

## Overview

### Useful For

Diagnosis of pheochromocytoma and paraganglioma, as an auxiliary test to fractionated plasma and urine metanephrine measurements (plasma metanephrine is the preferred test for this diagnosis)

Diagnosis and follow-up of patients with neuroblastoma and related tumors, as an auxiliary test to urine vanillylmandelic acid and homovanillic acid measurements

Evaluation of patients with autonomic dysfunction or failure or autonomic neuropathy

### Highlights

This test includes measurement of unconjugated norepinephrine, epinephrine, and dopamine.

### Method Name

High-Performance Liquid Chromatography (HPLC)

### NY State Available

Yes

## Specimen

### Specimen Type

Plasma EDTA Meta

### Ordering Guidance

To preserve the quality of the specimen, **this test should be its own collection**. Sharing the specimen could introduce unforeseen analysis interferences.

This test is not the first-tier test for pheochromocytoma, as plasma catecholamine levels may not be continuously elevated. For the recommended first-tier laboratory test for pheochromocytoma, order either:

- PMET / Metanephrines, Fractionated, Free, Plasma
- METAF / Metanephrines, Fractionated, 24 Hour, Urine

**Do not perform** this test on patients withdrawing from legal or illegal drugs known to cause rebound plasma catecholamine release during withdrawal (see Cautions for details)

### Specimen Required

#### Patient Preparation:

1. Discontinue drugs that release epinephrine, norepinephrine, or dopamine, or hinder their metabolism for at least one week before obtaining the specimen (see Cautions for details). If this is not possible for medical reasons, contact the

laboratory and discuss whether a shorter drug withdrawal period may be possible in a particular case.

2. Unless the purpose of the measurement is drug monitoring, discontinue any epinephrine, norepinephrine, or dopamine injections or infusions for at least 12 hours before specimen collection.
3. The **patient must refrain from eating, using tobacco, and drinking caffeinated beverages** for at least 4 hours before the specimen is collected.

**Supplies:** Catecholamine Tubes-EDTA (T066) (tubes contain sodium metabisulfite, may come as 10-mL or 6-mL tubes, and **have a 6-month expiration time**)

**Collection Container/Tube:**

**Preferred:** 10-mL Catecholamine tubes containing EDTA-sodium metabisulfite solution

**Acceptable:** 6-mL Catecholamine tubes containing EDTA-sodium metabisulfite solution

**Submission Container/Tube:** Plastic vial

**Specimen Volume:** 3 mL

**Collection Instructions:**

**Note: If the collection instructions are not followed, falsely elevated test results are highly likely.**

1. **Drawing from an indwelling intravenous (IV) line/catheter/butterfly is required.**
2. Calm the patient by giving complete instructions and reassurance regarding the procedure.
3. Insert an indwelling IV catheter. Flush with 3 mL of sodium chloride (NaCl), using positive pressure.
4. Have the patient rest for 30 minutes in the supine position in a quiet room.
5. At the end of the 30 minutes, withdraw and discard a minimum of 3 mL of blood to remove the saline out of the catheter.
6. If provocative sampling (eg, standing specimen) is required, perform provocative maneuver immediately after obtaining supine specimen. Obtain standing specimen immediately.
7. For each specimen, draw 10 mL of blood into the chilled 10 mL catecholamine tube containing EDTA-sodium metabisulfite solution. A 6 mL pink top EDTA-metabisulfite tube is an acceptable substitute.
8. Specimens must remain at refrigerated temperature during processing and transport.
9. Separate plasma in a refrigerated centrifuge within 30 minutes of collection.
10. Freeze specimen immediately.

**Forms**

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

**Specimen Minimum Volume**

2 mL

**Reject Due To**

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK

**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Plasma EDTA Meta	Frozen (preferred)	7 days	

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**Clinical & Interpretive****Clinical Information**

The catecholamines (dopamine, epinephrine, and norepinephrine) are derived from tyrosine via a series of enzymatic conversions. All 3 catecholamines are important neurotransmitters in the central nervous system and play a crucial role in the autonomic regulation of many homeostatic functions, namely, vascular tone, intestinal and bronchial smooth muscle tone, cardiac rate and contractility, and glucose metabolism. Their actions are mediated via alpha- and beta-adrenergic receptors and dopamine receptors, all existing in several subforms. The 3 catecholamines overlap but also differ in their receptor activation profile and consequent biological actions. The systemically circulating fraction of the catecholamines is derived almost exclusively from the adrenal medulla, with small contributions from sympathetic ganglia.

The catecholamines are normally present in the plasma in minute amounts, but levels can increase dramatically and rapidly in response to change in posture, environmental temperature, physical and emotional stress, hypovolemia, blood loss, hypotension, hypoglycemia, and exercise.

In patients with pheochromocytoma (a potentially curable tumor of catecholamine-producing cells of the adrenal medulla), or less commonly of sympathetic ganglia (paraganglioma), plasma catecholamine levels may be continuously or episodically elevated. This results in episodic or sustained hypertension and in intermittent attacks of palpitations, cardiac arrhythmias, headache, sweating, pallor, anxiety, tremor, and nausea. Intermittent or continuous elevations of the plasma levels of one or several of the catecholamines may also be observed in patients with neuroblastoma and related tumors (ganglioneuroblastomas and ganglioneuromas) and, very occasionally, in other neuroectodermal tumors.

