

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 (in milliliters) 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](#) for multiple collections.

Forms

[If not ordering electronically, complete, print, and send an Oncology Test Request](#) (T729) with the specimen.

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**.

| | |
|----------------------|-----------|
| Ambient | No |
| Refrigerate | OK |
| Frozen | OK |
| 50% Acetic Acid | Preferred |
| Boric Acid | Preferred |
| Diazolidinyl Urea | No |
| 6M Hydrochloric Acid | OK |
| 6M Nitric Acid | OK |
| Sodium Carbonate | OK |
| Thymol | No |
| Toluene | OK |

Specimen Minimum Volume

3 mL

Reject Due To

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

Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---------------|--------------------------|---------|-------------------|
| Urine | Refrigerated (preferred) | 28 days | |
| | Ambient | 28 days | |
| | Frozen | 28 days | |

Clinical & 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 younger than 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 younger than 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 younger than 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 younger than 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 younger than 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 younger than 36 months of age.

Hypertensives: <1,300 mcg/24 hours

For SI unit Reference Values, see 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 metanephrine levels of 1300 mcg/24 hours and lower can be detected in non-pheochromocytoma 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 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, monamine oxidase [MAO] inhibitors, methyldopa, phenacetin, ephedrine, or epinephrine).

This method is not subject to the known interference of acetaminophen (seen with the plasma metanephrine high performance liquid chromatography-electrochemical method).

Clinical Reference

1. van Duinen N, Corssmit EPM, de Jong WHA, Brookman D, Kema IP, Romijn JA: Plasma levels of free metanephrines and 3-methoxytyramine indicate a higher number of biochemically active HNPGL than 24-h urinary excretion rates of catecholamines and metabolites. *Eur J Endocrinol*. 2013 Aug 28;169(3):377-382. doi: 10.1530/EJE-13-0529
2. Pacak K, Linehan WM, Eisenhofer G, Walther MM, Goldstein DS: Recent advances in genetics, diagnosis, localization, and treatment of pheochromocytoma. *Ann Intern Med*. 2001 Feb 20;134(4):315-329
3. Sawka AM, Singh RJ, Young WF Jr: False positive biochemical testing for pheochromocytoma caused by surreptitious catecholamine addition to urine. *Endocrinologist*. 2001;11:421-423
4. Eisenhofer G, Grebe S, Cheung NKV: Monoamine-producing tumors. In: Rafai N, Horvath AR, Wittwer CT, eds. *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*. 6th ed. Elsevier; 2018:1421
5. Shen Y, Cheng L: Biochemical diagnosis of pheochromocytoma and paraganglioma. In: Mariani-Costantini R, ed. *Paraganglioma: A Multidisciplinary Approach*. Codon Publications; 2019. doi: 10.15586/paraganglioma.2019.ch2. Accessed: April 2020. Available at: www.ncbi.nlm.nih.gov/books/NBK543224/

Performance

Method Description

Urine samples are acidified and hydrolyzed in a heat block, metanephrine and normetanephrine are extracted from the specimens utilizing extraction cartridges. Analyte concentrations are determined through analysis performed by a liquid chromatography-tandem mass spectrometry method.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

3 to 5 days

Specimen Retention Time

2 weeks

Performing Laboratory Location

Rochester

Fees & 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 account representative. 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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

83835

LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---------|-------------------------------------|--------------------|
| METAF | Metanephrines, Fractionated, 24h, U | In Process |

| Result ID | Test Result Name | Result LOINC® Value |
|-----------|------------------|---------------------|
| 8552 | Metanephrine, U | 19049-6 |

| | | |
|-------|------------------------|---------|
| 21545 | Normetanephrine, U | 2671-6 |
| 83006 | Total Metanephrines, U | 2609-6 |
| TM50 | Collection Duration | 13362-9 |
| VL48 | Urine Volume | 3167-4 |
| 2434 | Comment | 48767-8 |