

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.

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

2 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 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 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, methyl dopa, 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

1. van Duinen N, Corssmit EPM, de Jong WHA, et al: 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 *European J Endocrinol* 2013;169:377-382 doi: 10.1530/EJE-13-0529
2. Pacak K, Linehan WM, Eisenhofer G, et al: Recent advances in genetics, diagnosis, localization, and treatment of pheochromocytoma. *Ann Intern Med* 2001;134:315-329
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: Chapter 63: Monoamine-Producing Tumors. In *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*. Sixth edition. Edited by N Rafai, AR Horvath, CT Wittwer. Elsevier, 2018. pp 1421
5. Shen Y, Cheng L: Chapter 2: Biochemical Diagnosis of Pheochromocytoma and Paraganglioma. In *Paraganglioma: A Multidisciplinary Approach*. Edited by R. Mariani-Costantini. Codon Publications; 2019. doi:10.15586/paraganglioma.2019.ch2. Accessed: April 2020. Available at: www.ncbi.nlm.nih.gov/books/NBK543224/

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, Rafflesberg 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



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