MAST CELL ACTION

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Patient Information Forum

Primary Care Guide to MCAS

A Comprehensive Guide to Mast Cell Activation Syndrome for Primary Care Physicians



> As a primary healthcare practitioner, understanding MCAS has helped me to build better and more effective referrals for diagnosis and treatment options for my patients.



Registered Charity Number 1164917

MAST CELL ACTION

Welcome

Do you have patients with multiple, systemic inflammatory symptoms?

Thank you for your interest in learning about Mast Cell Activation Syndrome (MCAS).

MCAS is a complex and often under-recognised condition in which mast cells release excessive amounts of mediators, causing a wide range of systemic symptoms. Many doctors tell us that they are increasingly seeing MCAS in their patients, and need the tools to help them confidently manage it in primary care.

Patients with MCAS can take many years to get a correct diagnosis. They often undergo multiple expensive and invasive medical tests, and are referred to multiple specialists. This costs the NHS in time and money, and is also distressing for patients.

Although often considered a rare disease, recent studies show that up to 17% of the population may be affected.

We hope that this guide will serve as a useful, practical tool to support you with recognising and treating MCAS in your practice.

How To Use This Guide

We've split the information into different sections, so you can find 'at a glance' information, or more in-depth detail, which we hope you will return to again and again.

- There is a 1-page Overview on Page 4 if you are looking for a quick guide.
- Sections 2 - 11 cover the aetiology and pathology, the clinical features and symptoms, diagnosis and testing, and the medical management of MCAS. These can be read together or as stand-alone leaflets.
- You'll find case studies on Pages 8 and 14 to help you recognise MCAS in your clinic.

The coloured boxes throughout are coded, according to the type of information within.

Key Information **Clinical Pearls** **Action** **Caution**

We hope that this guide will help you provide best practice care for your MCAS patients and improve their health outcomes significantly.

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Key Information

Clinical Pearls

Action

Caution

1 Recognising & Managing MCAS Overview

Key Information
Clinical Pearls
Action
Caution

Mast Cell Activation Syndrome (MCAS) is part of a spectrum of mast cell disorders characterised by abnormal mast cell activation and mediator release, without evidence of clonal mast cell proliferation.

MCAS affects both children and adults and may present at any age. Symptoms are often long-standing but under-recognised, there may be mild or intermittent symptoms from childhood which escalate in adulthood, or symptoms may be severe from birth. Sometimes a clear precipitating event precedes escalation of symptoms, including infection, surgery, stress, hormonal changes.
The condition is frequently characterised by unpredictable, relapsing–remitting symptoms involving multiple organ systems.

Patient presents with a multisystem constellation of allergy-like and inflammatory symptoms that remains unexplained by conventional investigation and are refractory to standard treatment.

Obtain a detailed history of symptoms and triggers (Checklist on P18 may help)

Use clinical judgement to rule out differential diagnoses.

Consider - Does the patient have any of the following?

Multi-speciality referral history

Other historical symptoms that are potentially mast-cell mediated?

A relapsing–remitting pattern of illness, often without an obvious unifying diagnosis

Family history of similar symptoms

Food, medication, or environmental intolerances

Common co-morbid conditions?
- Hypermobility spectrum disorders, EDS. Hypermobility
- PoTS and autonomic nervous system dysfunction
- Long COVID, (ME/CFS)
- Autism, ADHD

Symptoms affecting multiple body systems, such as:
- Skin (flushing, rashes, hives, itching, dermographism)
- Gastrointestinal (abdominal pain, diarrhoea, constipation, nausea, bloating)
- Respiratory (wheeze, throat tightness, breathlessness)
- Cardiovascular (palpitations, dizziness, fainting, chest pain)
- Neurological (headaches, brain fog, fatigue, mood changes)
- General (fatigue, muscle or joint pain, chemical/medication/food sensitivities

Referrals
Many patients with MCAS may be adequately managed in Primary Care. However, referral may be required for
- Ongoing symptoms that are not adequately controlled by first-line treatment
- Patients with recurrent anaphylaxis
- Those needing psychological support to cope with severe symptoms
- History of anaphylaxis
- Need for advanced diagnostic testing
- Suspected clonal mast cell disorders

Affirmative answers to the above are often indicative of MCAS, but absence does not rule out MCAS.

Does Patient meet diagnostic criteria?
- Inflammatory symptoms, 2 or more body systems
- Response to treatment - improvement with mast cell–targeted therapies
- Mediator testing where available - Elevated mast cell mediators N-Methyl Histamine /Prostaglandins (blood or urine)
- Exclusion of alternative diagnoses - Differential diagnosis is essential, as symptom overlap is common.

