By **Eric Gordon, MD** and **Nafysa Parpia, ND**

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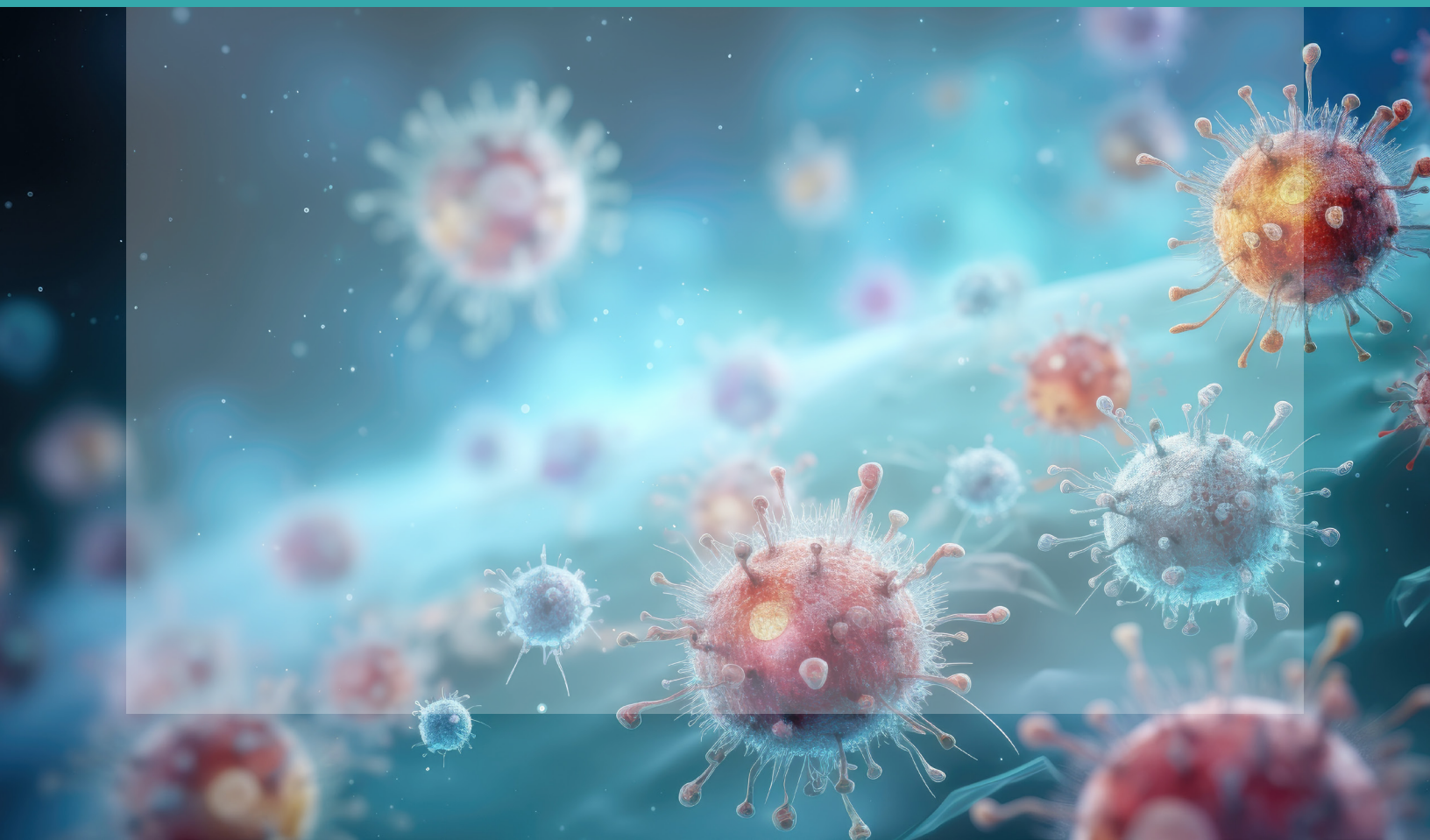
When Symptoms Don't Add Up

What Your Doctor Might Be Missing About

Mast Cell Activation Syndrome



ABOUT THE AUTHORS

Eric Gordon, MD

Eric Gordon, MD, Clinical Director at Gordon Medical Associates and President of Gordon Medical Research Center. He has focused on bringing together leading international medical researchers and cutting-edge clinicians focusing on ME/CFS, Lyme disease, environmentally acquired illness, and autoimmune diseases.

He also combined forces with Dr. Robert Naviaux and his research into metabolomics, mitochondrial function, and chronic inflammatory disease. Dr. Gordon has co-authored with Dr. Naviaux the groundbreaking study, "Metabolic Features of Chronic Fatigue Syndrome," published in the Proceedings of the National Academy of Science (PNAS).

Gordon Medical Associates is also a collection site for the Lyme Disease Biobank, providing patient samples to researchers worldwide.

