Overview

Useful For
A first- and second-order screening test for the presumptive diagnosis of catecholamine-secreting pheochromocytomas and paragangliomas

Confirming positive plasma metanephrine results

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

Method Name
Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) Stable Isotope Dilution Analysis

NY State Available
Yes

Specimen

Specimen Type
Urine

Necessary Information
24-Hour volume is required.

Specimen Required

Patient Preparation: Tricyclic antidepressants, labetalol, and sotalol medications may elevate levels of metanephrines producing results that cannot be interpreted. If clinically feasible, it is optimal to discontinue these medications at least 1 week before collection. For advice on assessing the risk of removing patients from these medications and alternatives, consider consultation with a specialist in endocrinology or hypertension.

Supplies: Urine Tubes, 10 mL (T068)

Container/Tube: Plastic urine tube

Specimen Volume: 10 mL

Collection Instructions:

1. Collect urine for 24 hours.

2. Add 10 g (pediatric: 3 g) of boric acid or 25 mL (pediatric: 15 mL) of 50% acetic acid as preservative at start of collection.

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

Forms
If not ordering electronically, complete, print, and send an Oncology Test Request (T729) with the specimen.
Test Definition: METAF
Metanephrines, Fractionated, 24h, U

Urine Preservative Collection Options

Note: The addition of preservative must occur prior to the start of the collection or application of temperature controls must occur during collection.

<table>
<thead>
<tr>
<th>Preservative</th>
<th>Acceptance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambient</td>
<td>No</td>
</tr>
<tr>
<td>Refrigerate</td>
<td>OK</td>
</tr>
<tr>
<td>Frozen</td>
<td>OK</td>
</tr>
<tr>
<td>50% Acetic Acid</td>
<td>Preferred</td>
</tr>
<tr>
<td>Boric Acid</td>
<td>Preferred</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>
<td>OK</td>
</tr>
<tr>
<td>Thymol</td>
<td>No</td>
</tr>
<tr>
<td>Toluene</td>
<td>OK</td>
</tr>
</tbody>
</table>

Specimen Minimum Volume
2 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>
</tr>
</thead>
<tbody>
<tr>
<td>Urine</td>
<td>Refrigerated (preferred)</td>
<td>7 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>7 days</td>
<td></td>
</tr>
</tbody>
</table>

Clinical and Interpretive

Clinical Information
Pheochromocytoma is a rare, though potentially lethal, tumor of chromaffin cells of the adrenal medulla that produces episodes of hypertension with palpitations, severe headaches, and sweating (spells). Patients with pheochromocytoma may also be asymptomatic and present with sustained hypertension or an incidentally discovered adrenal mass.

Pheochromocytomas and other tumors derived from neural crest cells (eg, paragangliomas and neuroblastomas) secrete catecholamines (epinephrine, norepinephrine, and dopamine).
Metanephrine and normetanephrine are the 3-methoxy metabolites of epinephrine and norepinephrine, respectively. Metanephrine and normetanephrine are both further metabolized to vanillylmandelic acid.

Pheochromocytoma cells also have the ability to oxymethylate catecholamines into metanephrines that are secreted into circulation.

In patients that are highly suspect for pheochromocytoma, it may be best to screen by measuring plasma free fractionated metanephrines (a more sensitive assay). The 24-hour urinary fractionated metanephrines (a more specific assay) may be used as the first test for low suspicion cases and also as a confirmatory study in patients with a less than 2-fold elevation in plasma free fractionated metanephrines. This is highly desirable, as the very low population incidence rate of pheochromocytoma (<1:100,000 population per year) will otherwise result in large numbers of unnecessary, costly, and sometimes risky imaging procedures.

Complete 24-hour urine collections are preferred, especially for patients with episodic hypertension; ideally the collection should begin at the onset of a spell.

Reference Values

Metanephrine

Males
Normotensives
3-8 years: 29-92 mcg/24 hours
9-12 years: 59-188 mcg/24 hours
13-17 years: 69-221 mcg/24 hours
> or =18 years: 44-261 mcg/24 hours
Reference values have not been established for patients that are <36 months of age.
Hypertensives: <400 mcg/24 hours

Females
Normotensives
3-8 years: 18-144 mcg/24 hours
9-12 years: 43-122 mcg/24 hours
13-17 years: 33-185 mcg/24 hours
> or =18 years: 30-180 mcg/24 hours
Reference values have not been established for patients that are <36 months of age.
Hypertensives: <400 mcg/24 hours

Normetanephrine
Males

Normotensives

3-8 years: 34-169 mcg/24 hours
9-12 years: 84-422 mcg/24 hours
13-17 years: 91-456 mcg/24 hours
18-29 years: 103-390 mcg/24 hours
30-39 years: 111-419 mcg/24 hours
40-49 years: 119-451 mcg/24 hours
50-59 years: 128-484 mcg/24 hours
60-69 years: 138-521 mcg/24 hours
> or =70 years: 148-560 mcg/24 hours

Reference values have not been established for patients that are <36 months of age.

Hypertensives: <900 mcg/24 hours

Females

Normotensives

3-8 years: 29-145 mcg/24 hours
9-12 years: 55-277 mcg/24 hours
13-17 years: 57-286 mcg/24 hours
18-29 years: 103-390 mcg/24 hours
30-39 years: 111-419 mcg/24 hours
40-49 years: 119-451 mcg/24 hours
50-59 years: 128-484 mcg/24 hours
60-69 years: 138-521 mcg/24 hours
> or =70 years: 148-560 mcg/24 hours

Reference values have not been established for patients that are <36 months of age.