Prescribe medication for mast cell mediated symptoms

Encourage diary to log symptoms and triggers

Educate on Patient Management Strategies

Book a follow up appointment

Medical Management
- H1 and H2 Blockers
- Antileukotrienes
- Mast Cell Stabilisers
- Corticosteriods
- Epi-Pens where necessary

Slow, systematic, trial of drugs may be necessary.

Patient Management
- Symptom Diary
- Trigger identification and avoidance
- Dietary modification to lessen/ avoid high histamine or other trigger foods
- Stress management

Stabilisation
Review medication response
Adjust accordingly
Trial different categories of medication, different medications within the same category, different brands and different combinations until symptoms are well controlled

If symptom control cannot be achieved, consider referral.

Ongoing Management
Review medication regularly for continued effectiveness, and adjust as appropriate

Viral infections, surgeries, stressful life events, unexpected trigger exposure etc may cause temporary or permanent illness progression which may necessitate adjustment of medication.

Consider Possible Triggers
- Foods (particularly high-histamine foods)
- Medications
- Fragrances, perfumes, and chemicals
- Household detergents and laundry products
- Pollen, dust, pet dander, and moulds
- Temperature changes, heat, sunlight
- Physical exertion or exercise
- Stress
- Hormonal fluctuations (e.g. puberty, menopause)
- Viral/bacterial/fungal/infections

Anaphylaxis in MCAS
Anaphylaxis is a mast cell mediated reaction.
People with MCAS are potentially at increased risk of anaphylaxis, affecting around 7% of MCAS patients.
May be atypical presentation
Emergency management follows standard UK guidance
- Establish whether there is a history of anaphylaxis
- Explain the signs, triggers and symptoms of anaphylaxis to the patient
- Prescribe 2 Epi-Pens
- Provide Personalised Management Plan

Useful Resources
Mast Cell Action's 'Brief Guide to MCAS'
Mast Cell Action's 'Self-management Toolkit'
CAMRare passports or medical bracelet can be helpful
Mast cell action have services and resources to help individuals navigate life with MCAS

Caution
- Medication sensitivities are common.
- Introduce drugs cautiously, titrate slowly.
- Avoid problematic medications eg Opioids, NSAIDs, contrast agents, alcohol, certain local and general anaesthetics, excipients like colourings, flavourings, fillers, binders etc.
- Patients may only tolerate specific brands.
- Medications may need to be compounded from specialist pharmacies.
- Surgeries and investigative procedures can trigger flares, consider premedication protocol.

View this Flowchart Online

What is MCAS? Aetiology and Pathology

2

Mast Cell Activation Syndrome (MCAS) is a mast cell disorder. There is primary, secondary and idiopathic. It is distinct from Systemic Mastocytosis because there is no excess accumulation of mast cells, and distinct from primary mast cell disorders because it is not IgE mediated. It is characterised by inappropriate or excessive mast cell activation leading to a wide range of inflammatory and allergy-like symptoms.

MCAS may present at any age. Symptoms are often long-standing but under-recognised, with many patients reporting mild or intermittent symptoms from childhood before a sudden escalation in severity.

In some cases, a clear precipitating event precedes deterioration, such as:

- Viral or bacterial infection
- Surgery or medical procedures
- Physical or psychological stress

Others are unwell from birth or early childhood with no clear precipitating event.

> **"Previously I had experienced mild symptoms but then in 2019 they developed rapidly out of control after a streptococcus throat infection"**
> Tasmin

The condition is characterised by unpredictable, relapsing–remitting symptoms involving multiple organ systems.

Understanding the diagnostic debate

There is disagreement on the diagnostic criteria for MCAS. Two approaches, known as Consensus-1 and Consensus-2, differ in how MCAS is identified and diagnosed.* Consensus-1 uses more restrictive criteria, while Consensus-2 recognises a broader range of symptoms and clinical evidence. This debate can affect access to diagnosis and treatment, and more research and greater clinical agreement is needed.

Mast cells release hundreds of biologically active mediators when triggered; the full extent of their effects is an evolving area of research. Preformed mediators are released immediately, while newly synthesised mediators are released over minutes to hours after exposure to a trigger.