Nafysa Parpia, ND

Dr. Nafysa Parpia is a board-certified naturopathic doctor and the Director of Naturopathic Medicine at Gordon Medical Associates.

Throughout her career in holistic medicine, she has focused on treating patients with complex chronic illnesses. She specializes in tick-borne illness/Lyme disease, environmentally acquired illness, mold/mycotoxin illness, autoimmunity, Long COVID, ME/CFS and MCAS (mast cell activation syndrome).

Dr. Parpia's extensive knowledge has helped people worldwide overcome difficult-to-treat medical conditions. She uses cutting-edge laboratory tests and deep intuition applied to the full range of scientific data to create comprehensive treatment plans that are highly personalized.

Her targeted system of care includes a synergistic blend of allopathic and functional medicine diagnoses paired with treatment that includes regenerative medicine, micronutrient therapies, peptide therapies, bioidentical hormone therapy, botanical medicine, pharmaceuticals, and psychoemotional support.

INTRODUCTION

Mast Cell Activation Syndrome (MCAS) represents one of medicine's most complex and frequently misunderstood conditions.

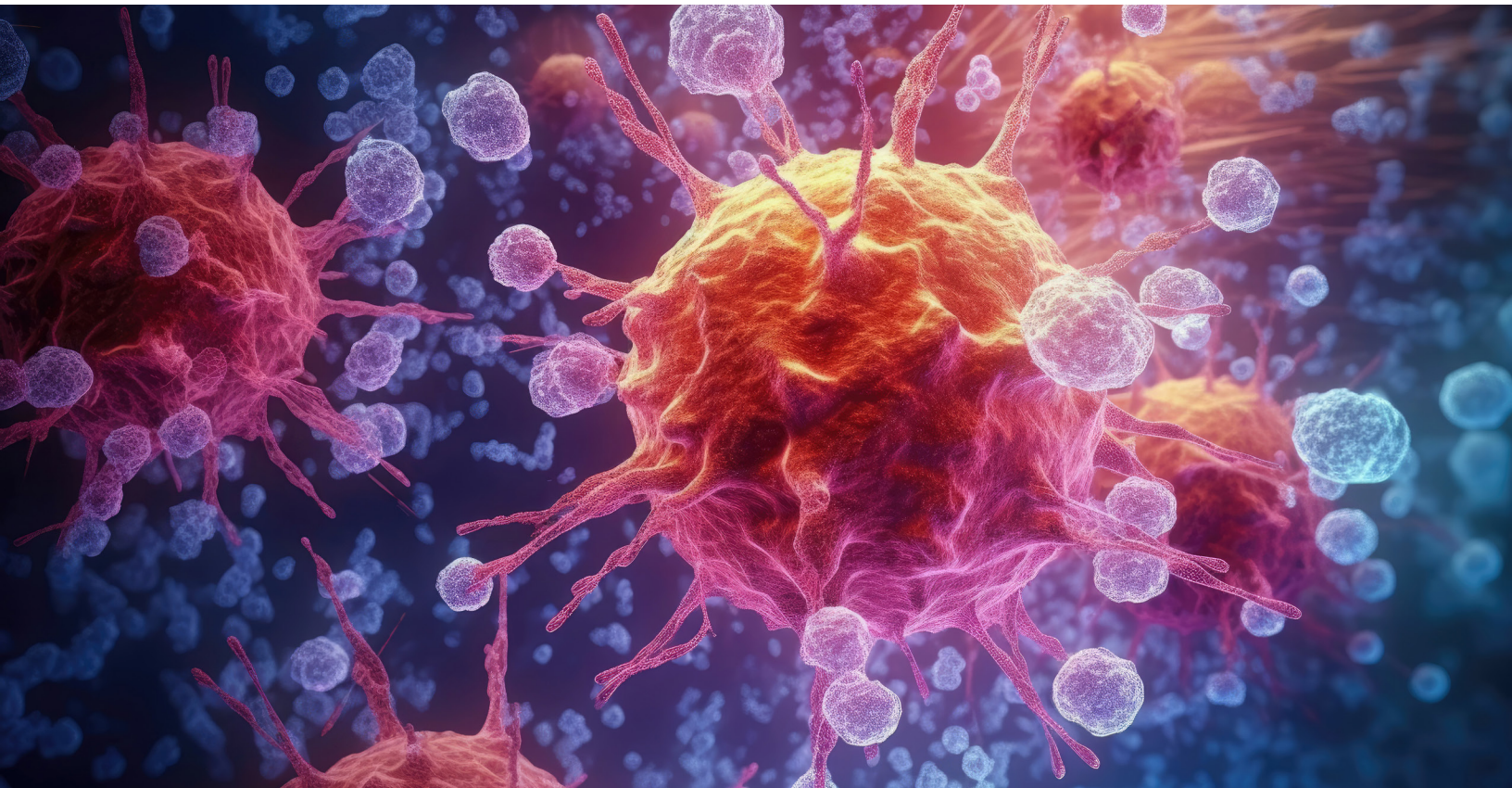
As our understanding of immune system disorders continues to evolve, MCAS has emerged as a critical piece in explaining why many patients experience multiple, seemingly unrelated symptoms across various body systems.

