

## Overview

### Useful For

Diagnosis of pheochromocytoma and paraganglioma in specimens collected from individuals in a standing position, as an auxiliary test to fractionated plasma and urine metanephrite measurements

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/failure or autonomic neuropathy

### Method Name

Only orderable as part of a profile. For more information see CATPA / Catecholamine, Endocrine Study, Plasma.

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

### NY State Available

Yes

## Specimen

### Specimen Type

Plasma EDTA Meta

### Specimen Required

Only orderable as part of a profile. For more information see CATPA / Catecholamine, Endocrine Study, Plasma.

#### Patient Preparation:

1. Discontinue drugs that release epinephrine, norepinephrine, or dopamine, or hinder their metabolism, for at least 1 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/infusions for at least 12 hours before specimen draw.
3. The patient **must not eat, use tobacco, or drink caffeinated beverages** for at least 4 hours before the specimen is collected.

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

Sarstedt Aliquot Tube, 5 mL (T914)

#### 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 plasma per collection

**Collection Instructions:**

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

1. **Drawing from a catheter is required.**
2. Calm the patient by giving complete instructions and reassurance regarding the procedure.
3. Insert an indwelling intravenous catheter. Flush with 3 mL of saline, 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 blood into the chilled EDTA-sodium metabisulfite 10-mL tube.
8. Specimens **must** remain at refrigerated temperature at all times.
9. Within 30 minutes of collection, centrifuge in a refrigerated centrifuge and aliquot plasma into a plastic vial.
10. Freeze specimen immediately. Ship frozen.

**Specimen Minimum Volume**

Plasma: 2 mL per collection

**Reject Due To**

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Plasma EDTA Meta	Frozen	28 days	

**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 also 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 and dopamine receptors, all existing in several subforms. The 3 catecholamines overlap but 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.

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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, paraganglioma (a tumor of the sympathetic ganglia that also produces catecholamine), 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 1 or several of the catecholamines may 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/failure and autonomic neuropathies are characterized by either inadequate production of 1 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

Only orderable as part of a profile. For more information see CATPA / Catecholamine, Endocrine Study, Plasma.

### Interpretation

Diagnosis of Pheochromocytoma:

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 metanephhrines (catecholamine metabolites) appears to be increased continuously.

The recommended first-line laboratory tests for pheochromocytoma are:

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

However, plasma catecholamine measurements can be useful in patients whose plasma metanephhrine or urine metanephhrine measurements do not completely exclude the diagnosis. In such cases, plasma catecholamine specimens, if drawn during a "spell," have a 90% to 95% diagnostic sensitivity when cutoffs of 750 pg/mL for norepinephrine and 110 pg/mL for epinephrine are employed. A lower value during a "spell," particularly when plasma and/or urinary metanephhrine measurements were also normal, essentially rules out pheochromocytoma. Unfortunately, the specificity of these high-sensitivity cutoff levels is not good 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 using 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

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in these tumors.

**Diagnosis of Autonomic Dysfunction/Failure and Autonomic Neuropathy:**

Depending on the underlying cause and pathology, autonomic dysfunction/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:

1. Substances which result in increased release or diminished metabolism of endogenous catecholamines
  - Monoamine 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, particularly 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 [ie, 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 in patients taking these drugs will be artificially elevated. Since isolated dopamine elevations are extremely rare, they should always be viewed with suspicion. A review of the liquid chromatography tandem mass spectrometry (LC-MS/MS) trace should be requested. On a careful review, our methodology usually, but not always, allows us to identify the unmetabolized parent drug, alongside dopamine.

Historically, a third category of potentially interfering substances was represented by molecules, which 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 LC-MS/MS-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), methyldopa, methylprednisolone, nitrofurantoin, nitroglycerine, oxazepam, pentazocine, phenacetin, phenformin, phenobarbital, phenytoin, prednisone, probenecid, progesterone, propoxyphene, propranolol, quinidine, spironolactone, tetracycline, thyroxine, and tripelennamine.

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

The variability associated with age, gender, and renal failure is uncertain.

### **Clinical Reference**

1. Jain A, Baracco R, Kapur G. Pheochromocytoma and paraganglioma-an update on diagnosis, evaluation, and management. *Pediatr Nephrol*. 2020;35(4):581-594. doi:10.1007/s00467-018-4181-2
2. Bergmann ML, Schmedes A. Highly sensitive LC-MS/MS analysis of catecholamines in plasma. *Clin Biochem*. 2020;82:51-57. doi:10.1016/j.clinbiochem.2020.03.006
3. Cheshire WP Jr, Goldstein DS. Autonomic uprising: the tilt table test in autonomic medicine. *Clin Auton Res*. 2019;29(2):215-230. doi:10.1007/s10286-019-00598-9

### **Performance**

#### **Method Description**

Catecholamines are adsorbed onto activated alumina at pH 8.6, washed with 50% acetonitrile and clinical laboratory reagent water, and eluted with 2% acetic acid. The eluate is derivatized with acetaldehyde and then analyzed for norepinephrine, epinephrine, and dopamine using liquid chromatography tandem mass spectrometry.(Unpublished Mayo method)

#### **PDF Report**

No

#### **Day(s) Performed**

Monday through Friday

#### **Report Available**

2 to 9 days

**Specimen Retention Time**

14 days

**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**

82384

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
CTP10	Catecholamine, Fract, Standing, P	95056-8

Result ID	Test Result Name	Result LOINC® Value
33865	Norepinephrine, Standing	17368-2
33866	Epinephrine, Standing	95054-3
33867	Dopamine, Standing	95055-0