Preformed Mediators (released within minutes):

- Histamine: immediate (~1 min) (vasodilation, itching, gastric acid secretion, bronchoconstriction)
- Tryptase: tissue remodelling, inflammation marker
- Heparin: anticoagulant effects (also increases bradykinin leading to angioedema)
- Proteases: tissue remodelling, inflammatory modulation

Newly Synthesized Mediators (released over minutes to hours):

- Leukotrienes: short-term (~15 min) smooth muscle contraction, inflammation
- Prostaglandins: pain, fever, vascular permeability
- Cytokines / Chemokines: delayed (up to 3 hours) immune signalling, recruit inflammatory cells

MCAS Triggers

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For patients with MCAS, symptoms are usually triggered by exposure to an agent which causes inappropriate mast cell degranulation, in the absence of IgE mediation. People with MCAS may react to a wide variety of triggers, including, but not limited to:

- Foods (particularly high-histamine foods)
- Medications
- Fragrances, perfumes, and chemicals
- Household detergents and laundry products
- Pollen, dust, pet dander, and moulds
- Temperature changes, heat, sunlight
- Physical exertion or exercise
- Stress
- Hormonal fluctuations (e.g. puberty, menopause, premenstrual)
- Infections - Covid-19, EBV, Lyme disease, SIBO (small intestine bacterial overgrowth), chronic infections eg sinus, UTI)

"Becoming aware of my triggers like stress, hot and cold temperatures, strenuous exercise, and fragrances, I was able to improve my symptoms. Being more in control of my symptoms felt amazing"
Lydia

Everyone's experience with MCAS is different. While some people may have clear, consistent triggers, others may struggle with reactions that seem unpredictable or vary day to day. Sometimes just one trigger is enough to cause a reaction; other times, it's the combined effect of several small triggers that pushes the body over its threshold. Keeping a diary to monitor the correlation between symptoms and exposures can be very helpful in identifying patterns.

The Mediator Bucket Theory is a simple but powerful visual aid that is often used to help patients understand how mediators build up in the body - and why we might experience symptoms when levels get too high.

Rather than seeing symptoms as isolated or random, the bucket analogy helps patients recognise that multiple small exposures, each seemingly manageable on their own, can add up over time, and lead to the onset of symptoms.



Clinical Features - When to Consider MCAS

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You may wish to consider MCAS where patients present with:

- Symptoms affecting multiple body systems, such as:
  - Skin (flushing, hives, itching)
  - Gastrointestinal (abdominal pain, bloating, reflux, diarrhoea, constipation, nausea)
  - Respiratory (wheeze, throat tightness, breathlessness)
  - Cardiovascular (palpitations, fainting, chest pain)
  - Neurological (headaches, brain fog, fatigue)
  - Genitourinary symptoms (prostate pain, vulval pain, UTI)
  - Gynaecological issues (heavy, painful periods, etc)
  - Musculoskeletal (joint pain, muscle pain)
- A relapsing–remitting pattern of illness, often without an obvious unifying diagnosis
- Allergy-type reactions (e.g. flushing, hives, throat closing, anaphylaxis) with negative or inconclusive IgE/RAST testing
- Non-specific or medically unexplained symptoms, such as fatigue, chronic pain, headaches, abdominal symptoms, or anxiety, particularly where routine investigations are normal or inconclusive

> **In total I've seen 21 different specialists, ranging from gastroenterology to gynaecology**
> Lydia

MCAS Patients Often Present With

- Multiple referrals across specialties
- Multiple diagnoses eg irritable bowel syndrome, endometriosis, POTS, prostatitis, interstitial cystitis, vasovagal syncope, spontaneous urticaria, angioedema, migraine.
- A wide range of unexplained or poorly explained symptoms
- A history of food, medication, or excipient intolerance
- Intolerance to environmental triggers (e.g. fragrances, temperature changes, stress)
- Symptoms occurring in different organ systems concurrently- eg - itchy eyes, GI symptoms, flushing.
- A family history of similarly affected individuals

Clinical Features That May Be Helpful

- Symptoms span more than one body system
- Reactions are often trigger-dependent but inconsistent
- Severity can fluctuate significantly over time
- Patients may have extensive healthcare contact without diagnostic clarity
- Reactions which are not adequately explained by allergy testing

> **My experiences have been happening since I was a child, and I've only recently been diagnosed at 38**
> Claire

Case Study 1 - Cynthia's Story

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From childhood, I developed increasing allergic-type reactions to a wide range of foods. Over time, I also became reactive to many environmental triggers - heat, stress, fragrances, pollen, dust, sunlight, unfiltered water, loud sounds, bright lights, exercise, cooking, and even strong emotions. My symptoms range from fatigue, bloating, and nausea to hives and anaphylaxis.

The journey to diagnosis was long and difficult. Along the way, I received a number of other diagnoses, including PoTS, Adrenal Insufficiency, PTSD, chronic inflammatory response syndrome, and polycystic ovarian syndrome. Despite seeing multiple specialists and experiencing significant symptoms, my tests for mast cell mediators were initially normal.