Current estimates suggest that as many as one in six people may have some predisposition to this condition, making it far more common than previously recognized.

What makes MCAS particularly challenging is its ability to affect multiple body systems simultaneously and its tendency to present differently in each individual. Traditional medical approaches struggle with the diagnosis of MCAS for several reasons. The first is the issue of diagnosis itself. The conventional allergists use a handful of tests to diagnose MCAS and are still stuck thinking of it as a variant of mastocytosis, a cancer of mast cells.

The second reason primary care providers and specialists do not consider MCAS is because they tend to compartmentalize symptoms by organ system, while MCAS can create symptoms across every part of the body. This leads to treatments for many specific ailments, such as migraines, asthma, reflux esophagitis, gastritis, IBS, recurrent sterile urinary tract infections, menstrual symptoms, etc.

Without realizing this, in many people, MCAS is driving or exacerbating all these diverse ailments.



The Role of Mast Cells in Health and Disease

Understanding Your Body's First Line of Defense

Mast cells are sophisticated components of your immune system that serve as a crucial line of defense against external and internal threats. These specialized cells are found throughout your body, particularly in areas that interface with the environment. Think of them as highly trained security guards strategically positioned at every entry point and throughout your internal systems, ready to protect you from potential dangers.

The positioning of mast cells is not random.

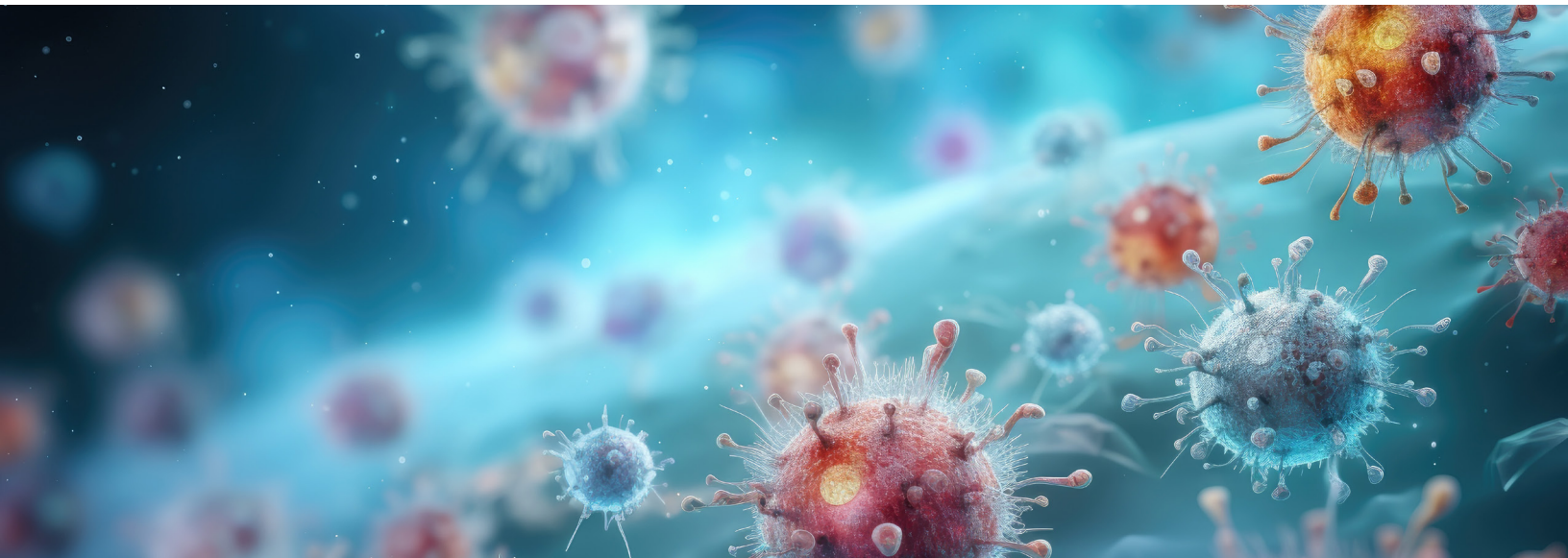
Their particular concentration is in areas where your body meets the outside world, including the skin, respiratory tract, digestive system, and urogenital system tissues. This strategic placement allows them to be among the first immune cells to encounter and respond to potential threats, whether they're viruses, bacteria, toxins, or other harmful substances. Mast cells are also found in the bones, the brain, and surrounding the nerves as an important part of the innate immune system.

In a healthy person, mast cells respond appropriately to threats through a complex series of defensive actions. When they encounter a potentially dangerous substance, they alert other immune cells and help coordinate the body's defense response.

When dysfunctional, the mast cell can undergo persistent release of more than a thousand different chemicals and inflammatory mediators designed to protect the body during an acute insult. How many of these chemicals, and which ones, depend upon the circumstances.

