecified". Dr. Theoharides added that stress could be a significant exacerbating factor. Through the release of corticotropin-releasing hormone (CRH), stress can also activate mast cells without histamine involvement, leading to vascular changes and amplified sensitivity to environmental triggers. This may help explain why MCS symptoms often worsen following trauma, infection, or emotionally distressing events. This could explain the positive-feedback cycle of MCS. Individuals with MCS often lose their social lives following their diagnosis, leading to stress, and further worsening of their symptoms.

Another major focus of his talk was on potential therapeutic approaches, particularly natural flavonoids in relieving symptoms of mast cell activation syndrome. Dr.Theoharides presented data comparing luteolin—a plant-derived flavonoid—with cromolyn sodium, a traditional mast cell stabilizer. In head-to-head studies using cultured human mast cells, luteolin consistently outperformed cromolyn in reducing inflammatory mediator release. In some cases, cromolyn paradoxically increased cytokine production. Testing the efficacy of similar treatment for individuals with MCS syndrome will further strengthen the link between mast cell activation and multiple chemical sensitivities.

In closing, Dr. Theoharides stressed that whether or not mast cell activation is ultimately deemed the root cause of MCS is less important than our responsibility to help patients. Given the overlap between MCS symptoms and those seen in mast cell-related conditions, addressing mast cell activity through avoidance of triggers and evidence-based supplementation could meaningfully improve patient outcomes. He urged the medical community to move past outdated psychosomatic interpretations of MCS and recognize the condition as a biologically plausible and treatable illness. His concluding remarks called for continued research, compassionate care, and the development of diagnostic tools that validate patient experiences and support clinical decision-making.

Citations

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