Eventually, a bone marrow biopsy confirmed MCAS, and I was finally able to access treatment. My medications include ketotifen, montelukast, and cromolyn sodium oral solution. I also use Benadryl, famotidine, and sondansetron intravenously, and carry an EpiPen for anaphylaxis, alongside albuterol sulfate, cromolyn sodium inhalation solution, promethazine, diphenhydramine, and methylprednisolone as needed.



Careful trigger avoidance and adequate rest are essential. Living with MCAS can be profoundly isolating and physically limiting - on some days I rely on a wheelchair - but finding understanding and support has been life-changing.

Learning Point: Normal mast cell mediator tests do not exclude MCAS. Where clinical presentation suggests recurrent, multi-system allergic-type symptoms without clear cause, ongoing mast cell activation should be considered. Collaboration across specialties may be essential to validate and support the patient effectively.

To read more patient stories, visit our webpage here

MCAS Symptoms

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MCAS symptoms arise from inappropriate mast cell activation. Activated mast cells release inflammatory mediators, including histamine, prostaglandins, leukotrienes and cytokines. The pattern of mast cell mediator release is influenced by what triggers activation. This in turn influences the type of symptoms patients experience

Symptoms typically wax and wane, with severity fluctuating over time. Exacerbations may follow identifiable triggers such as infection, surgery, hormonal changes, medical procedures, or significant physical or psychological stress. Most patients experience multiple co-occurring symptoms across several body systems, and the cumulative burden can be substantial, with marked impact on daily functioning and quality of life. Patients' accounts of their symptoms and patterns over time can provide important and reliable information alongside clinical clues.

Dermatological

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

Cardiovascular

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

Respiratory

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

Hormonal

- Menorrhagia
- Dysmenorrhoea
- Onset of systemic symptoms at puberty
- Deterioration of symptoms mid cycle and/or with perimenopause
- Poor tolerance of HRT

Genital or urinary

- Genital pain or swelling
- Vaginal pain or itching
- Bladder urgency or loss of control
- Post coital vaginal irritation
- Chronic bladder pain
- Interstitial Cystitis

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
- Low mood
- Behavioural issues, irritability
- Vestibular issues, balance, vertigo

Musculoskeletal

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

Nasal-ocular

- Nose congestion
- Eye-watering and itching
- Sinus issues

General

- Extreme tiredness
- Possible anaphylaxis (not essential)

The systemic nature of MCAS means it can be missed if only one issue or symptom is considered at a time. A correct diagnosis is more likely when symptoms are considered collectively, as part of a broader clinical picture.

By the age of 6, my daughter had 9 different consultants. Now, aged 15, she has just one, who manages her symptoms through MCAS treatments.
Joy

Diagnosis and Testing

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Diagnostic Criteria

Diagnosis requires a systematic, structured approach and typically includes:

1. Typical constellation of symptoms - Episodic or persistent inflammatory symptoms involving two or more body systems.
2. Response to treatment - Symptom improvement with mast cell–targeted therapies (e.g. antihistamines, mast cell stabilisers).
3. Mediator testing - Evidence of elevated mast cell mediators in 24-hour urine (N-Methyl Histamine, Tryptase, Prostaglandins D2, DM, F2a), typically obtained during or shortly after symptomatic episodes. These must be kept chilled throughout collection and frozen before transportation, as mast cell mediators degrade if not kept cold. For more information on testing, see the MCAS Testing for Healthcare Professionals and Diagnosing MCAS pages on our website.
4. Exclusion of alternative diagnoses - consider and investigate other possible cause of symptoms as symptom overlap is common.

In some cases, full diagnostic criteria cannot be met despite a suggestive clinical picture. These patients may be classified as having "suspected MCAS", and can still benefit from treatment.

MCAS is typically diagnosed based on clinical findings, urinary mediator testing and the response to mast cell-directed medications. Tissue biopsies with mast cell staining (for example CD117) may provide supporting evidence of mast cell involvement but are not required for diagnosis if those criteria are met. - Risk of solid cancer in patients with mast cell activation syndrome - National Library of Medicine

Commonly referenced diagnostic frameworks include:

1. Molderings et al. (2011)
2. Valent et al. (2019)
3. Giannetti et al. (2021)
4. Afrin et al. (2021) – Global "Consensus-2" criteria

Additional testing should include FBC, Ferritin, CRP, Vit D, TSH, 9am Cortisol and any other tests that are indicated by the presenting symptoms of the patient.

Diagnostic Challenges



MCAS presents significant diagnostic complexity in primary care due to its heterogeneous and fluctuating nature:

- Variable presentation between individuals
- Multisystem involvement
- Relapsing–remitting symptom pattern
- Symptoms often present for years or decades before recognition
- Symptoms may not be evident during consultations if the triggering exposure has resolved
- Tests degrade if not kept chilled, leading to false negatives

This variability can lead to repeated investigations, fragmented care, and delayed recognition.

