Test Definition: BGABS

Beta-Galactosidase, BS

Overview

Useful For

Diagnosis of beta-galactosidase deficiency (GM1 gangliosidosis, Morquio B disease and galactosialidosis) in blood spot specimens

Testing Algorithm

See Lysosomal Storage Disorders Diagnostic Algorithm, Part 1 in Special Instructions.

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Lysosomal Storage Disorders Diagnostic Algorithm, Part 1
- Blood Spot Collection Instructions

Method Name

Fluorometric Enzyme Assay

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Necessary Information

Provide a reason for referral with each specimen.

Specimen Required

Supplies: Card-Blood Spot Collection (Filter Paper) (T493)

Container/Tube:

Preferred: Blood spot collection card (T493)

Acceptable: Ahlstrom 226 Filter Paper and Whatman Protein Saver 903 Paper

Specimen Volume:2 blood spots

Collection Instructions:

1. An alternative blood collection option for a patient >1 year of age is fingerstick.

2. Let blood dry on the filter paper at ambient temperature in a horizontal position for 3 hours.

3. Do not expose specimen to heat or direct sunlight.

4. Do not stack wet specimens.

5. Keep specimen dry.

Additional Information:

1. For collection instructions, see Blood Spot Collection Instructions in Special Instructions.

2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777) in Special Instructions.

3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800) in Special Instructions.

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

Blood spot: 1

Reject Due To

Blood spot	Shows serum rings or has multiple layers

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	28 days	FILTER PAPER
	Frozen	90 days	FILTER PAPER
	Refrigerated	90 days	FILTER PAPER

Clinical and Interpretive

Clinical Information

Beta-galactosidase is a lysosomal enzyme responsible for catalyzing the hydrolysis of gangliosides. The deficiency of this enzyme can be seen in the following conditions: GM1 gangliosidosis, Morquio syndrome B, and

galactosialidosis. Enzymatic testing is not reliable for carrier detection of these conditions.

GM1 gangliosidosis is an autosomal recessive lysosomal storage disorder caused by reduced or absent beta-galactosidase activity. Absent or reduced activity leads to the accumulation of GM1 gangliosides, oligosaccharides, and keratan sulfate. The disorder can be classified into 3 subtypes that vary with regard to age of onset and clinical presentation. Type 1, or infantile onset, typically presents between birth and 6 months with a very rapid progression of hypotonia, dysostosis multiplex, hepatosplenomegaly, central nervous system degeneration, and death usually by 1 to 2 years. Type 2 is generally classified as late infantile or juvenile with onset between 7 months and 3 years, presenting with developmental delays, and a having a slower progression. Type 3 is an adult or chronic variant with onset between 3 and 30 years and is typically characterized by slowly progressive dementia with Parkinsonian features and dystonia. The incidence has been estimated to be 1 in 100,000 to 200,000 live births.

Mucopolysaccharidosis type IVB (MPS IVB, Morquio B) is an autosomal recessive lysosomal storage disorder caused by reduced or absent beta-galactosidase activity. The mucopolysaccharidoses are a group of disorders caused by the deficiency of any of the enzymes involved in the stepwise degradation of dermatan sulfate, heparan sulfate, keratan sulfate, or chondroitin sulfate (glycosaminoglycans; GAGs). Accumulation of GAGs (also known as mucopolysaccharides) in lysosomes interferes with normal functioning of cells, tissues, and organs. MPS IVB is caused by a reduced or absent activity of the beta-galactosidase enzyme and gives rise to the physical manifestations of the disease. Clinical features and severity of symptoms of MPS IVB are widely variable ranging from severe disease to an attenuated form, which generally presents at a later onset with a milder clinical presentation. In general, symptoms may include coarse facies, short stature, hepatosplenomegaly, hoarse voice, stiff joints, cardiac disease, but no neurological involvement.

Galactosialidosis is an autosomal recessive lysosomal storage disease associated with a combined deficiency of beta-galactosidase and neuraminidase secondary to a defect in the cathepsin A protein. The disorder can be classified into 3 subtypes that vary with regard to age of onset and clinical presentation. Typical clinical presentation is coarse facial features, cherry-red spots, and skeletal dysplasia. The early infantile form is associated with fetal hydrops, skeletal dysplasia, and early death. The late infantile form typically presents with short stature dysostosis multiplex, coarse facial features, corneal clouding, hepatosplenomegaly, and heart valve problems. The juvenile/adult form is typically characterized by progressive neurologic degeneration, ataxia, and angiokeratomas. The incidence of the juvenile/adult form is greater in individuals with Japanese ancestry.

Patients with mucolipidosis II/III (I-cell disease) may also demonstrate deficiency of beta-galactosidase in leukocytes, in addition to deficiency of other hydrolases. I-cell disease is an autosomal recessive lysosomal storage disorder resulting in impaired transport and phosphorylation of newly synthesized lysosomal proteins to the lysosome due to deficiency of N-acetylglucosamine 1-phosphotransferase (GlcNAc). Characteristic clinical features include short stature, skeletal and cardiac abnormalities, and developmental delay. Measurement of beta-galactosidase activity is not the preferred diagnostic test for I-cell disease but may be included in the testing strategy.

