Test Definition: CATP

Catecholamine Fractionation, Free, Plasma

Overview

Useful For

Diagnosing pheochromocytoma and paraganglioma, as an auxiliary test to fractionated plasma and urine metanephrine measurements

Diagnosis 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

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

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. 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

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 2 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 at all times.
9. Separate plasma in a refrigerated centrifuge within 30 minutes of collection.
10. Freeze specimen immediately. Transport frozen.

Forms

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

Specimen Minimum Volume

Plasma: 2 mL

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 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.

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 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 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: 200-1700 pg/mL

Epinephrine
Supine: <111 pg/mL
Standing: <141 pg/mL

Dopamine
<30 pg/mL (no postural change)

For International System of Units (SI) conversion for Reference Values, see

www.mayocliniclabs.com/order-tests/si-unit-conversion.html.

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 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 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 750 pg/mL for norepinephrine and 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 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 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:
1. Substances that 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 [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 liquid chromatography tandem mass spectrometry (LC-MS/MS) 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 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, labetolol, 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 occasions when interference cannot be resolved, an interference comment will be reported.

The variability associated with age, sex, and kidney 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 Definition: CATP

Catecholamine Fractionation, Free, Plasma

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