Differential Diagnoses

- Micronutrient deficiencies such as Vitamin D deficiency, Iron deficiency
- Endocrine disorders such as hypothyroidism, adrenal insufficiency, phaeochromocytoma
- Immunological, inflammatory and rheumatologic diseases, including autoimmune disorders, Fibromyalgia, acute IgE allergic reactions
- Chronic Infections such as Lyme Disease
- Post-viral syndromes such as Myalgic Encephalomyelitis (ME/CFS), Long Covid
- Patients with recurrent anaphylaxis should be referred to rule out allergies or clonal mast cell disorders such as Systemic Mastocytosis

Note - the presence of these disorders does not exclude the diagnosis of MCAS.

Testing to assist with differential diagnoses should include FBC, Ferritin, CRP, Vit D, TSH, 9am Cortisol and specific tests relevant to the presenting symptoms of the patient.

Co-Existing Conditions/Comorbidities

MCAS frequently coexists with other conditions, although the precise pathophysiological relationships remain under investigation. Common associations include:

- Connective tissue disorders: Ehlers-Danlos syndromes (EDS), other Hypermobility syndromes, Marfan syndrome
- Postural Tachycardia Syndrome (PoTS) and other autonomic nervous system dysfunction
- Post-infectious and fatigue syndromes: Long COVID, Myalgic Encephalomyelitis (ME/CFS)
- Neurodevelopmental Conditions, Autism, ADHD
- For more information, see The Overlapping Illness Alliance and Co-existing Conditions

Diagnostic Best Practice in Primary Care

- Consider MCAS as a possible cause of your patient's symptoms, especially where symptoms do not fit neatly into existing diagnoses
- Exclude differential diagnoses, including mastocytosis where indicated
- Encourage symptom tracking by body system to aid pattern recognition
- Take a whole-person, longitudinal history
- Consider childhood atopy: Eczema, Asthma, recurrent tonsillitis, recurrent ear infection.
- Use targeted questioning, as patients may not recognise patterns independently - ask about chemical sensitivity, family members with similar symptoms, life events at onset of symptoms such as viral infection, environmental exposures, trauma or stress (See checklist P18-19)
- Look for patterns between symptoms, triggers, timing, and organ systems
- Explore multisystem involvement, rather than single presenting symptom
- Allow longer appointments where possible, as histories are often complex
- Use investigations to support (not replace) clinical judgement
- Always consider the possibility of co-existing conditions

The primary goal of treatment is symptom control and stabilisation and improved quality of life.

How MCAS is Managed

While no medications are currently licensed specifically for MCAS, many patients achieve improved symptom burden and stability through a combination of:

- Trigger identification and avoidance
- Dietary modification to lessen/ avoid high histamine or other trigger foods
- Stress management
- Pharmacological therapy (see next page)
- A slow, systematic trial-and-error approach often results in improved tolerability and meaningful symptom reduction.

Self-Management.

Patient self-management is key for the successful stabilisation of MCAS, and patients may need support to help them make lifestyle and dietary changes. Strategies include identifying and avoiding triggers, implementing dietary modifications, and utilising stress management techniques alongside appropriate pharmacological support. The support of knowledgeable dietitians, therapists, health coaches and other allied professionals can be invaluable in supporting patients to make lifestyle adjustments and cope with the mental and emotional strain of living with this condition. A detailed diary can be a helpful place to start.

Mast Cell Action has a lot of free downloadable resources about diet and lifestyle modifications here.

Follow-Up

Some patients may achieve effective symptom control through diet and lifestyle modifications for extended periods; however, pharmacologic intervention is often necessary during flares or disease progression. Regular review appointments are helpful to ensure long-term stability of symptoms.

When she was 5, Millie's consultant prescribed Nalcrom, which made a massive difference – in fact, Millie was totally well for the first time ever.

Jo, Millie's Mum

In 2019 I finally got to see an NHS specialist who diagnosed me with MCAS. Montelukast was a game-changer for me. My symptoms stabilised and I began introducing foods back into my diet.