Patients and doctors alike tend to think only about histamine, however this is only one of the many chemicals released.

These defensive chemicals serve multiple purposes. Some help fight off invading organisms directly, while some signal other immune cells to join the response. Still, others help modify local tissue conditions to make them less hospitable to invaders. After the threat is eliminated, normal mast cells return to their resting state, ready to respond to the next challenge.



When Protection Becomes Problematic

MCAS develops when these normally protective cells become dysfunctional, leading to inappropriate and excessive activation. Many patients who develop MCAS may have had discrete populations of dysfunctional mast cells from an early age. This is seen with inhalant allergies, skin sensitivity to mild irritants, and many other mild allergic-type symptoms.

Generally, MCAS develops after either a persistent trigger or chronic low-grade inflammation.

Some acute infections, such as COVID, can also act as the event that produces MCAS.

These triggers vary widely and might include:

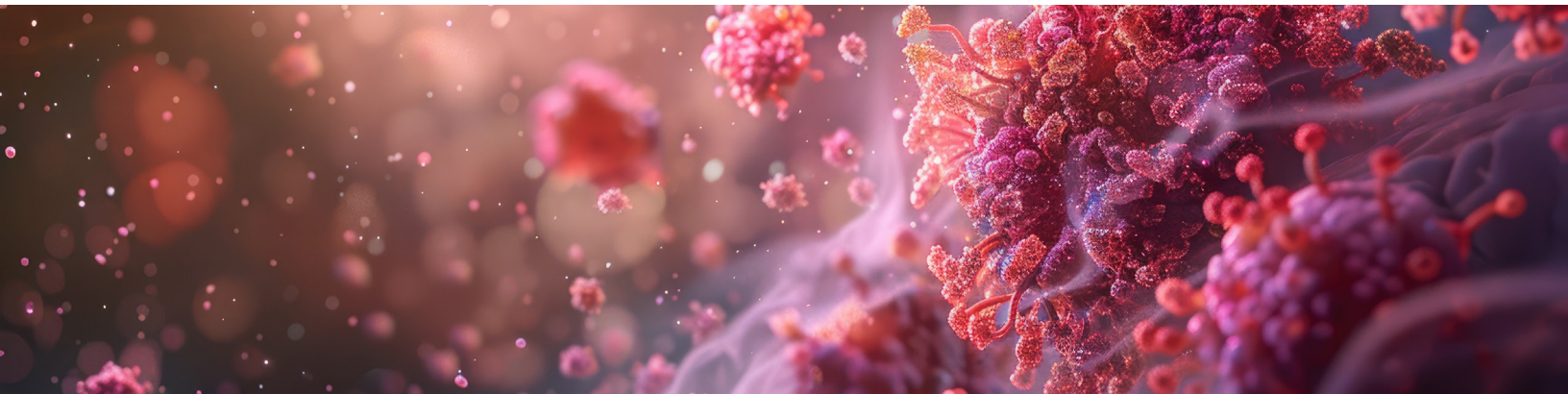
- Infections (viral, bacterial, or other types)
- Environmental toxins
- Physical trauma
- Severe emotional stress
- Chemical exposures
- Mold exposure
- Various other environmental challenges

The progression of MCAS can take different paths. Some individuals report a lifetime of subtle symptoms that suddenly worsen after a specific trigger event. These patients often realize in retrospect that they had been dealing with minor manifestations of the condition for years before a major event pushed their system over a threshold. Others can identify a clear starting point for their symptoms, often following a severe illness or significant life stress.

What makes MCAS particularly challenging is that once mast cells become dysfunctional, they may continue to react inappropriately even after the initial trigger is removed. This creates a chronic condition that requires ongoing management rather than a simple one-time treatment.

The Athletic Paradox

An interesting aspect of MCAS that challenges conventional understanding is its occurrence in seemingly healthy, athletic individuals. Many MCAS patients were highly functional before their condition became apparent, including professional athletes and other physically active individuals. However, upon careful examination of their medical histories, subtle signs of underlying dysfunction often become apparent. These individuals were often able to compensate for their mast cell dysfunction through their overall health and fitness until a triggering event overwhelmed their compensatory mechanisms.



Beyond Histamine
The Complex Chemistry of Mast Cells

The chemistry of mast cells is far more complex than many people, including healthcare providers, realize. While most doctors learn about mast cells primarily in relation to allergic responses and histamine release, these cells can produce more than 1,000 different chemical mediators, each serving specific functions in the immune response.

Understanding Mast Cell Mediators

Histamine, while important, represents just one piece of a much larger puzzle. Here's a closer look at some key mediators:

Histamine acts as a crucial signaling molecule that can:

- Control blood vessel dilation
- Affect stomach acid production
- Influence brain function
- Regulate sleep-wake cycles
- Impact mood and energy levels

Heparin, a natural blood thinner produced by mast cells, plays multiple roles:

- Prevents inappropriate blood clotting
- Influences blood vessel function
- Affects healing processes
- Can impact menstrual bleeding patterns
- Contributes to tissue repair

Cytokines serve as powerful communication molecules that:

- Coordinate immune responses
- Direct inflammation
- Influence mood and behavior
- Affect tissue repair and healing
- Impact energy levels and metabolism

These mediators don't act in isolation. Instead, they work together in complex ways, which helps explain why MCAS can cause such diverse symptoms and why treatment often requires a multi-faceted approach.

