

Overview

Useful For

A second-order screening test for the presumptive diagnosis of pheochromocytoma in patients with non-episodic hypertension

Confirming positive plasma metanephrine results in patients with non-episodic hypertension

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
METAU	Metanephrines, Fractionated, U	No	Yes
CRETR	Creatinine, Random, U	Yes, (Order RCTUR)	Yes

Method Name

METAU: Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) Stable Isotope Dilution Analysis

CRETR: Enzymatic Colorimetric Assay

NY State Available

Yes

Specimen

Specimen Type

Urine

Specimen Required

Patient Preparation: Patient should refrain from cold medicines, nose drops, and nasal sprays for at least 48 hours prior to test. Tricyclic antidepressants and labetalol and sotalol (beta blockers) may elevate levels of metanephrines. If clinically feasible, these medications should be discontinued at least 1 week before collection.

Supplies: Urine Tubes, 10 mL (T068)

Collection Container/Tube: Clean, plastic urine collection container

Submission Container/Tube: Plastic, 10 mL urine tube

Specimen Volume: 10 mL

Collection Instructions:

1. Collect a random urine specimen.
2. No preservative.

Forms

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

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	
	Frozen	28 days	
	Ambient	14 days	

Clinical & Interpretive

Clinical Information

Pheochromocytoma is a rare, potentially lethal, tumor of chromaffin cells of the adrenal medulla that produces episodes of hypertension with palpitations, severe headaches, and sweating ("spells").

Pheochromocytomas and other tumors derived from neural crest cells (eg, paragangliomas and neuroblastomas) secrete catecholamines (epinephrine and norepinephrine).

Metanephrine and normetanephrine are the 3-methoxy metabolites of epinephrine and norepinephrine, respectively. Both are further metabolized to vanillylmandelic acid.

Pheochromocytoma cells are also able to oxymethylate catecholamines into metanephrines that are secreted into circulation.

Reference Values

METANEPHRINE/CREATININE

Normotensives

- 0-2 years: 82-418 mcg/g creatinine
- 3-8 years: 65-332 mcg/g creatinine
- 9-12 years: 41-209 mcg/g creatinine
- 13-17 years: 30-154 mcg/g creatinine
- > or =18 years: 29-158 mcg/g creatinine

NORMETANEPHRINE/CREATININE

Males

Normotensives

- 0-2 years: 121-946 mcg/g creatinine
- 3-8 years: 92-718 mcg/g creatinine
- 9-12 years: 53-413 mcg/g creatinine

13-17 years: 37-286 mcg/g creatinine
18-29 years: 53-190 mcg/g creatinine
30-39 years: 60-216 mcg/g creatinine
40-49 years: 69-247 mcg/g creatinine
50-59 years: 78-282 mcg/g creatinine
60-69 years: 89-322 mcg/g creatinine
> or =70 years: 102-367 mcg/g creatinine

Females

Normotensives

0-2 years: 121-946 mcg/g creatinine
3-8 years: 92-718 mcg/g creatinine
9-12 years: 53-413 mcg/g creatinine
13-17 years: 37-286 mcg/g creatinine
18-29 years: 81-330 mcg/g creatinine
30-39 years: 93-379 mcg/g creatinine
40-49 years: 107-436 mcg/g creatinine
50-59 years: 122-500 mcg/g creatinine
60-69 years: 141-574 mcg/g creatinine
> or =70 years: 161-659 mcg/g creatinine

TOTAL METANEPHRINE/CREATININE

Males

Normotensives

0-2 years: 241-1,272 mcg/g creatinine
3-8 years: 186-980 mcg/g creatinine
9-12 years: 110-582 mcg/g creatinine
13-17 years: 78-412 mcg/g creatinine
18-29 years: 96-286 mcg/g creatinine
30-39 years: 106-316 mcg/g creatinine
40-49 years: 117-349 mcg/g creatinine
50-59 years: 130-386 mcg/g creatinine
60-69 years: 143-427 mcg/g creatinine
> or =70 years: 159-472 mcg/g creatinine

Females

Normotensives

0-2 years: 241-1,272 mcg/g creatinine
3-8 years: 186-980 mcg/g creatinine
9-12 years: 110-582 mcg/g creatinine
13-17 years: 78-412 mcg/g creatinine
18-29 years: 131-467 mcg/g creatinine
30-39 years: 147-523 mcg/g creatinine
40-49 years: 164-585 mcg/g creatinine
50-59 years: 184-655 mcg/g creatinine

60-69 years: 206-733 mcg/g creatinine
> or =70 years: 230-821 mcg/g creatinine

Interpretation

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

Increased urine metanephrines can be detected in non-pheochromocytoma hypertensive patients; quantification may help distinguish these patients from those with tumor-induced symptoms.

Cautions

While screening for pheochromocytoma is best accomplished by measuring plasma free fractionated metanephrines (a more sensitive assay), follow-up testing with urinary fractionated metanephrines (a more specific assay) may identify false-positive results. Twenty-four-hour urine collections are preferred, especially for patients with episodic hypertension; ideally the collection should begin at the onset of a "spell."

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, monoamine oxidase inhibitors, methyl dopa, phenacetin, ephedrine, or epinephrine).

This method is also not subject to the known interference of acetaminophen, which is seen with the plasma metanephrine high performance liquid chromatography-electrochemical detection method.

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

1. van Duinen N, Corssmit EPM, de Jong WHA, Brookman D, Kema P, 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: Rifai N, Horvath AR, Wittwer CT, eds. *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*. 6th ed. Elsevier; 2018:1421
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6. Hernandez FC, Sanchez M, Alvarez A, et al: A five-year report on experience in the detection of pheochromocytoma. *Clin Biochem*. 2000 Nov;33(8):649-55. doi: 10.1016/s0009-9120(00)00172-7
7. van Duinen N, Steenvoorden D, Kema IP, et al: Increased urinary excretion of 3-methoxytyramine in patients with head and neck paragangliomas. *J Clin Endocrinol Metab*. 2010 Jan;95(1):209-14. doi: 10.1210/jc.2009-1632
8. Le Jacques A, Abalain JH, Le Saos F, Carre JL: Significance of 3-methoxytyramine urine measurement in the diagnosis of pheochromocytomas and paragangliomas: about 28 patients. *Ann Biol Clin (Paris)*. 2011 Sep-Oct;69(5):555-9. French.

doi: 10.1684/abc.2011.0612

9. Muskiet FA, Thomasson CG, Gerding AM, Fremouw-Ottevangers DC, Nagel GT, Wolthers BG: Determination of catecholamines and their 3-O-methylated metabolites in urine by mass fragmentography with use of deuterated internal standards. Clin Chem. 1979 Mar;25(3):453-60

10. Hirsch D, Grossman A, Nadler V, Alboim S, Tsvetov G: Pheochromocytoma: Positive predictive values of mildly elevated urinary fractionated metanephrines in a large cohort of community-dwelling patients. J Clin Hypertens (Greenwich). 2019 Oct;21(10):1527-1533. doi: 10.1111/jch.13657

Performance

Method Description

Metanephrine and Normetanephrine:

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)

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)

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
82570

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
METRN	Metanephrintest, Fractionated, Random, U	68317-7

Result ID	Test Result Name	Result LOINC® Value
21546	Metanephrintest/Creatinine	9645-3
21547	Normetanephrintest/Creatinine	13783-6
21548	Total Metanephrintest/Creatinine	13771-1
CRETR	Creatinine, Random, U	2161-8