Overview

Useful For

Screening for and monitoring of mastocytosis and disorders of systemic mast-cell activation, such as anaphylaxis and other forms of severe systemic allergic reactions

Monitoring therapeutic progress in conditions that are associated with secondary, localized, low-grade persistent, mast-cell proliferation and activation such as interstitial cystitis

Profile Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>NMH</td>
<td>N-Methylhistamine, U</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>NCTU</td>
<td>Creatinine Concentration</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Special Instructions

- [Urine Preservatives-Collection and Transportation for 24-Hour Urine Specimens](#)

Method Name

NMH: Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

NCTU: Enzymatic Colorimetric Assay

NY State Available

Yes

Specimen

Specimen Type

Urine

Advisory Information

Individuals who are taking monoamine oxidase inhibitors (MAOIs) or aminoguanidine would have increased N-methylhistamine (NMH) results, which would be uninterpretable.

Specimen Required

Supplies: Aliquot Tube, 5 mL (T465)

Container/Tube: Plastic, 5-mL tube

Specimen Volume: 5 mL

Collection Instructions:

1. Collect urine for 24 hours.
2. No preservative.

Additional Information:

1. 24-Hour collection is preferred, but a random specimen is also acceptable.

2. See Urine Preservatives-Collection and Transportation for 24-Hour Urine Specimens in Special Instructions for multiple collections.

Urine Preservative Collection Options

**Note:** The addition of preservative or application of temperature controls must occur within 4 hours of completion of the collection.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Ambient</td>
<td>Yes</td>
</tr>
<tr>
<td>Refrigerate</td>
<td>Preferred</td>
</tr>
<tr>
<td>Frozen</td>
<td>Yes</td>
</tr>
<tr>
<td>50% Acetic Acid</td>
<td>Yes</td>
</tr>
<tr>
<td>Boric Acid</td>
<td>Yes</td>
</tr>
<tr>
<td>Diazolidinyl Urea</td>
<td>No</td>
</tr>
<tr>
<td>6M Hydrochloric Acid</td>
<td>Yes</td>
</tr>
<tr>
<td>6M Nitric Acid</td>
<td>Yes</td>
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<tr>
<td>Sodium Carbonate</td>
<td>Yes</td>
</tr>
<tr>
<td>Thymol</td>
<td>No</td>
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<tr>
<td>Toluene</td>
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</table>

Specimen Minimum Volume

3 mL

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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</thead>
<tbody>
<tr>
<td>Urine</td>
<td>Refrigerated (preferred)</td>
<td>8 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td>14 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ambient</td>
<td>24 hours</td>
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</table>
N-methylhistamine (NMH) is the major metabolite of histamine, which is produced by mast cells. Increased histamine production is seen in conditions associated with increased mast-cell activity, such as allergic reactions, but also in mast-cell proliferation disorders, in particular mastocytosis.

Mastocytosis is a rare disease. Its most common form, urticaria pigmentosa (UP), affects the skin and is characterized by multiple persistent small reddish-brown lesions that result from infiltration of the skin by mast cells. Systemic mastocytosis is caused by the accumulation of mast cells in other tissues and can affect organs such as the liver, spleen, bone marrow, and small intestine. The mast-cell proliferation in systemic mastocytosis can be either benign or malignant. In children, benign systemic mastocytosis tends to resolve over time, while in most, but not all adults, the disease is progressive. Systemic mastocytosis may or may not be accompanied by UP. Patients with UP or systemic mastocytosis can have symptoms ranging from itching, gastrointestinal distress, bone pain, and headaches; to flushing and anaphylactic shock.

Diagnosis of mastocytosis is made by bone marrow biopsy; however, patients with systemic mastocytosis usually exhibit elevated levels of NMH. Other biochemical markers include 11-beta prostaglandin F(2) alpha, a metabolite of prostaglandin D2 (23BP / 2,3 Dinor-11Beta-Prostaglandin F2 Alpha, Urine), and alpha or beta tryptase (TRYPT / Tryptase, Serum).

**Reference Values**

- 0-5 years: 120-510 mcg/g creatinine
- 6-16 years: 70-330 mcg/g creatinine
- >16 years: 30-200 mcg/g creatinine

**Interpretation**

Increased concentrations of urinary N-methylhistamine (NMH) are consistent with urticaria pigmentosa (UP), systemic mastocytosis, or mast-cell activation. Because of its longer half-life, urinary NMH measurements have superior sensitivity and specificity than histamine, the parent compound. However, not all patients with systemic mastocytosis or anaphylaxis will exhibit concentrations outside the reference range and healthy individuals may occasionally exhibit values just above the upper limit of normal.

The extent of the observed increase in urinary NMH excretion is correlated with the magnitude of mast-cell proliferation and activation, UP patients, or patients with other localized mast-cell proliferation and activation, show usually only mild elevations, while systemic mastocytosis and anaphylaxis tend to be associated with more significant rises in NMH excretion (2-fold or more). There is, however, significant overlap in values between UP and systemic mastocytosis, and urinary NMH measurements should not be relied upon alone in distinguishing localized from systemic disease.

Up to 25% variability in spot-urine excreted levels may be observed, making 24-hour urine collections preferable for cases with borderline results.

Children have higher NMH levels than adults. By the age of 16, adult levels have been reached.

**Cautions**

While an average North American diet has no effect on urinary N-methylhistamine NMH levels, mild elevations (around 30%) may be observed on very histamine-rich diets. This problem is more pronounced if spot-urine specimens rather than 24-hour urine specimens are used and the spot-urine specimen is collected following a histamine-rich meal.

NMH levels may be depressed in individuals who have a polymorphism in the histamine-N-methyl transferase gene, which encodes the enzyme that catalyzes NMH formation. This polymorphism results in an amino acid change that
decreases the rate of NMH synthesis.

When N-acetylcysteine is administered at levels sufficient to act as an antidote for the treatment of acetaminophen overdose, it may lead to falsely decreased creatinine results.

**Clinical Reference**


**Performance**

**Method Description**

N-methylhistamine (NMH) is extracted from urine using solid-phase extraction. The elute is analyzed using liquid chromatography-tandem mass spectrometry (LC-MS/MS) and quantified using a stable isotope labeled internal standard. (Martens-Lobenhoffer J, Neumann HJ: Determination of 1-methylhistamine and 1-methylimidazole acetic acid in human urine as a tool for the diagnosis of mastocytosis. J Chromatogr B Biomed Sci Appl 1999;721[1]:135-140)

**PDF Report**

No

**Day(s) and Time(s) Test Performed**

Tuesday, Thursday; 10 a.m.

**Analytic Time**

3 days

**Maximum Laboratory Time**

7 days

**Specimen Retention Time**

14 days

**Performing Laboratory Location**

Rochester

**Fees and Codes**
Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

82542

LOINC® Information

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<th>Test Order Name</th>
<th>Order LOINC Value</th>
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<tr>
<td>NMHIN</td>
<td>N-Methylhistamine, U</td>
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<th>Test Result Name</th>
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