How MCAS Affects the Body

The systemic nature of MCAS means it can affect virtually every system in the body. Understanding these diverse effects helps explain why diagnosis can be challenging and why treatment often requires a comprehensive approach.

The Respiratory System

The respiratory system frequently shows significant effects from MCAS. The presence of mast cells throughout the respiratory tract, from the nasal passages to the smallest airways in the lungs, means that activation can cause widespread inflammation and reactivity. Patients may experience anything from mild nasal congestion to severe asthma-like episodes.

These respiratory manifestations can be particularly challenging because they often mimic other conditions like asthma or allergies. However, unlike traditional allergic responses, MCAS-related respiratory symptoms may occur without obvious triggers and may not respond well to conventional treatments. Many patients find their breathing problems are accompanied by other systemic symptoms, providing a clue that MCAS might be the underlying cause.

The impact on breathing can significantly affect daily life, limiting exercise tolerance and making routine activities more challenging. Some patients find their symptoms worsen with physical exertion or exposure to environmental triggers that wouldn't bother most people.

The Gastrointestinal System

The digestive tract contains an especially high concentration of mast cells, making it particularly vulnerable to MCAS-related symptoms. Patients often experience a complex array of digestive issues that can include nausea, vomiting, diarrhea, constipation, and abdominal pain. These symptoms can vary in intensity and may seem to have no clear pattern or trigger.

One particularly challenging aspect of gastrointestinal involvement is the development of food sensitivities. Many MCAS patients find they react to foods they previously tolerated well. These reactions aren't typical allergic responses but rather mast cell activation events that can cause both local and systemic symptoms. The unpredictable nature of these reactions can make eating a stressful experience and may lead to significant dietary restrictions.

Gastroparesis, or delayed stomach emptying, can also occur in MCAS patients. This condition can cause feelings of fullness, bloating, and discomfort, even with small meals. The connection between MCAS and gastroparesis illustrates how mast cell dysfunction can affect not just the immune response but also basic organ function.

Diarrhea is a common manifestation of MCAS and inflammatory bowel disorders such as Crohn's disease and Ulcerative colitis can have significant mast cell components.

The Neurological System

The neurological manifestations of MCAS can be among the most debilitating and confusing for both patients and healthcare providers. Mast cells are present throughout the nervous system, including in the brain, and their activation can lead to a wide range of neurological symptoms.

Cognitive difficulties, often described as “brain fog,” represent one of the most common neurological manifestations. Patients may struggle with memory, concentration, and word-finding. These cognitive impacts can significantly affect daily life; making work, study, and even basic tasks more challenging.

Anxiety and mood changes often accompany MCAS, though it’s important to understand these are physiological rather than purely psychological responses. The release of inflammatory mediators can directly affect brain function and neurotransmitter systems, leading to changes in mood and emotional regulation.

The Reproductive System

MCAS can significantly impact reproductive health in both women and men. In the uterus, where mast cells are abundant, activation can lead to abnormal bleeding patterns, pelvic pain, and various types of dysfunction. These effects can be particularly challenging because they may be dismissed as normal menstrual problems rather than recognized as part of a systemic condition.

For women, MCAS can affect:

- Menstrual patterns
- Fertility
- Pregnancy
- Hormonal balance
- Sexual function

In men, MCAS might impact:

- Reproductive organ health
- Fertility
- Hormonal function
- Sexual health

The Cardiovascular and Autonomic Systems

MCAS can significantly impact heart function and autonomic nervous system regulation. Many patients develop POTS (Postural Orthostatic Tachycardia Syndrome) or other forms of dysautonomia as part of their MCAS presentation. The connection between MCAS and autonomic dysfunction appears to be bidirectional, with mast cell activation potentially triggering autonomic symptoms and autonomic stress potentially triggering mast cell activation.

Understanding the Connection to Chronic Illness

MCAS rarely exists in isolation. Instead, it often appears alongside other chronic conditions, creating complex patterns of illness that can be challenging to untangle. Understanding these connections is crucial for both diagnosis and treatment.

The Chronic Infection Connection

Chronic infections play a crucial role in many cases of MCAS. Conditions such as Lyme disease, Bartonella, Epstein-Barr virus, and other persistent infections can trigger mast cell dysfunction. Many patients who initially appear to have purely infection-related symptoms may actually be experiencing MCAS triggered by these infections.