Ivy

Medical Management

- The therapeutic goal is to inhibit mediator effects and stabilise mast cell activity to prevent further degranulation.
- Choose medication based on individual tolerance and symptom profile
- Start medications at lower-than-usual doses, titrating slowly with close monitoring
- Encourage patients to keep a diary and monitor any changes carefully
- Trial alternative brands or compounded formulations if excipient sensitivity is suspected
- If adverse reaction occurs to a drug, another drug within the same drug class may be better tolerated (eg, if Cetirizine is not tolerated, Fexofenadine may be)
- Some patients require more frequent-than-standard antihistamine doses. The NICE evidence summary on chronic urticaria supports incremental up-dosing of antihistamines up to fourfold in poor responders (off-licence use), a principle often also applied in MCAS
- Prescribing antihistamines (rather than OTC use) may support adherence and consistent access at higher doses.
- More information here www.mastcellaction.org/management

Category	Medication	Purpose
Prescription Drugs		
H1 blockers	Cetirizine, Fexofenadine	Reduce histamine effects
H2 blockers	Famotidine	Reduce gastric acid and may reduce systemic histamine effects
Leukotriene blockers	Montelukast	Blocks leukotriene effects
Mast cell stabilisers	Sodium cromoglicate	Reduce mediator release
Mast cell stabilisers and antihistamine	Ketotifen	Reduce mediator release
Corticosteroids	Prednisolone	Reduce inflammation symptoms in short-term flare management
Emergency meds	Adrenaline	Anaphylaxis management
Useful Additional Treatments		
Bioflavonoids	Quercetin	Natural mast cell stabilisers
Vitamins	Vitamin C, Vitamin D, Probiotics, Magnesium	Support stabilising mast cells, control histamine levels & histamine production
	Low Dose Naltrexone*	Anti-inflammatory agent

** Evidence base is limited, but numerous reports suggest potential benefits.*
Visit The LDN Research Trust for more information & prescriber info: ldnresearchtrust.org

Case Study 2 - Kellye's Story

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"As a child, I reacted to many environmental triggers such as grass and pollen, which caused skin and respiratory symptoms. In my mid-thirties, I began experiencing extreme fatigue and muscle soreness after exercise, and new digestive problems. Two years later, I developed severe headaches after a cerebrospinal fluid leak, and was also diagnosed with postural orthostatic tachycardia syndrome (POTS).

Then my food intolerances, bloating, nausea, and skin rashes became increasingly severe, and I began to gain weight despite feeling full after only small amounts of food. I had a long list of triggers - including dairy, tuna, egg whites, fragrances, sorbic and benzoic acid, neomycin, propolis, benzyl salicylate, and stress.

My diagnostic journey was long and often disheartening. I saw more than 40 different specialists.

I was repeatedly misdiagnosed with stress, anxiety, or functional neurological disorder, and at times even accused of fabricating symptoms. The lack of understanding and validation was deeply distressing.

Although my tryptase levels were normal, a biopsy with CD117 staining eventually confirmed MCAS, as did a gastrointestinal scope and duodenal biopsy. Starting treatment with fexofenadine and famotidine brought almost immediate relief from many of my symptoms.

Even with treatment, MCAS remains unpredictable - what works one day may not the next. I've had to adjust my life significantly, prioritising rest, managing stress, and maintaining a careful diet. Finding a diagnosis and a care plan has allowed me to rebuild confidence and regain some control over my health."

Learning Point: MCAS may underlie complex, multi-system sensitivities that appear inconsistent with conventional allergic mechanisms. For unexplained systemic reactions, clinicians should consider mast cell activation, even when tryptase is normal. A patient-centred approach that explores therapeutic trials with antihistamines or mast cell stabilisers can significantly improve outcomes.

To read more patient stories, visit our webpage here

Caution

Medication sensitivities are common. Drugs should be introduced cautiously and titrated slowly.

Medications commonly associated with adverse reactions include:

- Opioids (e.g. morphine, codeine)
- NSAIDs (e.g. ibuprofen, aspirin)
- Radiographic contrast agents
- Neuromuscular blocking agents
- Alcohol-containing formulations and preservatives
- Certain local and general anaesthetics
- Excipients like colourings, flavourings, fillers, binders etc are an issue for some, and patients may only tolerate specific brands.
- Medications may need to be compounded from specialist pharmacies

However, individual tolerance varies, and some patients may tolerate these medications well.

> **My health issues really began after an adverse reaction to a medication**
> Claire

Onward referral

Although many patients with MCAS may be adequately managed in Primary Care, consider referral to secondary care if symptoms are severe, significantly impact daily life, do not respond to first-line treatments or if specialist input is needed for further diagnostic evaluation & management.

Referral may be appropriate to allergy/immunology, haematology, gastroenterology, cardiology, or other relevant specialties, depending on the predominant symptom profile and clinical concern.

> **The right specialists have literally changed my life and given me a future - I can't thank them enough. A decade ago I couldn't stand or eat. After 4 years of MCAS treatment, I'm training to trek 120km to raise awareness.**
> Sophie

Be Aware

Medical procedures and surgery may trigger flares.

