MAYO CLINIC LABORATORIES

Test Definition: RLTE4

Leukotriene E4, Random, Urine

Overview

Useful For

An aid to evaluate patients suspected of having systemic mastocytosis using random urine collections

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
LTE4R	Leukotriene E4, Random, U	No	Yes
CRETR	Creatinine, Random, U	No	Yes

Highlights

Systemic mastocytosis is a heterogeneous disorder, including N-methylhistamine and 11 beta-prostaglandin F2 alpha analysis along with this test provides a clinical sensitivity is greater than 90% and specificity is greater than 60%.

Method Name

LTE4R: Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)
CRETR: Enzymatic Colorimetric Assay

NY State Available

Yes

Specimen

Specimen Type

Urine

Ordering Guidance

A 24-hour urine collection is the preferred specimen type. Order TLTE4 / Leukotriene E4, 24 Hour, Urine.

Specimen Required

Supplies: Sarstedt 5 mL Aliquot Tube (T914)
Container/Tube: Plastic vial
Specimen Volume: 5 mL
Collection Instructions:
1. Collect a random urine specimen.
2. No preservative preferred.

Specimen Minimum Volume

2 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	Frozen (preferred)	30 days	
	Refrigerated	7 days	
	Ambient	24 hours	

Clinical & Interpretive

Clinical Information

Leukotrienes (LT) are eicosanoids generated from arachidonic acid via the 5-lipoxygenase pathway. Leukotriene E4 (LTE4) is the stable end product of this pathway and therefore regarded as a biomarker of total cysteinyl leukotriene production. Assessment of LTE4 in urine allows for noninvasive specimen collection and avoids artifactual formation of LT during phlebotomy. Generation of LTE4 occurs nonspecifically from active mast cells, basophils, eosinophils, and macrophages, and is modulated through a variety of mechanisms. Elevated concentrations of LTE4 are associated with inflammatory and accelerated mast cell activation conditions, specifically in patients with systemic mast cell disease.(1)

Systemic mastocytosis (SM), or systemic mast cell disease, is a myeloproliferative neoplasm that has infiltrated extracutaneous organs. Release of mast cell inflammatory mediators leads to disease symptoms including those associated with allergic and anaphylactic reactions, while increased mast cell number leads to organ dysfunction. Consensus diagnostic criteria for SM include one major criterion: imaging of the multifocal infiltrates; and 4 minor criteria: 1) identifying morphological features of above 25% of mast cells from bone marrow biopsy, 2) detection of the point alteration at codon 816 in the *KIT* gene, 3) CD2 and/or CD25 expression in mast cells, and 4) persistently elevated serum tryptase. Diagnosis requires either one major plus one minor criterion or 3 minor criteria.(2)

Measurement of urinary mast cell activation biomarkers can aid in the initial evaluation of suspected cases of systemic mast cell disease, potentially avoiding the need for imaging and bone marrow examination. Patients with SM frequently have elevated urine concentrations of LTE4,(1) N-methylhistamine,(3,4) and/or 2,3-dinor 11 beta-prostaglandin F2 alpha.(4)

Urinary LTE4 has also demonstrated significant utility in patients with asthma and respiratory diseases. In a study of adults with mild to moderate asthma on 5-lipoxygenase inhibitors, urine LTE4 concentrations decreased approximately 40% compared to asthma control subjects, suggesting modest decreases in LTE4 production correlates with clinical improvements in asthma severity.

Reference Values

LEUKOTRIENE E4
< or =104 pg/mg creatinine

CREATININE

> or =18 years old: 16-326 mg/dL
Reference values have not been established for patients who are younger than 18 years of age.

Interpretation

Elevated urinary leukotriene E4 (LTE4) concentrations greater than 104 pg/mg creatinine are consistent with the diagnosis of systemic mast cell disease when combined with clinical signs and symptoms. Pharmacological treatment with 5-lipoxygenase inhibitors or leukotriene receptor antagonists has been shown to decrease production of LTE4.

Urinary LTE4 may be used together with serum tryptase, urinary 2,3-dinor 11 beta-prostaglandin F2 alpha, and/or urinary N-methyl histamine.

Cautions

Patients taking 5-lipoxygenase inhibitor zileuton/Zyflo may have decreased concentrations of leukotriene E4 (LTE4) if dosage has not been discontinued for 48 hours.

Systemic mastocytosis is a heterogenous disease and lack of elevated LTE4 does not exclude the diagnosis of mast cell disease.

Increased excretion of LTE4 has also been reported in the following conditions: asthma, eosinophilic pneumonia, respiratory syncytial virus infection, atopic dermatitis, Crohn disease, and rheumatoid arthritis.

11-trans-LTE4 interferes with the LTE4 analysis.

Clinical Reference

1. Divekar R, Hagan J, Rank M, et al: Diagnostic utility of urinary LTE4 in asthma, allergic rhinitis, chronic rhinosinusitis, nasal polyps, and aspirin sensitivity. J Allergy Clin Immunol Pract. 2016 Jul-Aug;4(4):665-670
2. Gotlib J, Pardanani A, Akin C, et al: International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) and European Competence Network on Mastocytosis (ECNM) consensus response criteria in advanced systemic mastocytosis. Blood. 2013 Mar 28;121(13):2393-2401
3. Oranje AP, Mulder PGH, Heide R, Tank B, Riezebos P, van Toorenenbergen AW: Urinary N-methylhistamine as an indicator of bone marrow involvement in mastocytosis. Clin Exp Dermatol. 2002 Sep;27(6):502-506. doi: 10.1046/j.1365-2230.2002.01072.x
4. Van Gysel D, Oranje AP, Vermeiden I, de Raadt JDL, Mulder PG, van Toorenenbergen AW: Value of urinary N-methylhistamine measurements in childhood mastocytosis. J Am Acad Dermatol. 1996 Oct;35(4):556-558
5. Lueke AJ, Meeusen JW, Donato LJ, Gray AV, Butterfield JH, Saenger AK: Analytical and clinical validation of an LC-MS/MS method for urine leukotriene E4: A marker of systemic mastocytosis. Clin Biochem. 2016 Sep;49(13-14):979-982
6. Roberts LJ II, Sweetman BJ, Lewis RA, Austen KF, Oates JA: Increased production of prostaglandin D2 in patients with systemic mastocytosis. N Engl J Med. 1980 Dec 11;303(24):1400-1404

Performance

Method Description

The specimen and an internal standard are assayed by liquid chromatography-tandem mass spectrometry. The analyte is detected by multiple-reaction monitoring.(Unpublished Mayo method)

Creatinine:
The enzymatic method is based on the determination of sarcosine from creatinine with the aid of creatininase, creatinase, and sarcosine oxidase. The liberated hydrogen peroxide is measured via a modified Trinder reaction using a colorimetric indicator. Optimization of the buffer system and the colorimetric indicator enables the creatinine concentration to be quantified both precisely and specifically.(Package insert: Creatinine plus ver 2. Roche Diagnostics; V15.0, 03/2019)

PDF Report
No

Day(s) Performed
Monday, Thursday

Report Available
2 to 6 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
82542
82570

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
RLTE4	Leukotriene E4, Random, U	33343-5

Test Definition: RLTE4

Leukotriene E4, Random, Urine

Result ID	Test Result Name	Result LOINC® Value
CRETR	Creatinine, Random, U	2161-8
603457	Leukotriene E4, Random, U	33343-5