A diagnostic workup in an individual with GM1 gangliosidosis, Morquio B, or galactosialidosis typically demonstrates decreased beta-galactosidase enzyme activity in leukocytes or fibroblasts; however, additional testing and consideration of the patientÃ¢â‚¬â„¢s clinical findings are necessary to differentiate between these conditions. Individuals with GM1 gangliosidosis can have characteristic abnormalities on urine oligosaccharides and have elevated keratan sulfate in urine (however to a lesser degree than seen in patients with Morquio B). Individuals with Morquio B can have increased keratan sulfate in urine. Molecular sequence analysis of the *GLB1* gene allows for detection of the disease-causing mutations in affected patients with GM1 gangliosidosis or Morquio B. Individuals with galactosialidosis demonstrate abnormalities on urine oligosaccharides as well as decreased neuraminidase activity in fibroblasts. Sequencing of the *CTSA* gene allows for detection of disease-causing mutations in patients with galactosialidosis.

Reference Values

> or =5.0 nmol/hour/mL

An interpretive report will be provided.

Interpretation

Properly submitted specimens with results less than 5.0 nmol/h/mL are consistent with beta-galactosidase deficiency (GM1 gangliosidosis, Morquio B disease, or galactosialidosis). Further differentiation between GM1, Morquio B, and galactosialidosis is dependent on the patient's clinical findings and results of additional biochemical testing.

Normal results (> or =5.0 nmol/hour/mL) are not consistent with beta-galactosidase deficiency.

Cautions

This test cannot reliably determine carrier status.

This test does not differentiate between GM1 gangliosidosis, Morquio B, and galactosialidosis.

Clinical Reference

1. Suzuki Y, Nanba E, Matsuda J, et al: Beta-Galactosidase Deficiency (Beta-Galactosidosis): GM1 Gangliosidosis and Morquio B Disease. In *The Online Metabolic and Molecular Bases of Inherited Disease.* Edited by D Valle, AL Beaudet, B Vogelstein, et al. New York, McGraw-Hill; 2014. Accessed January 27, 2017. Available at www.ommbid.mhmedical.com/content.aspx?bookid=971&sectionid=62645114

2. Chamoles NA, Blanco M, Gaggioli D, Casentini C: Hurler-like phenotype: enzymatic diagnosis in dried blood spots on filter paper. Clin Chem 2001;47:2098-2102

3. Regier DS, Tifft CJ: GLB1-Related Disorders. In GeneReviews. Edited by RA Pagon, MP Adam, HH Ardinger et al. Accessed January 30, 2017. Available at www.ncbi.nlm.nih.gov/books/NBK164500/

4. Fernandes, Saudubray, van den Berghe, Walter. Inborn Metabolic Diseases: Diagnosis and Treatment. Fourth edition. Edited by J Fernandes, JM Saudubray, G van den Berghe, JH Walter. Springer Science. 2006

Performance

Method Description

Whole blood collected in ACD or EDTA anticoagulant tubes is spotted onto filter paper. A 1/8-inch (3-mm) disk is punched out of the dried blood spot (DBS) into a 96-well, round-bottom plate containing 40 microliters of 50 mM cit-phos buffer as elution liquid and 20 microliters of 0.8 mM 4-methylumbelliferyl-beta-D-galactopyranoside in water as the substrate (60 microliters total volume + DBS). A blank is prepared using only elution liquid, substrate, and filter paper punches containing no blood (60 microliters total volume + blank punches). All patients, controls, and blank are set up in duplicate (2 punches total, 1 punch per well). After the incubation period (3 hours at 37 degrees C), all of the liquid from the plate is manually transferred to a 96-well, flat-bottom black plate. A calibration curve is prepared and analyzed on every plate to calculate enzyme activity results, based on fluorescence units in patient wells vs. calibrators. The calibration is derived from 4-methylumbelliferone (4-MU) that is serially diluted manually in the plate with the highest calibrator being equivalent to an enzyme activity of 10.4 nmol/hour/mL. Two hundred microliters of stop buffer (150 mM EDTA, pH 11.4) is added to all wells (patients, QC, blanks, calibrators). The plate is then read on the spectrofluorometer. Fluorescence readings for duplicate wells are averaged, and the average fluorescence is used to calculate the enzyme activity result.(Civallero G, Michelin K, de Mari J, et al: Twelve different enzyme assays on dried-blood filter paper samples for detection of patients with selected inherited lysosomal storage diseases. Clin Chim Acta 2006;372:98-102)

PDF Report

No

Day(s) and Time(s) Test Performed

Varies

Analytic Time

8 days

Maximum Laboratory Time

15 days

Specimen Retention Time

1 year

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

82657

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
BGABS	Beta-Galactosidase, BS	55916-1

Result ID	Test Result Name	Result LOINC Value
60986	Beta-Galactosidase, BS	55916-1
34430	Interpretation	69047-9
34429	Reason for Referral	42349-1
34431	Reviewed By	18771-6