Consider premedication protocols similar to those used in systemic mastocytosis (e.g. H1/H2 blockers ± corticosteroids).

Anaphylaxis in MCAS

11

Anaphylaxis at a Glance

Anaphylaxis is a potentially life-threatening systemic reaction, involving rapid mast cell mediator release. It may occur in around 7% of MCAS patients. (Characterization of Mast Cell Activation Syndrome - National library of Medicine)
Presentations may be atypical. A low threshold for recognition and awareness of variable presentations is critical in MCAS, as delayed recognition can be fatal.

Identification of Anaphylaxis - ABCDE (Recommended by Resuscitation Council UK)

- Airways – eg swelling of the lips, tongue, or throat (angioedema), difficulty swallowing or speaking, hoarseness, persistent cough
- Breathing - eg shortness of breath, rapid breathing, wheezing, a blue tint (cyanosis) around the lips or skin (in severe cases)
- Circulation - eg sudden drop in blood pressure (hypotension), feeling faint, dizzy, lightheaded, pale, cold, or clammy skin, rapid or weak pulse. Note, a significant minority of cases may present with hypertension. (Solmazgul eg al)
- Disability - eg confusion or unresponsiveness, including sudden confusion or agitation, new-onset drowsiness, lethargy, or unresponsiveness
- Exposure - physical signs of exposure including hives (urticaria), generalized erythema (widespread rash), signs of an allergen trigger (eg a bee sting site) (May not be present in MCAS)

Emergency MCAS management follows standard UK guidance.
In severe and/or rapidly progressing allergic reaction:

- Immediate intramuscular epinephrine (0.01 mg/kg up to 0.5 mg adult dose) as first-line treatment.
- Prompt transfer to A&E for observation and care
- MCAS patients may experience rebound, or biphasic reactions up to 12 hours afterwards.

Epi-Pen Prescribing In Brief

For all individuals at risk of anaphylaxis -

- Prescribe two Adrenaline Auto Injectors (AAIs)
- Patients should carry both at all times
- Ensure pens are in-date. Patients must check dates and replace regularly
- Provide written anaphylaxis management plans - ensure patients and carers have training and are confident in how and when to use them
- Personal plan for individuals prescribed EpiPen are available here
  - **Adults**
  - **Children**

FAQs

12

1. What is MCAS and how does it differ from Mastocytosis?
In MCAS there is inappropriate activation of mast cells but mast cell numbers are normal. In mastocytosis there is a clonal increase in mast cells and there may also be inappropriate activation.

2. When should I suspect MCAS in a patient?
Consider MCAS in patients with recurrent, unexplained multisystem allergic-type symptoms such as flushing, itching, hives, abdominal pain, diarrhoea or other inflammatory symptoms.

3. What initial tests should I order?
If allergy is suspected check specific IgE for triggers. Check FBC, vitamin D, ferritin and CRP. Specialist mast cell mediator testing includes tryptase and urinary mediators (n-methylhistamine, prostaglandins d2 DM and F2alpha) but are not always available. See our Testing Leaflet for more information.

4. How do I manage mild to moderate MCAS symptoms in primary care?
Treatment is aimed at blocking the effects of mast cell mediators and stabilising mast cells to reduce mediator release. Start with an H1 antihistamine and consider addition of H2 blockers, and mast cell stabilisers like oral sodium cromoglicate and ketotifen. Use a step wise approach and avoid multiple simultaneous drug changes. Be aware that excipients in medications may be a problem. Avoid known triggers and educate patient about emergency self-care

5. When is it appropriate to prescribe an EpiPen?
Prescribe adrenaline auto-injectors for patients with a history of anaphylaxis or severe systemic reactions, or those at high risk of such events.

6. How should I approach referral for MCAS?
Refer based on specific symptoms or complications, such as recurrent anaphylaxis, severe GI symptoms, suspected clonal mast cell disorders, or multisystem involvement rather than solely on a diagnosis of MCAS.

7. Can MCAS cause psychiatric or neurological symptoms?
Yes, patients may experience brain fog, anxiety, depression, headaches, and neuropathic pain due to mast cell mediator effects.

8. Are there any contraindicated medications in MCAS?
Some NSAIDs, opioids, and certain antibiotics can trigger mast cell activation. Always review medication history carefully. Each patient will have individual triggers, but there are some, like opioids, that are problematic for many.

9. What lifestyle advice should I give?
Advise avoidance of known triggers (e.g., temperature extremes, stress, certain foods), encourage regular meals, hydration, and consider referral to dietetics if diet is very restricted.

10. How can I support patients with MCAS long term?
Regular review, symptom monitoring, mental health support, and coordination with specialist services when needed. Patients who experience flares or progression may need medication review or referral.