At the other end of the spectrum, inherited and acquired syndromes of autonomic dysfunction or failure and autonomic neuropathies are characterized by either inadequate production of one or several of the catecholamines or by insufficient release of catecholamines upon appropriate physiological stimuli (eg, change in posture from supine to standing, cold exposure, exercise, stress).

**Reference Values****NOREPINEPHRINE**

Supine: 70-750 pg/mL

Standing: 200-1,700 pg/mL

**EPINEPHRINE**

Supine: &lt; or =111 pg/mL

Standing: &lt; or =141 pg/mL

**DOPAMINE**

&lt;30 pg/mL (no postural change)

For SI unit Reference Values, see [www.mayocliniclabs.com/order-tests/si-unit-conversion.html](http://www.mayocliniclabs.com/order-tests/si-unit-conversion.html)

**Interpretation**

Diagnosis of Pheochromocytoma:

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This test should not be used as the first-line test for pheochromocytoma, as plasma catecholamine levels may not be continuously elevated but only secreted during a "spell." By contrast, production of metanephrines (catecholamine metabolites) appears to be increased continuously. The recommended first-line laboratory tests for pheochromocytoma are:

- PMET / Metanephrines, Fractionated, Free, Plasma: the most sensitive assay
- METAF / Metanephrines, Fractionated, 24 Hour, Urine: highly specific and almost as sensitive as PMET

However, plasma catecholamine measurements can still be useful in patients whose plasma metanephrine or urine metanephrine measurements do not completely exclude the diagnosis. In such cases, plasma catecholamine specimens, if collected during a "spell," have a 90% to 95% diagnostic sensitivity when cutoffs of greater than 750 pg/mL for norepinephrine and greater than 110 pg/mL for epinephrine are employed. A lower value during a "spell," particularly when plasma or urinary metanephrine measurements were also normal, essentially rules out pheochromocytoma. Unfortunately, the specificity of these high-sensitivity cutoff levels is not adequate for separating tumor patients from other patients with similar symptoms. When more specific (95%) decision levels of 2000 pg/mL for norepinephrine or 200 pg/mL for epinephrine are used, the assay's sensitivity falls to about 85%.

#### Diagnosis of Neuroblastoma:

Vanillylmandelic acid, homovanillic acid, and sometimes urine catecholamine measurements on random urine or 24-hour urine collections are the mainstay of biochemical diagnosis and follow-up of neuroblastoma. Plasma catecholamine levels can aid diagnosis in some cases, but diagnostic decision levels are not well established. The most useful finding is disproportional elevations in 1 of the 3 catecholamines, particularly dopamine, which may be observed in these tumors.

#### Diagnosis of Autonomic Dysfunction or Failure and Autonomic Neuropathy:

Depending on the underlying cause and pathology, autonomic dysfunction or failure and autonomic neuropathies are associated with subnormal resting norepinephrine levels, or an absent rise of catecholamine levels in response to physiological release stimuli (eg, change in posture from supine to standing, cold exposure, exercise, stress), or both. In addition, there may be significant abnormalities in the ratios of the plasma values of the catecholamines to each other (normal: norepinephrine>epinephrine>dopamine). This is observed most strikingly in the inherited dysautonomic disorder dopamine-beta-hydroxylase deficiency, which results in markedly elevated plasma dopamine levels and a virtually total absence of plasma epinephrine and norepinephrine.

#### Cautions

Catecholamines in plasma are chemically labile and the specimens must be handled carefully, both because of rapid specific metabolism and rapid oxidation on exposure to air. For example, plasma-free norepinephrine has a half-life of approximately 2 minutes. To enhance accuracy, one must pay careful attention to the circumstances of specimen collection and to the preparation of the patient (see Specimen Required).

Many alterations in physiologic and pathologic states can profoundly affect catecholamine concentrations.

Any environmental factor that may increase endogenous catecholamine production should be avoided. These include noise, stress, discomfort, body position, and the consumption of food, caffeinated beverages, or nicotine. Caffeine and nicotine effects are short term, a few minutes to hours only.

