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 using 24-hour urine collection specimens

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>
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</thead>
<tbody>
<tr>
<td>NMH1D</td>
<td>N-Methylhistamine, 24 Hr, U</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>CRT24</td>
<td>Creatinine, 24 Hour, U</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Special Instructions

- Urine Preservatives-Collection and Transportation for 24-Hour Urine Specimens

Method Name
NMH1D: Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

CRT24: Enzymatic Colorimetric Assay

NY State Available
Yes

Specimen

Specimen Type
Urine

Advisory Information
Random urine collections are preferred for patients with episodic symptoms, for example in the context of allergic reactions, brought on by specific environmental factors. See NMHR / N-Methylhistamine, Random, Urine.

Specimen Required

Patient Preparation: Patient must not be taking monoamine oxidase inhibitors (MAOIs) or aminoguanidine as these medications increase N-methylhistamine (NMH) levels.

Supplies: Aliquot Tube, 5 mL (T465)

Container/Tube: Plastic, 5-mL tube

Specimen Volume: 5 mL
**Test Definition: NMH24**  
N-Methylhistamine, 24 Hr, U

**Collection Instructions:**

1. Collect urine for 24 hours.

2. No preservative.

3. Aliquot into plastic tube and send at refrigerate temperature.

**Additional Information:** 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.

<table>
<thead>
<tr>
<th>Preservative Type</th>
<th>Status</th>
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<tbody>
<tr>
<td>Ambient</td>
<td>OK</td>
</tr>
<tr>
<td>Refrigerate</td>
<td>Preferred</td>
</tr>
<tr>
<td>Frozen</td>
<td>OK</td>
</tr>
<tr>
<td>50% Acetic Acid</td>
<td>OK</td>
</tr>
<tr>
<td>Boric Acid</td>
<td>OK</td>
</tr>
<tr>
<td>Diazolidinyl Urea</td>
<td>No</td>
</tr>
<tr>
<td>6M Hydrochloric Acid</td>
<td>OK</td>
</tr>
<tr>
<td>6M Nitric Acid</td>
<td>OK</td>
</tr>
<tr>
<td>Sodium Carbonate</td>
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<tr>
<td>Thymol</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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<tr>
<td>Urine</td>
<td>Refrigerated (preferred)</td>
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<tr>
<td></td>
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**Clinical and Interpretive**
Clinical Information

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.(1,3) 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.(1-5) Other biochemical markers include 11-beta prostaglandin F(2) alpha, a metabolite of prostaglandin D2 (23BPG / 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 random-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 random-urine specimens are used and collected following a histamine-rich meal.

NMH levels may be depressed in individuals who have an alteration in the histamine-N-methyltransferase gene.
(HNMT), which encodes the enzyme that catalyzes NMH formation. This alteration 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**


Creatinine:

The enzymatic method is based on the determination of sarcosine from creatinine with the aid of creatininase, creatinase, and sarcosine oxidase. The liberated hydrogen peroxide is measured via a modified Trinder reaction using a colorimetric indicator. Optimization of the buffer system and the colorimetric indicator enables the creatinine concentration to be quantified both precisely and specifically.(Package insert: Creatinine plus ver 2. Roche Diagnostics; V15.0 03/2019)
Test Definition: NMH24
N-Methylhistamine, 24 Hr, U

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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