Hypertensives: <900 mcg/24 hours
TOTAL METANEPHRINE

Males

Normotensives

3-8 years: 47-223 mcg/24 hours

9-12 years: 201-528 mcg/24 hours

13-17 years: 120-603 mcg/24 hours

18-29 years: 190-583 mcg/24 hours

30-39 years: 200-614 mcg/24 hours

40-49 years: 211-646 mcg/24 hours

50-59 years: 222-680 mcg/24 hours

60-69 years: 233-716 mcg/24 hours

> or =70 years: 246-753 mcg/24 hours

Reference values have not been established for patients that are <36 months of age.

Hypertensives: <1,300 mcg/24 hours

Females

Normotensives

3-8 years: 57-210 mcg/24 hours

9-12 years: 107-394 mcg/24 hours

13-17 years: 113-414 mcg/24 hours

18-29 years: 142-510 mcg/24 hours

30-39 years: 149-535 mcg/24 hours

40-49 years: 156-561 mcg/24 hours

50-59 years: 164-588 mcg/24 hours

60-69 years: 171-616 mcg/24 hours

> or =70 years: 180-646 mcg/24 hours

Reference values have not been established for patients that are <36 months of age.
Hypertensives: <1,300 mcg/24 hours

For SI unit Reference Values, see https://www.mayocliniclabs.com/order-tests/si-unit-conversion.html

**Interpretation**

Increased metanephrine and normetanephrine levels are found in patients with pheochromocytoma and tumors derived from neural crest cells.

Total urine metanephrines 1300 mcg/24 hours and lower can be detected in nonpheochromocytoma hypertensive patients.

Further clinical investigation (eg, radiographic studies) is warranted in patients whose total urinary metanephrine levels are above 1300 mcg/24 hours (approximately 2 times the upper limit of normal). For patients with total urinary metanephrine levels below 1300 mcg/24 hours, further investigations may also be indicated if either the normetanephrine or the metanephrine fraction of the total metanephrines exceed their respective upper limit for hypertensive patients. Finally, repeat testing or further investigations may occasionally be indicated in patients with urinary metanephrine levels below the hypertensive cutoff, or even normal levels, if there is a very high clinical index of suspicion.

**Cautions**

This test utilizes a high-performance liquid chromatography/tandem mass spectrometry method and is not affected by the interfering substances that affected the previously utilized spectrophotometric (Pisano reaction) method (ie, diatrizoate, chlorpromazine, hydrazine derivatives, imipramine, monoamine oxidase [MAO] inhibitors, methyldopa, phenacetin, ephedrine, or epinephrine).

This method is not subject to the known interference of acetaminophen (seen with the plasma metanephrine HPLC-EC method).

**Clinical Reference**


**Performance**

**Method Description**

Urinary metanephrines are determined by reverse phase liquid chromatography-tandem mass spectrometry (LC-MS/MS) stable isotope dilution analysis. Urinary metanephrines occur largely in conjugated form. After urine specimens are acidified and hydrolyzed for 20 minutes in a boiling water bath, metanephrine and normetanephrine are extracted from the specimens utilizing extraction cartridges. The metanephrine and normetanephrine are eluted from the cartridge using 20% methanol (MeOH) and analyzed by LC-MS/MS using multiple reaction monitoring in positive mode. Deuterated metanephrine (d3-metanephrine, 200 ng) and deuterated normetanephrine
(d3-normetanephrine, 500 ng) are added prior to the hydrolysis as an internal standard. The following ion pairs are used for analysis: metanephrine, (180/148); normetanephrine, (166/134); d3-metanephrine, (183/151); d3-normetanephrine, (169/137). The metanephrine and normetanephrine concentrations are quantified using ratios of the peak areas to deuterium-labeled internal standards by LC-MS/MS. A calibration curve, generated from 20% MeOH spiked standards, is included with each batch of patient specimens. (Taylor RL, Singh RJ: Validation of liquid chromatography-tandem mass spectrometry method for analysis of urinary conjugated metanephrine and normetanephrine for screening of pheochromocytoma. Clin Chem 2002;48:533-539; Roden M, Raffesberg W, Raber W, et al: Quantification of unconjugated metanephrine in human plasma without interference by acetaminophen. Clin Chem 2001;47:1061-1067)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday; 4 p.m.

Analytic Time
3 days (not reported on Sundays)

Maximum Laboratory Time
5 days

Specimen Retention Time
2 weeks

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
83835

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>METAF</td>
<td>Metanephrines, Fractionated, 24h, U</td>
<td>In Process</td>
</tr>
</tbody>
</table>
### Test Definition: METAF
Metanephrines, Fractionated, 24h, U

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>8552</td>
<td>Metanephrine, U</td>
<td>19049-6</td>
</tr>
<tr>
<td>21545</td>
<td>Normetanephrine, U</td>
<td>2671-6</td>
</tr>
<tr>
<td>83006</td>
<td>Total Metanephrines, U</td>
<td>2609-6</td>
</tr>
<tr>
<td>TM50</td>
<td>Collection Duration</td>
<td>13362-9</td>
</tr>
<tr>
<td>VL48</td>
<td>Urine Volume</td>
<td>3167-4</td>
</tr>
<tr>
<td>2434</td>
<td>Comment</td>
<td>48767-8</td>
</tr>
</tbody>
</table>