# Test Definition: METAF

Metanephrines, Fractionated, 24 Hour, Urine

## 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)

### 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. 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**.
2. Collect urine for 24 hours.
**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 1 of the following forms with the specimen:
-Oncology Test Request (T729)
-Renal Diagnostics Test Request (T830)

### 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 additive) | No |
| Refrigerate (no additive) | OK |
| Frozen (no additive) | OK |
| 50% Acetic Acid | Preferred |
| Boric Acid | Preferred |
| Diazolidinyl Urea | No |
| 6M Hydrochloric Acid | OK |
| 6M Nitric Acid | No |
| 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, which 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 or 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 h
9-12 years: 59-188 mcg/24 h
13-17 years: 69-221 mcg/24 h
> or =18 years: 44-261 mcg/24 h
Reference values have not been established for patients that are younger than 36 months.

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

Hypertensives: <400 mcg/24 h

NORMETANEPHRINE
Males
Normotensives
3-8 years: 34-169 mcg/24 h
9-12 years: 84-422 mcg/24 h
13-17 years: 91-456 mcg/24 h
18-29 years: 103-390 mcg/24 h
30-39 years: 111-419 mcg/24 h
40-49 years: 119-451 mcg/24 h

50-59 years: 128-484 mcg/24 h
60-69 years: 138-521 mcg/24 h
> or =70 years: 148-560 mcg/24 h
Reference values have not been established for patients that are younger than 36 months.

Hypertensives: <900 mcg/24 h

Females
Normotensives
3-8 years: 29-145 mcg/24 h
9-12 years: 55-277 mcg/24 h
13-17 years: 57-286 mcg/24 h
18-29 years: 103-390 mcg/24 h
30-39 years: 111-419 mcg/24 h
40-49 years: 119-451 mcg/24 h
50-59 years: 128-484 mcg/24 h
60-69 years: 138-521 mcg/24 h
> or =70 years: 148-560 mcg/24 h
Reference values have not been established for patients that are younger than 36 months.

Hypertensives: <900 mcg/24 h

TOTAL METANEPHRINE
Males
Normotensives
3-8 years: 47-223 mcg/24 h
9-12 years: 201-528 mcg/24 h
13-17 years: 120-603 mcg/24 h
18-29 years: 190-583 mcg/24 h
30-39 years: 200-614 mcg/24 h
40-49 years: 211-646 mcg/24 h
50-59 years: 222-680 mcg/24 h
60-69 years: 233-716 mcg/24 h
> or =70 years: 246-753 mcg/24 h
Reference values have not been established for patients that are younger than 36 months.

Hypertensives: <1,300 mcg/24 h

Females
Normotensives
3-8 years: 57-210 mcg/24 h
9-12 years: 107-394 mcg/24 h
13-17 years: 113-414 mcg/24 h
18-29 years: 142-510 mcg/24 h
30-39 years: 149-535 mcg/24 h

40-49 years: 156-561 mcg/24 h
50-59 years: 164-555 mcg/24 h
60-69 years: 171-616 mcg/24 h
> or =70 years: 180-646 mcg/24 h
Reference values have not been established for patients that are younger than 36 months.

Hypertensives: <1,300 mcg/24 h

For International System of Units (SI) conversion for 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 h 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 h (approximately 2 times the upper limit of normal). For patients with total urinary metanephrine levels below 1300 mcg/24 h, 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 older spectrophotometric (Pisano reaction) methods (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 methods).

## 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;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: 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 22, 2024. Available at: www.ncbi.nlm.nih.gov/books/NBK543224/

## Performance

### Method Description
Urine samples are acidified and hydrolyzed in a heat block, then 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
Mayo Clinic Laboratories - Rochester Superior Drive

## 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 | 104632-5 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|

| | | |
|---|---|---|
| 8552 | Metanephrine, U | 104629-1 |
| 21545 | Normetanephrine, U | 104631-7 |
| 83006 | Total Metanephrines, U | 104630-9 |
| TM50 | Collection Duration (h) | 13362-9 |
| VL48 | Volume (mL) | 3167-4 |
| 2434 | Comment | 48767-8 |