The relationship between infections and MCAS can take several forms:

- Acute or chronic infections may trigger initial MCAS development
- Chronic infections may perpetuate ongoing mast cell activation
- Persistent mast cell activation exacerbates immune dysregulation, making individuals more susceptible to chronic infections
- Treatment of underlying infections may help resolve MCAS symptoms

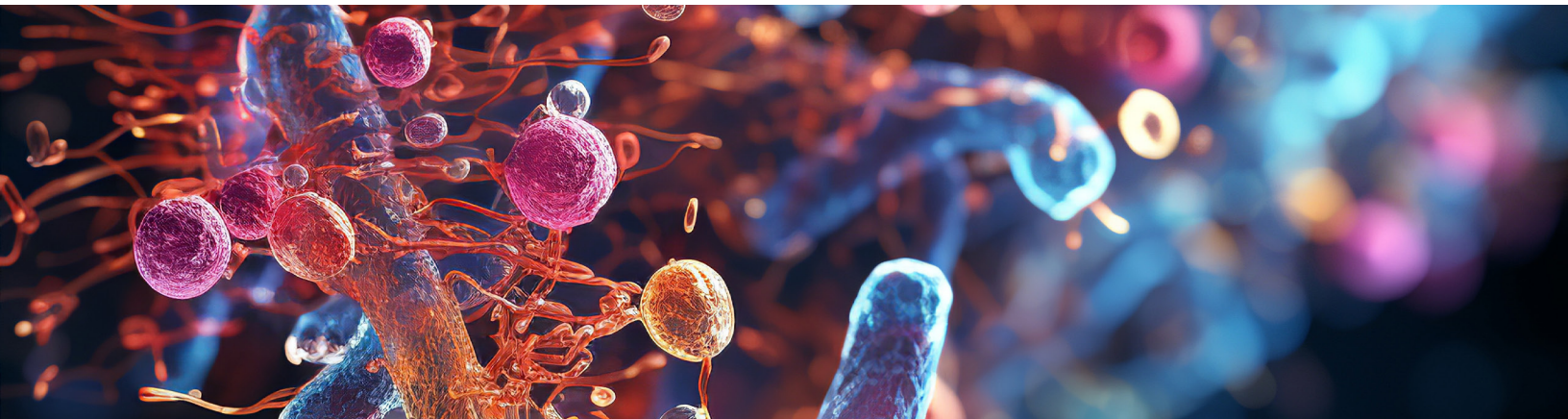
The Connective Tissue Connection

A significant pattern has emerged linking MCAS with connective tissue disorders, particularly Ehlers-Danlos Syndrome (EDS) and the EDS 3 subtype. This connection appears to be more than coincidental, as mast cells play a crucial role in connective tissue health and regulation.

The chemicals released persistently by mast cells can weaken connective tissue, thus aggravating hypermobility issues.

Understanding POTS and Dysautonomia

The connection between MCAS and dysautonomia, particularly POTS, represents another important pattern in chronic illness. Many patients experience both conditions and treating one often helps improve the other. This relationship highlights the interconnected nature of immune function, autonomic nervous system regulation, and the cardiovascular system.



Diagnosing MCAS
Challenges and Approaches

The diagnosis of MCAS presents unique challenges that can require both clinical expertise and careful testing procedures. Unlike many medical conditions, there isn't a single definitive test that can confirm or rule out MCAS. The complexity of diagnosis stems from several factors, including the wide range of symptoms and the technical challenges of testing.

The Testing Challenge

Laboratory testing for MCAS requires special handling and timing. The mediators released by mast cells are often unstable and break down quickly if samples aren't processed correctly. This means that blood and urine samples must be handled with specific protocols, including proper temperature control and rapid processing.

A refrigerated centrifuge is often necessary for processing samples, and even then, timing is crucial. The samples must be kept cold throughout the entire process, from collection through testing. This technical requirement alone can make accurate testing difficult in many medical settings.

