Test Definition: BIOTS

Biotinidase, S

Overview

Useful For

Preferred test for diagnosing biotinidase deficiency

Follow-up testing for certain organic acidurias

Genetics Test Information

Preferred test to rule-out biotinidase deficiency.

Second-tier molecular testing is available, see BTDZ / Biotinidase Deficiency, *BTD* Full Gene Analysis.

Highlights

Enzymatic testing for the diagnosis of biotinidase deficiency, usually in follow-up to an abnormal newborn screen.

Biotinidase deficiency is treatable with oral biotin supplements.

Individuals who are diagnosed presymptomatically (eg, by newborn screening) and who are treated with biotin supplementation do not develop the associated clinical features of biotinidase deficiency.

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Informed Consent for Genetic Testing (Spanish)

Method Name

Colorimetric

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Collection Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Submission Container/Tube: Plastic vial

Specimen Volume: 1 mL

Collection Instructions: Spin down immediately and remove serum.

Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

-Informed Consent for Genetic Testing (T576)

-Informed Consent for Genetic Testing-Spanish (T826)

2. Biochemical Genetics Patient Information (T602) in Special Instructions.

3. If not ordering electronically, complete, print, and send an Inborn Errors of Metabolism Test Request (T798) with the specimen.

Specimen Minimum Volume

0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	21 days	
	Refrigerated	5 days	

Clinical and Interpretive

Clinical Information

Biotinidase deficiency is an autosomal recessive disorder caused by mutations in the biotinidase gene (*BTD*). Age of onset and clinical phenotype vary among individuals depending on the amount of residual biotinidase activity. Profound biotinidase deficiency occurs in approximately 1 in 137,000 live births and partial biotinidase deficiency occurs in approximately 1 in 110,000 live births, resulting in a combined incidence of about 1 in 61,000. The carrier frequency for biotinidase deficiency within the general population is about 1 in 120.

Untreated profound biotinidase deficiency typically manifests within the first decade of life as seizures, ataxia, developmental delay, hypotonia, sensorineural hearing loss, vision problems, skin rash, and alopecia. Partial biotinidase deficiency is associated with a milder clinical presentation, which may include cutaneous symptoms without neurologic involvement. Certain organic acidurias, such as holocarboxylase synthase deficiency, isolated carboxylase synthase deficiency, and 3-methylcrotonylglycinuria, present similarly to biotinidase deficiency. Serum biotinidase levels can help rule out these disorders.

Treatment with biotin is successful in preventing the clinical features associated with biotinidase deficiency. In symptomatic patients, treatment will reverse many of the clinical features except developmental delay, vision, and

hearing complications. As a result, biotinidase deficiency is included in most newborn screening programs. This enables early identification and treatment of presymptomatic patients.

Molecular tests form the basis of confirmatory or carrier testing. When biotinidase enzyme activity is deficient, sequencing of the entire *BTD* gene (BTDZ / Biotinidase Deficiency, *BTD* Full Gene Analysis) allows for detection of disease-causing mutations in affected patients. Identification of familial mutations allows for testing of at-risk family members (FMTT / Familial Mutation, Targeted Testing).

While genotype-phenotype correlations are not well established, it appears that certain mutations are associated with profound biotinidase deficiency, while others are associated with partial deficiency.

Reference Values

3.5-13.8 U/L

Interpretation

The reference range is 3.5 U/L to 13.8 U/L.

Partial deficiencies and carriers may occur at the low end of the reference range.

Values below 3.5 U/L are occasionally seen in specimens from unaffected patients.

Cautions

A diet high in biotin may result in normal clinical presentation even when the biotinidase level is low.

Clinical Reference

1. Zempleni J, Barshop BA, Cordonier EL, et al: Disorders of biotin metabolism. In The Online Metabolic and Molecular Bases of Inherited Diseases. Edited by D Valle, AL Beaudet, B Vogelstein, et al. New York, McGraw-Hill Book Company. Accessed February 20, 2018. Available at http://ommbid.mhmedical.com/content.aspx?bookid=971&sectionid=62646613

2. Wolf B: Biotinidase Deficiency. In GeneReviews Edited by MP Adam, HH Ardinger, RA Pagon, et al. University of Washington, Seattle; 1993-2017. Updated 2016 Jun 9. Accessed February 20, 2018. Available at www.ncbi.nlm.nih.gov/books/NBK1322/

Performance

Method Description

Biotinidase activity is determined colorimetrically by measuring *p*-aminobenzoate liberation from *N*-biotinyl-*p*-aminobenzoate at 546 nm. Activity is determined from a standard curve of *p*-aminobenzoic acid. Modified Sigma substrate is used.(Wolf B, Grier RE, Allen RJ, et al: Biotinidase deficiency: the enzymatic defect in late-onset carboxylase deficiency. Clin Chim Acta 1983;131:273-281)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday, Thursday; set up at 8 a.m.

Analytic Time

4 days

Maximum Laboratory Time

8 days

Specimen Retention Time

30 days

Performing Laboratory Location

Rochester

Fees and 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 U.S. Food and Drug Administration.

CPT Code Information

82261

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
BIOTS	Biotinidase, S	1982-8

Result ID	Test Result Name	Result LOINC Value
50666	Specimen	31208-2
50667	Specimen ID	57723-9
50668	Source	31208-2
50669	Order Date	82785-7
50670	Reason For Referral	42349-1
50671	Method	49549-9
50672	Biotinidase, S	1982-8
50673	Interpretation	59462-2
50674	Amendment	48767-8
50675	Reviewed By	18771-6
50676	Release Date	82772-5