Other substances and drugs that may also affect the results include:

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1. Substances that result in increased release or diminished metabolism of endogenous catecholamines
    - Monamine oxidase inhibitors (MOIs): a class of antidepressants with marked effects on catecholamine levels, particularly if the patient consumes tyrosine rich foods, such as nuts, bananas, or cheese
    - Catecholamine reuptake inhibitors including cocaine and synthetic cocaine derivatives, such as many local anesthetics, some of which are also antiarrhythmic drugs (eg, lidocaine)
    - Some anesthetic gases, particularly halothane
    - Withdrawal from sedative drugs, medical or recreational, in particular alcohol, benzodiazepines (eg, Valium), opioids and some central-acting antihypertensive drugs, particularly clonidine, but, generally not cannabis or other hallucinogens such as lysergic acid diethylamide (LSD), mescal, or peyote
    - Vasodilating drugs (eg, calcium antagonists, alpha-blockers)
    - Tricyclic antidepressants usually exert a negligible effect
  2. Substances that reduce or increase plasma volume acutely (eg, diuretics, radiographic contrast media, synthetic antidiuretic hormone [eg, desmopressin 1-deamino-8-d-arginine vasopressin: DDAVP])
  3. Drugs that are metabolized to endogenous catecholamines. In the main, this concerns carbidopa and L-dopa. These drugs are converted to dopamine, and dopamine measurements for patients taking these drugs will be artifactually elevated. Since isolated dopamine elevations are extremely rare, they should always be viewed with suspicion. A review of the high-performance liquid chromatography (HPLC) trace should be requested. On a careful review, this methodology usually, but not always, allows identification of the unmetabolized parent drug, alongside dopamine.

Historically, a third category of potentially interfering substances was represented by molecules that are either similar in chemical structure, antibody epitopes, or chromatographic migration pattern to the catecholamines, or have metabolites that can be mistaken for the catecholamines. The current HPLC-based assay is not subject to any significant direct interference of this kind. In particular, the following drugs, which used to be considered potential interferences, do not cause problems that cannot be resolved, in most cases, with the current assay: acetaminophen, allopurinol, amphetamines and its derivatives (methamphetamine, methylphenidate [Ritalin], fenfluramine, methylenedioxymethamphetamine [MDMA: ecstasy]), atropine, beta-blockers (atenolol, labetalol, metoprolol, sotalol), buspirone, butalbital, carbamazepine, chlorazepate, chlordiazepoxide, chlorpromazine, chlorothiazide, chlorthalidone, clonidine, codeine, diazepam, digoxin, dimethindene, diphenhydramine, diphenoxylate, dobutamine, doxycycline, ephedrine and pseudoephedrine, fludrocortisone, flurazepam, guanethidine, hydralazine, hydrochlorothiazide, hydroflumethiazide, indomethacin, insulin, isoprenaline, isosorbide dinitrate, L-dopa, methenamine mandelate (mandelic acid), methyl dopa, methylprednisolone, nitrofurantoin, nitroglycerine, oxazepam, pentazocine, phenacetin, phenformin, phenobarbital, phenytoin, prednisone, probenecid, progesterone, propoxyphene, propranolol, quinidine, spironolactone, tetracycline, thyroxine, and tripeleminamine.

On occasion when interference cannot be resolved an interference comment will be reported.

The variability associated with age, gender, and kidney failure is uncertain

### Clinical Reference

1. Young WF Jr: Pheochromocytoma and primary aldosteronism. In: Arnold A, ed. Endocrine Neoplasms. Kluwer Academic Publishers; 1997:239-261
2. Hernandez FC, Sanchez M, Alvarez A, et al: A five-year report on experience in the detection of pheochromocytoma. *Ann Intern Med.* 2000;33:649-655

3. Pacak K, Linehan WM, Eisenhofer G, Walther MM, Goldstein DS : Recent advances in genetics, diagnosis, localization, and treatment of pheochromocytoma. *Ann Intern Med.* 2001;134:315-329
4. Alexander F: Neuroblastoma. *Urol Clin North Am.* 2000 Aug;27(3):383-392
5. McDougall AJ, McLeod JG: Autonomic neuropathy, I. Clinical features, investigation, pathophysiology, and treatment. *J Neurol Sci.* 1996;137:79-88
6. Lenders JW, Pacak K, Walther MM, et al: Biochemical diagnosis of pheochromocytoma: which test is best? *JAMA.* 2002;287:1427-1434
7. Jain A, Baracco R, Kapur G: Pheochromocytoma and paraganglioma-an update on diagnosis, evaluation, and management. *Pediatr Nephrol.* 2020 Apr;35(4):581-594. doi: 10.1007/s00467-018-4181-2

## Performance

### Method Description

Following chromatographic purification, which results in a highly purified and concentrated final eluate, the purified amines are quantitated by using high-performance liquid chromatography with electrochemical detection.(Jiang NS, Machacek D, Wadel OP: Further study on the two-column plasma catecholamine assay. *Mayo Clin Proc.* 1976;51:112-116; Jiang NS, Machacek D: Measurement of catecholamines in blood and urine by liquid chromatography with amperometric detection. In: Parvez V, ed. *Progress in HPLC. Vol 2.* VNU Science Press; 1987:397-426; published methods modified by Mayo Clinic Laboratories)

### PDF Report

No

### Day(s) Performed

Monday, Tuesday, Thursday, Friday

### Report Available

2 to 5 days

### Specimen Retention Time

14 days

### 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 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 US Food and Drug Administration.

**CPT Code Information**

82384

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
CATP	Catecholamine Fract, Free, P	34551-2

Result ID	Test Result Name	Result LOINC® Value
2846	Norepinephrine	2666-6
2901	Epinephrine	2230-1
2906	Dopamine	2216-0