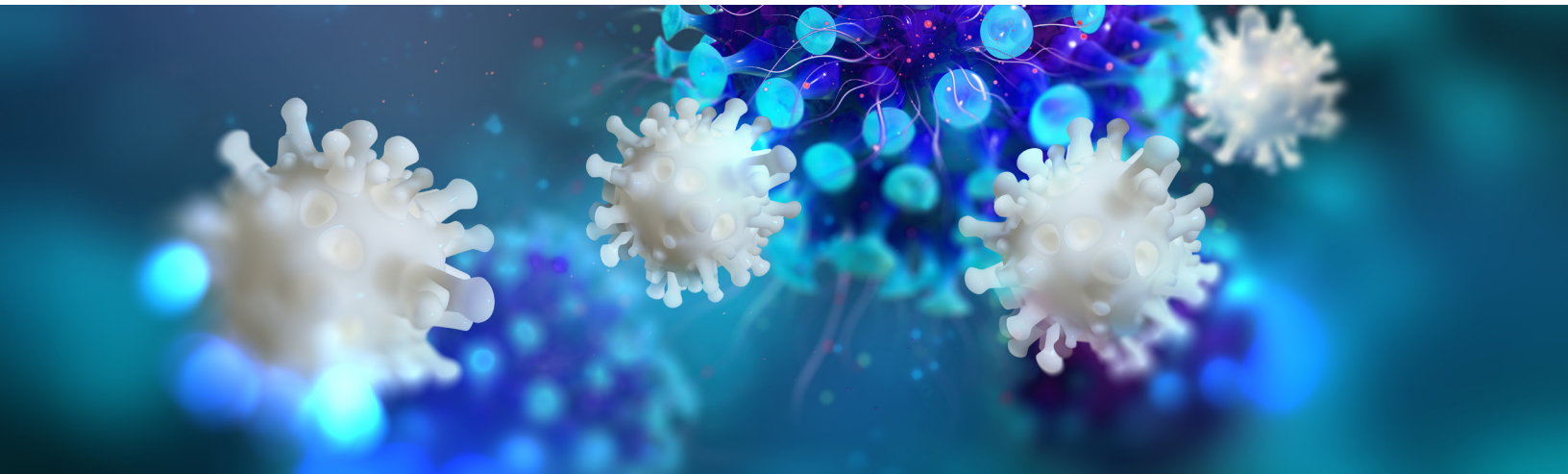
Even with perfect handling, current testing methods can only measure a small fraction of the mediators that mast cells produce. Given that mast cells can release over 1,000 different chemicals, testing for just a few may miss significant dysfunction in other areas.

Clinical Diagnosis

Because of these testing challenges, many practitioners have begun to rely more heavily on clinical presentation for initial diagnosis and treatment decisions. Key clinical indicators include:

- The presence of symptoms in multiple body systems
- Symptoms that wax and wane over time
- Reactions to triggers that are particular for that person
- Improvement with antihistamines or mast cell stabilizers
- Family history of similar symptoms
- Often MCAS patients do not have common allergy symptoms of hives, runny noses, and itchy eyes

Clinical experience suggests that about 90% of suspected cases show evidence of mast cell dysfunction when properly tested. However, negative test results don't necessarily rule out MCAS, particularly if clinical signs strongly suggest the condition.



Treatment Approaches
A Comprehensive Strategy

Treatment of MCAS typically requires a multi-faceted approach that must be tailored to each individual patient. The complexity of the condition means that no single treatment works for everyone, and most patients need a combination of approaches to achieve optimal results.

Foundation Treatments

The cornerstone of MCAS treatment often begins with a low histamine diet. Vitamin D optimization is also important. This seemingly simple intervention can have profound effects because mast cells have vitamin D receptors on their surface. When vitamin D levels are low, this can signal danger to mast cells, potentially triggering inappropriate activation. Correcting vitamin D deficiency can help stabilize mast cell function.

Antihistamines often form the first line of medication treatment. These include both second-generation H1 blockers (such as Claritin, Zyrtec, Allegra, and Xyzal) and H2 blockers (such as Pepcid and Tagamet). If there is a poor response to the 2nd generation H1 blockers, the first generation antihistamines are then trialed. However, many people are sensitive to the sedating and drying side effects of these medications.

Patients often need to try different formulations of these medications, as some people react to the inactive ingredients or fillers in certain brands. What works well for one patient might cause reactions in another. This variation in response often necessitates a careful trial and error approach to find the right combination for each individual.

Advanced Treatment Options

Cromolyn sodium represents an important treatment option for many MCAS patients. This medication is particularly interesting because it's not absorbed systemically - it primarily affects mast cells in the gastrointestinal tract. Despite Cromolyn's local effect in the gut it can lower inflammation systemically.

This generalized response occurs because calming mast cells in the gut reduces local inflammation and diminishes the release of inflammatory signals from the gut. The reduction of these inflammatory cytokines quiets mast cell activation throughout the body. This is just one example of the central role an inflamed gut can have on our whole physiology.

Ketotifen, another valuable medication, can help stabilize mast cells not only in the gut but throughout multiple systems in the body. When patients can tolerate or adjust to its sedating side effects, it can provide significant relief from the full array of MCAS symptoms. Like all MCAS treatments, responses to ketotifen vary considerably between individuals.

Natural Approaches

Several natural treatments can play important roles in MCAS management:

- **Vitamin C** serves as a natural antihistamine and can help stabilize mast cells. Some patients find regular vitamin C supplementation helps reduce their reactivity and improve their symptoms.

- **Quercetin** and **luteolin** are natural compounds that can stabilize mast cells. These are an excellent place to start trying to modulate MCAS symptoms.

- The addition of **DAO (diamine oxidase)**, an enzyme in our gut that breaks down excess histamine, can also be helpful. This is particularly helpful for patients with genetically lower production of this enzyme.

Living with MCAS
A Patient's Perspective

Living successfully with MCAS requires patience, persistence, and a comprehensive approach to health. Many patients find their journey involves both triumphs and setbacks, making emotional resilience particularly important.

Finding the Right Healthcare Team

Working with healthcare providers who understand MCAS is crucial. The condition's complexity means that treatment often needs to be personalized and adjusted based on individual response. Patients may need to try various combinations of medications and treatments before finding what works best for them.

