

Metanephrines, Fractionated, Random, Urine

# 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,	No	Yes
	Fractionated, U		
CRETR	Creatinine, Random, U	Yes, (Order RCTUR)	Yes

### **Method Name**

METAU: Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

CRETR: Enzymatic Colorimetric Assay

#### **NY State Available**

Yes

# Specimen

## **Specimen Type**

Urine

# **Specimen Required**

# **Patient Preparation:**

- 1. For at least 48 hours prior to test, patient should avoid use of cold medicines, nose drops, and nasal sprays.
- 2. Patients taking tricyclic antidepressants and labetalol and sotalol (beta blockers) may have falsely elevated levels of metanephrines. If medically feasible, for at least 1 week before specimen collection, the patient should not take these medications.

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.



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#### **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	
	Ambient	14 days	
	Frozen	28 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



Metanephrines, Fractionated, Random, Urine

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



Metanephrines, Fractionated, Random, Urine

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 free fractionated metanephrines in plasma (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 [MAOI], methyldopa, phenacetin, ephedrine, or epinephrine).

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

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;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;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
- 5. Shen Y, Cheng L. Biochemical diagnosis of pheochromocytoma and paraganglioma. In: Mariani-Costantini R, ed. Paraganglioma: A Multidisciplinary Approach. Codon Publications; 2019. Accessed May 2, 2024. Available at www.ncbi.nlm.nih.gov/books/NBK543224/
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Metanephrines, Fractionated, Random, Urine

- 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;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;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;21(10):1527-1533. doi:10.1111/jch.13657

#### **Performance**

# **Method Description**

Urinary metanephrines are determined by liquid chromatography tandem mass spectrometry (LC-MS/MS). Urinary metanephrines occur largely in conjugated form. After urine samples are acidified and hydrolyzed in a heat block, metanephrine and normetanephrine are extracted from the specimens utilizing extraction cartridges. The metanephrine, normetanephrine, and 3-methoxytyramine (3MT) are eluted from the cartridge and analyzed by LC/MS/MS using multiple reaction monitoring in positive mode. Deuterated metanephrine (d3-metanephrine), deuterated normetanephrine (d3-normetanephrine), and deuterated 3MT (d4-3MT) are added prior to the hydrolysis as internal standards. The metanephrine, normetanephrine, and 3-MT concentrations are quantified using ratios of the peak areas to deuterium labeled internal standards by LC-MS/MS.(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**

Mayo Clinic Laboratories - Rochester Superior Drive



Metanephrines, Fractionated, Random, Urine

# **Fees & Codes**

### **Fees**

- Authorized users can sign in to <u>Test Prices</u> for detailed fee information.
- Clients without access to Test Prices can contact <u>Customer Service</u> 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact <u>Customer Service</u>.

### **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	Metanephrines, Fract., Random, U	68317-7

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