Mast Cell Activation Syndrome - A Physicians Guide

MAST CELL ACTION

What is Mast Cell Activation Syndrome (MCAS)?

MCAS is a mast cell disorder that involves an over-activation of mast cells without an increase in their number. It differs from mastocytosis which is characterised by abnormal accumulation of proliferation of mast cells. Mastocytosis is therefore typically associated with an elevated serum mast cell tryptase level; usually normal in MCAS. MCAS presents with a wide range of allergic or inflammatory symptoms across multiple body systems. These symptoms can be quiescent for periods and then flare, with flares or exacerbations varying in duration or intensity. MCAS affects both children and adults; onset is unpredictable.

Symptoms

Symptoms are often chronic and persistent. Treatment, drug and non-drug (e.g. acupuncture, physiotherapy, and psychology), aim to help mitigate and control but not necessarily totally alleviate symptoms. Triggers can vary widely. They need not be classical allergens, and therefore can include:

- Hormonal fluctuations and intercurrent acute infections.
- Aerosols, perfumes, odours (from for example cleaning agents)
- Medications and chemicals (such as drug colourants or excipients).
- Foods and pollens.
- Temperature changes. exercise and stress.

Dermographic

- Flushing/redness
- Hives or wheals
- Itching with or without a rash
- Swelling

Cardiovascular

- Chest pain
- Low blood pressure
- Fast heart rate
- Fainting or light-headedness

Respiratory

- Sore throat
- Hoarseness
- Wheezing
- Shortness of breath
- Throat swelling

Genital and urinary

- Genital pain or swelling
- Pain when urinating
- Vaginal pain, discharge or itching
- Bladder urgency or loss of control

Gastrointestinal

- Bloating
- Stomach cramps or pain
- Reflux
- Feeling or being sick
- Diarrhoea
- Constipation
- Dumping syndrome
- Food allergies or intolerance

Neurological

- Headache, migraine
- Brain fog
- Numbness, pain or tingling skin
- Anxiety
- Behavioural issues, irritability

Musculoskeletal

- Joint & muscle pain
- Osteoporosis
- Loss of bone mass

Nasal-ocular

- Nose congestion
- Eye watering and itching

General

- Extreme tiredness
- Anaphylaxis

Diagnostic Criteria

Blood tests may consistently be normal. Diagnosis requires a systematic approach:

1. Clinical Symptoms: Episodic or persistent, involving multiple body systems.
2. Response to Treatment: Symptom improvement with mast cell-targeted therapies.
3. Mediator Tests: Elevated mast cell mediators in blood or urine during symptoms.
4. Exclusion of Other Conditions: Differential diagnosis is essential as some symptoms overlap.

In some cases, a definitive diagnosis may not be possible, leading to a classification of "suspected MCAS." Diagnostic frameworks include Molderings et al. (2011), Valent et al. (2019), and Giannetti et al. (2021) and Diagnosis of mast cell activation syndrome: a global “consensus-2” L Afrin et al (2021)

Comorbidities

MCAS frequently coexists with other conditions. The exact relationship between MCAS and these conditions remains under investigation. Comorbidities include:

- Connective Tissue Disorders: Ehlers-Danlos Syndrome (EDS), Marfan Syndrome
- Dysautonomia: Postural Orthostatic Tachycardia Syndrome (PoTS)
- Long Covid and Chronic Fatigue Syndrome (CFS)
- Neurological Conditions: migraine, Autism

Management and Treatment

The primary goal of treatment is symptom management through a combination of self-care and pharmacological interventions. While no medications are currently licensed specifically for MCAS, various drugs can help stabilise mast cells and alleviate symptoms. Key management strategies include identifying and avoiding triggers, implementing dietary modifications, and utilising stress management techniques alongside appropriate pharmacological support.

Treatment typically follows a stepwise approach, starting with H1 and H2 antihistamines, followed by mast cell stabilisers, leukotriene receptor antagonists, and other adjuncts as needed. Dosing is often individualised, with some patients requiring higher-than-standard doses for symptom control. NICE Evidence Summary on Chronic Urticaria advises that the standard dose of antihistamine could increase up to 4-fold where required (incremental up-dosing in poor response, off-licence use)

Excipients in medications can act as triggers, leading to variable tolerability between different brands. Any changes in medication should be made one at a time, with patients keeping a symptom diary to monitor their response. If a patient experiences issues with a specific brand, prescribing an alternative formulation may improve tolerability. Although antihistamines are available over the counter, prescribing them may be more appropriate for patients requiring higher doses to ensure consistent access and adherence to treatment.

Category	Medication	Purpose
H1 blockers	Cetirizine, Fexofenadine, Loratadine	Reduce histamine effects
H2 blockers	Famotidine	Manage gastric symptoms
Leukotriene blockers	Montelukast	Address leukotriene effects
Mast cell stabilisers	Sodium cromoglicate	Prevent mediator release
Mast cell stabilisers	Ketotifen	Prevent mediator release
Corticosteroids	Prednisolone	Reduce inflammation symptoms
Bioflavonoids	Quercetin	Natural mast cell stabilisers
Vitamins	Vitamin C, Vitamin D, Probiotics, Magnesium	Support stabilising mast cells, control histamine levels & histamine production
Emergency medication	Adrenaline	Anaphylaxis management
	Low Dose Naltrexone*	Mast cell stabilisers

** Evidence base is limited, but numerous reports suggest potential benefits.*

Visit The LDN Research Trust for more information & prescriber info: ldnresearchtrust.org

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Additional Information: For further guidance and resources, including more on testing and management, see the 'Health Professionals' tab on the Mast Cell Action website (www.mastcellaction.org). You can also join our professional network to receive important updates

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