DIAGNOSING MCAS

KEY DIAGNOSTIC CRITERIA 1,2

1. The presence of typical clinical MCAS symptoms across multiple body systems.
2. Evidence of raised levels of mast cell mediators (see "Mediator Tests").
3. Substantial systemic response to inhibitors of mast cell activation or inhibitors of mast cell mediator production or action.
4. Exclusion of other potential diagnoses.

MEDIATOR TESTS 3, 4, 5, 6, 7, 8

<table>
<thead>
<tr>
<th>Test</th>
<th>Normal Range</th>
<th>Comments</th>
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</thead>
</table>
| Serum tryptase            | 2 to 14 ug/L                      | • Most specific to mast cells  
• Often raised in clonal MCAS but normal in non-clonal MCAS  
• Must be measured within 4 hours of a suspected episode and compared with baseline values measured 24 to 48 hours later  
• An increase of at least 20% over the individual's baseline plus 2ng/ml may indicate anaphylaxis* |
| Urinary N-methyl histamine | NMH/creatinine ratio (mcg/mmol)   | <25  
• Fairly specific to mast cells, however also present in basophils  
• No validated diagnostic threshold  
• May be influenced by diet or bacterial contamination |
| Urinary Prostaglandins    | PG/creatinine ratio (ng/mmol)     | PGD2: <825  
PGDM and PGF2α: <2300  
PGF2α: <105  
• Not specific - not recommended as a single marker of mast cell activation  
• No validated diagnostic threshold  
• Positive results for all three PGs is more likely in clonal MCAS  
• A single positive result is more likely in non-clonal MCAS  
• NSAIDs may reduce PGs, inflammation may raise PGs  
• Ovulation, menstruation, PCOS and endometriosis may raise PGF2α |

*The “20% + 2” tryptase formula has not been validated for MCAS. Although the formula may be useful for anaphylaxis, it is not optimal. Tryptase elevation correlates with the severity of anaphylaxis; serum tryptase is elevated in some severe anaphylaxis cases but often remains normal in patients with mild or moderate anaphylaxis. N.B. If serum tryptase is >8 ng/ml, check for hereditary alpha tryptasemia.

IMPORTANT INFORMATION 6, 9

• 24-hour urine samples are recommended as mast cell mediators with short half lives may show normal results in spot urine samples.  
• Sample collection starts after the first urination of day 1 and includes the first urination of day 2.  

• As many mast cell mediators are thermolabile, samples must be kept chilled throughout collection, storage and transport and frozen in the lab.  
• The container used for sample collection must be chilled prior to sampling.  
• Each sample must be collected in a different container and then chilled.  

• Multiple tests are often conducted; ideally two abnormal biochemical values are required to diagnose MCAS.  
• Urine samples must be collected in an acid free container.
**IMPORTANT INFORMATION**

**Analysis**
- A single positive result does not say that a person certainly has MCAS, and a single negative result is insufficient to rule out MCAS. When considered alongside other evidence, these mediator tests can provide reasonable confidence in a diagnosis.
- MCAS patients may not have raised mast cell mediator levels unless they are symptomatic.

**MEDIATORS AND SYMPTOMS**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Mediators</th>
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<tbody>
<tr>
<td>Cardiovascular</td>
<td>CHR, chymase, histamine, interleukin-6, PAF, renin, TNF, tryptase</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>CRH, histamine, interleukin-6, 8, 33, PAF, TNF, tryptase</td>
</tr>
<tr>
<td>Digestive</td>
<td>CHR, histamine, interleukin-6, neurotensin, PAF, PGD2, serotonin, TNF, tryptase, VIP</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Interleukin-6, PGD2, RANKL, TNF, tryptase</td>
</tr>
<tr>
<td>Neurologic</td>
<td>CRH, histamine, interleukin-6, neurotensin, PAF, PGD2, TNF</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Histamine, interleukin-6, CysLTs, PAF, PGD2</td>
</tr>
<tr>
<td>Systemic</td>
<td>CRH, histamine, interleukin-6, TNF</td>
</tr>
</tbody>
</table>

**OTHER MEDIATOR TESTS**

<table>
<thead>
<tr>
<th>Test</th>
<th>Comments</th>
</tr>
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<tbody>
<tr>
<td>Leukotriene E4</td>
<td>• Not available in the UK.</td>
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<tr>
<td>Carboxypeptidase</td>
<td>• Elevated levels may indicate anaphylaxis.</td>
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<tr>
<td></td>
<td>• May reduce false negatives by picking up serum tryptase-negative cases.</td>
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**MCAS-associated symptoms and the mast cell mediators driving these symptoms. Information taken from Theoharides et al. 2015.**

**ACKNOWLEDGEMENTS**

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References