Understanding Triggers and Patterns

Many MCAS patients learn to identify their personal triggers and patterns over time.

These might include:

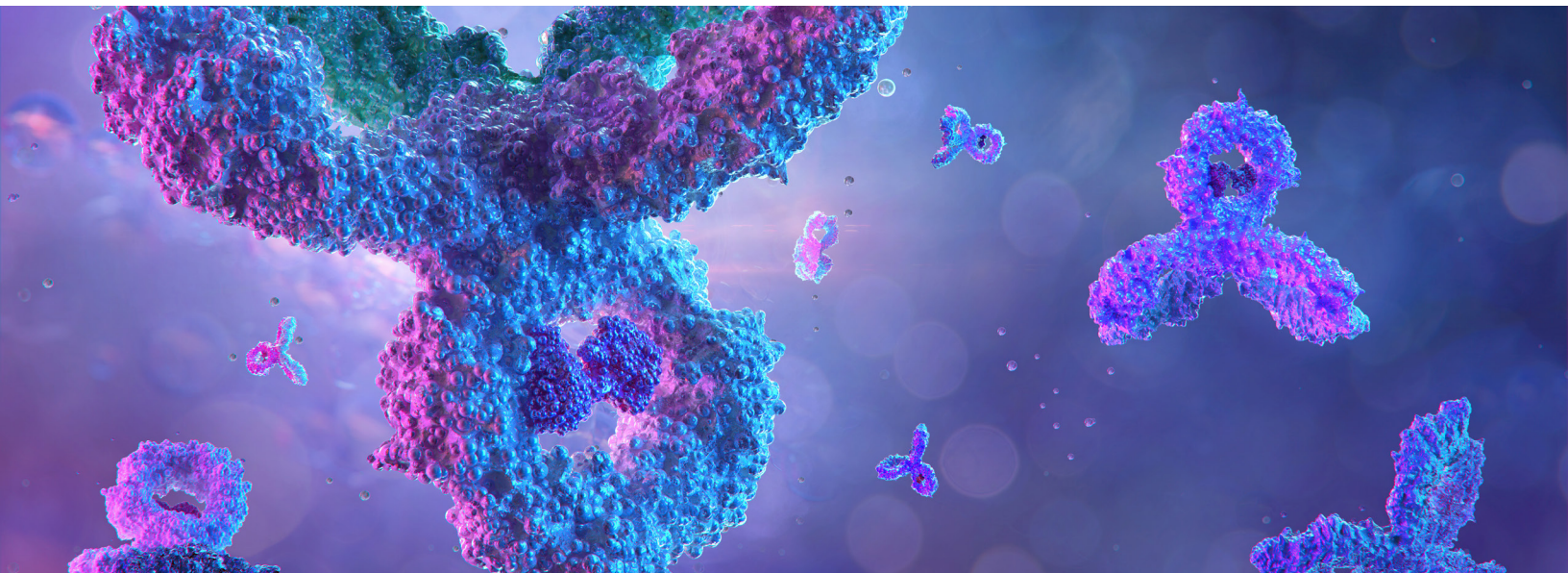
- Environmental exposures
- Foods
- Physical stressors
- Emotional stress
- Weather changes
- Hormonal fluctuations

Managing Daily Life

Successfully managing MCAS often requires adjustments to daily routines and lifestyle.

This might involve changes to:

- Diet and eating patterns
- Sleep habits
- Exercise routines
- Work environments
- Social activities



The Future of MCAS Treatment and Research

The field of MCAS treatment continues to evolve as medical understanding grows. Current research focuses on several key areas:

Improving Diagnosis

Better testing methods are being developed to more accurately identify mast cell dysfunction. These may eventually allow for earlier diagnosis and more targeted treatment approaches.

Understanding Triggers

Research continues into what causes mast cell dysfunction and how to prevent it. This includes studying both environmental triggers and genetic factors that might predispose individuals to MCAS.

Developing New Treatments

Work is ongoing to develop more effective treatments for MCAS. This includes both new medications and a better understanding of how to use existing treatments more effectively.

MCAS represents a complex medical condition that requires a comprehensive understanding and individualized approach to treatment.

While it presents significant challenges, proper management can lead to substantial improvements in quality of life. The key lies in working with knowledgeable healthcare providers, maintaining patience during the treatment process, and taking a holistic approach to health and wellness.

As research continues and medical knowledge expands, new opportunities for diagnosis and treatment will emerge. For now, focusing on comprehensive care while remaining hopeful about future developments offers the best path forward for most patients.

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About Gordon Medical Associates

As the premier clinic for Lyme disease, tick-borne illnesses, and environmentally acquired illnesses on the West Coast, we've earned a reputation as the go-to destination for those seeking answers and solutions.

Our clinic serves as a sought-after think tank for complex and chronic illnesses, where cutting-edge research and compassionate care converge to provide unparalleled support for our patients.

Learn more at: www.GordonMedical.com

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