MAYO CLINIC LABORATORIES

Test Definition: META3

Metanephrines with 3-Methoxytyramine, 24 Hour, Urine

Overview

Useful For

A first- and second-tier screening test for the presumptive diagnosis of catecholamine-secreting pheochromocytomas and paragangliomas

Testing in conjunction with or as an alternative to plasma metanephrine or catecholamine testing

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
3MT1	3-Methoxytyramine, U	Yes, (Order 3MT)	Yes
METAF	Metanephrines, Fractionated, 24h, U	Yes	Yes

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

Ordering Guidance

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.

Necessary Information

24-Hour volume (in milliliters) is required.

Specimen Required

Supplies: Urine Tubes, 10 mL (T068)
Submission Container/Tube: Plastic urine tube
Specimen Volume: 10 mL
Collection Instructions:
1. Complete 24-hour urine collections are preferred, especially for patients with episodic hypertension; ideally the collection should begin at the onset of a "spell."
2. Collect urine for 24 hours.
3. 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.

Urine Preservative Collection Options

Note: The addition of preservative or application of temperature controls **must occur at the start** of the collection.

Ambient	OK
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

4 mL

Reject Due To

Gross hemolysis	OK
Gross icterus	OK

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). Dopamine secreting tumors are rarer than norepinephrine and epinephrine secreting tumors.

3-Methoxytyramine (3MT), metanephrine, and normetanephrine are the metabolites of dopamine, epinephrine, and norepinephrine, respectively. These metabolites are 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). This test 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 or catecholamines. 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

3-Methoxytyramine:
Males: < or =306 mcg/24 hours
Females: < or =242 mcg/24 hours

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: <1300 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: <1300 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.

Increased 3-methoxytyramine (3MT) levels are found in patients with pheochromocytoma and dopamine-secreting tumors.

Total urine metanephrine levels of 1300 mcg/24 hours and less, and 3MT levels of 306 mcg/24 hours or less in males and 242 mcg/24 hours or less in females, 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) or whose 3MT levels are elevated and there is a very high clinical index of suspicion.
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 exceeds 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

Tricyclic antidepressants, levodopa, and significant physical stress (eg, hypertensive stroke) may elevate levels of

3-methoxytyramine (3MT). L-Dopa use will definitely increase results for 3-MT and the results cannot be interpreted. If clinically feasible, these medications should be discontinued at least 1 week before collection.

These tests utilizes a liquid chromatography/tandem mass spectrometry (LC-MS/MS) method and is not affected by the interfering substances that affected older spectrophotometric (Pisano reaction) (ie, diatrizoate, chlorpromazine, hydrazine derivatives, imipramine, monoamine oxidase [MAO] inhibitors, methyldopa, phenacetin, ephedrine, or epinephrine) or high-performance liquid chromatography (HPLC) methods (acetaminophen).

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 Eur J Endocrinol. 2013;169:377-382. doi: 10.1530/EJE-13-0529
2. 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):209-214. doi: 10.1210/jc.2009-1632
3. Kantorovich V, Pacak K; Interest of urinary dosage of 3- methoxytyramine in the diagnosis of pheochromocytoma and paraganglioma: report of 28 cases. Ann Clin Biol. 2011;69(5):555-559. doi: 10.168 4 /abc.2011.0612
4. Muskiet FA, Thomasson CG, Gerding AM, et al: 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):453-460
5. Hernandez FC, Sanchez M, Alvarez A, et al: A five-year report on experience in the detection of pheochromocytoma. Clin Biochem. 2000;33:649-655
6. 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
7. 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

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. Deuterated metanephrine, deuterated normetanephrine, and deuterated 3MT are added prior to the hydrolysis as an internal standard. 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)

PDF Report

No

Day(s) Performed

Monday through Friday

Test Definition: META3

Metanephrines with 3-Methoxytyramine, 24 Hour, Urine

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
82542
83835

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
META3	Metanephrines with 3-MT, 24h, U	101400-0

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
VL48	Urine Volume	3167-4
2434	Comment	48767-8
609422	3-Methoxytyramine, U	32618-1