11. How can Mast Cell Action help GP's?
Mast Cell Action is a charity, not a clinical service, so we do not accept formal referrals. However, we can signpost both clinicians and patients to relevant information, support resources, and patient-led tools to aid in diagnosis and management. Email info@mastcellaction.org

Patient Symptom Checklist

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The following checklist can be used to identify the main treatment priorities for a patient with MCAS. Patients can complete it before each appointment and bring it with them, helping to quickly identify the key issues and areas of focus for that consultation.

Name:	Date:_____/_____/_____	NHS no
	Frequency: 0=never, 1 = once/mo., 2 = few times/mo., 3 = few times/wk., 4 = few times/day, 5 = constantly	Severity: 0 = never, 1 = mild, 2 = mild to moderate, 3 = moderate to severe, 4 = severe
Symptoms	**Frequency**	**Severity**
GENERAL - Constitutional		
Chills		
Fever		
Fatigue		
Weight loss		
Skin		
Flushing		
Flushing with sweating		
Itchy skin		
Hives (red, itchy bumps)		
Swelling of lips, eyes or face		
Respiratory		
Itchy eyes or nose		
Runny nose		
Blocked nose		
Problems taking a deep breath (throat swelling)		
Feeling short of breath		
Hoarseness		
Wheezing		

Symptoms	Frequency	Severity
Cardiovascular		
Palpitations with rapid heart beats		
Fainting or near fainting episodes		
Chest pain		
Gastrointestinal		
Abdominal pain		
Abdominal cramping		
Bloating		
Constipation and / or diarrhoea		
Heartburn		
Nausea		
Neurological		
Headaches		
Tingling or numbness		
Trouble with memory /thinking		
Sleep problems		
Dizziness (head spinning)		
Anxiety/panic attacks / depression		
Musculo-skeletal		
Muscle pain and / or tenderness		
Joint pain		
Obstetric/Gynae		
Heavy periods? Endometriosis? PCOS ?		
Pregnancy issues		
Comorbid Conditions?		
? EDS Y/N		
? PoTs Y/N		

With thanks to Dr Bethan Myers for permission to include her symptom checklist

Signposting and Further Resources

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Mast Cell Activation Syndrome (MCAS) can be life-altering and isolating. In addition to medical management, patients benefit greatly from emotional support, practical resources, and help navigating day-to-day challenges.

Mast Cell Action is the UK's only charity dedicated solely to supporting people affected by Mast Cell Activation Syndrome (MCAS). Led by lived experience, we work to ensure people with MCAS are believed, informed and supported, while helping healthcare professionals to better understand, recognise and manage this complex and often poorly understood condition. We offer a range of information, resources and support for people living with MCAS and those who care for them. Please signpost patients and families to Mast Cell Action to access our support and connect with the wider MCAS community.

Useful Resources for you and your patients include :

MCAS Triggers mastcellaction.org/mcas-triggers
MCAS Symptoms mastcellaction.org/mcas-symptoms
Managing MCAS mastcellaction.org/managing-mcas
MCAS Case Studies mastcellaction.org/patient-stories
Mast Cell Action's online events for patients mastcellaction.org/mast-cell-action-events
Support and Resources mastcellaction.org/support-and-resources
Information for Carers and Loved-Ones mastcellaction.org/caring-for-someone-with-mcas
Support Services mastcellaction.org/peer-parent-support-services
Resources mastcellaction.org/resources
Symptom Log mastcellaction.org/articles/mcas-symptom-log
HCP Resources mastcellaction.org/health-professionals
Testing mastcellaction.org/testing
Children with MCAS mastcellaction.org/parents-carers-of-children-with-mcas
MCAS Bibliography and Research Papers mastcellaction.org/mcas-bibliography
Quick Guide to MCAS for Patients mastcellaction.org/articles/a-brief-guide-to-mcas
Dietary Advice for MCAS mastcellaction.org/articles/nourishing-health-and-happiness-with-mcas
Dietitians for MCAS mastcellaction.org/dietetic-advisory-board
YouTube https://www.youtube.com/@mastcellaction
Podcast 'Let's Talk MCAS' on Spotify, Amazon Music and Apple Podcasts

I am thankful to have discovered Mast Cell Action, they helped me accept my condition and expand my knowledge about it. Discovering the online community at Mast Cell Action was a pivotal moment for me.
Mia

How to refer or signpost:
Patients and carers and doctors can access support and download resources directly from the charity's website at www.mastcellaction.org or by emailing info@mastcellaction.org
You can also join our professional network to receive important updates.

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Make your legacy a lifeline for people with MCAS, leave a gift in your will to Mast Cell Action.