MAYO CLINIC LABORATORIES

Test Definition: NAGR

Hexosaminidase A and Total, Leukocytes/Molecular Reflex, Whole Blood

Overview

Useful For

Carrier detection and diagnosis of Tay-Sachs disease

Carrier detection and diagnosis of Sandhoff disease

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
HEXBZ	HEXB Gene, Full Gene Analysis	Yes	No
CULFB	Fibroblast Culture for Genetic Test	Yes	No
HEXAN	HEXA Gene Analysis	Yes	No
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
MATCC	Maternal Cell Contamination, B	Yes	No

Testing Algorithm

If result interpretation is consistent with carrier, indeterminate, or affected for Tay-Sachs disease or Sandhoff disease, then next-generation sequencing to detect single nucleotide and copy number variants for *HEXA* or *HEXB*, respectively, will be performed at an additional charge.

For more information see Tay-Sachs and Related Disorders Diagnostic Testing Algorithm

Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Tay-Sachs and Related Disorders Diagnostic Testing Algorithm
- Informed Consent for Genetic Testing (Spanish)
- Hexosaminidase Test Selection Quick-Reference Comparison

Method Name

Heat Inactivation/Fluorometric/Semiautomated

NY State Available

Yes

Specimen

Specimen Type
Whole Blood ACD

Ordering Guidance
The following tests are available for diagnostic and carrier testing for Tay-Sachs and Sandhoff diseases:
NAGR / Hexosaminidase A and Total, Leukocytes/Molecular Reflex, Whole Blood
NAGW / Hexosaminidase A and Total Hexosaminidase, Leukocytes
NAGS / Hexosaminidase A and Total Hexosaminidase, Serum
MUGS / Hexosaminidase A, Serum

For information on hexosaminidase test selection see Hexosaminidase Test Selection Quick-Reference Comparison.

Shipping Instructions
For optimal isolation of leukocytes, it is recommended the specimen arrive refrigerated within 6 days of collection to be stabilized.

Pre-analytical processing is performed Monday through Friday and Sunday. This test may be canceled if specimens are outside of stability when processing occurs. Collect and package specimens for arrival on days when processing is performed.

Specimen Required
Container/Tube:
Preferred: Yellow top (ACD solution B)
Acceptable: Yellow top (ACD solution A)
Specimen Volume: 6 mL
Collection Instructions: Send whole blood specimen in original tube. **Do not aliquot**.

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:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
2. Biochemical Genetics Patient Information (T602)
3. If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume
5 mL

Reject Due To

Gross hemolysis	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood ACD	Refrigerated (preferred)	6 days	YELLOW TOP/ACD
	Ambient	6 days	YELLOW TOP/ACD

Clinical & Interpretive

Clinical Information

Tay-Sachs and Sandhoff diseases, also referred to as GM2 gangliosidoses, are lysosomal storage disorders caused by deficiencies of hexosaminidase A and hexosaminidase B, respectively. These related enzymes are dimers that differ by subunit composition. Hexosaminidase A is a heterodimer composed of 1 alpha and 1 beta subunit, whereas hexosaminidase B is a homodimer composed of 2 beta subunits. The alpha subunit is encoded by the *HEXA* gene and the beta subunit is encoded by *HEXB*. Defective lysosomal degradation leads to excessive accumulation of GM2 ganglioside and related glycolipids, resulting in the clinical features associated with Tay-Sachs and Sandhoff diseases.

Both Tay-Sachs and Sandhoff diseases are inherited in an autosomal recessive manner. Tay-Sachs disease is caused by 2 disease-causing variants in *HEXA*, resulting in hexosaminidase A deficiency. An increased carrier frequency for Tay-Sachs disease is observed in individuals of Ashkenazi Jewish, Celtic, and French-Canadian ancestry. Sandhoff disease is caused by 2 disease-causing variants in *HEXB*, resulting in deficiencies of both hexosaminidase A and hexosaminidase B. Sandhoff disease does not exhibit an increased carrier frequency in any specific population.

Clinical Phenotypes:
Phenotypically, patients with Tay-Sachs and Sandhoff diseases are virtually indistinguishable. Variability is observed with respect to age of onset and clinical symptoms. Enzyme analysis is generally required to distinguish between the 2 disorders.

The acute infantile forms of Tay-Sachs and Sandhoff diseases typically present with progressive motor deterioration beginning at 3 to 6 months of age. Patients exhibit weakness, hypotonia, and decreasing attentiveness. Motor skills learned previously, such as crawling or sitting alone, are nearly always lost by 1 year of age. Other symptoms include rapid diminishing of vision, seizures, macrocephaly due to cerebral gliosis, and the characteristic cherry-red spot in the retina. Affected individuals typically do not survive past early childhood.

The juvenile or subacute forms often present between 2 and 10 years of age with ataxia and clumsiness. Patients develop difficulties with speech and cognition. Neurologic features progressively get worse, and death typically occurs 2 to 4 years later.

Disease progression is slower in patients with chronic or adult-onset Tay-Sachs and Sandhoff diseases. Early signs and symptoms may be subtle and nonspecific, involving muscle and/or neurologic findings, often resulting in initial

misdiagnoses. Affected individuals may exhibit abnormalities of gait and posture, spasticity, dysarthria, and progressive muscle wasting and weakness. Cognitive impairment, dementia, or psychiatric findings are observed in some patients. Significant clinical variability exists both between and within families.

Testing Options:
Several tests are available for the detection of carriers of, and individuals affected with, Tay-Sachs and Sandhoff diseases (see Table, Ordering Guidance, and Testing Algorithm). This test is the recommended test for both diagnostic and carrier testing. Testing begins with enzyme analysis and when indicated reflexes to the appropriate molecular analysis for either the *HEXA* or *HEXB* gene.

Follow-up molecular testing is recommended for all individuals with enzyme results in the carrier, possible carrier, or affected ranges. This differentiates between nondisease-causing pseudodeficiency alleles and disease-causing variants. In addition, molecular analysis allows for the facilitation of carrier testing and prenatal diagnosis for at-risk individuals.

For additional information on hexosaminidase test selection see Hexosaminidase Test Selection Quick-Reference Comparison.

Reference Values

Hexosaminidase Total
< or =15 years: > or =20 nmol/min/mg
> or =16 years: 16.4-36.2 nmol/min/mg

Hexosaminidase Percent A
< or =15 years: 20-80% of total
> or =16 years: 63-75% of total

Interpretation

Interpretation is provided with report.

Cautions

A small percentage (<0.5%) of carriers may exhibit normal hexosaminidase A activity and will not be detected by this method.(1)

GM2 activator deficiency (AB variant, *GM2A*) is a rare disorder with clinical features similar to Tay-Sachs and Sandhoff diseases; however, levels of both hexosaminidase A and B are normal. GM2 activator deficiency is not detected with this assay. Molecular genetic analysis of *GM2A* is available, see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies.

Clinical Reference

1. Triggs-Raine BL, Feigenbaum ASJ, Natowicz M, et al. Screening for carriers of Tay-Sachs disease among Ashkenazi Jews-A comparison of DNA-based and enzyme-based tests. N Engl J Med. 1990;323(1):6-12
2. Delnooz CCS, Lefeber DJ, Langemeijer SMC, et al. New cases of adult-onset Sandhoff disease with a cerebellar or lower motor neuron phenotype. J Neurol Neurosurg Psychiatry. 2010;81(9):968-972
3. Vallance H, Morris TJ, Coulter-Mackie M, Lim-Stelle J, Kaback M. Common HEXB polymorphisms reduce serum HexA and HexB enzymatic activities, potentially masking Tay-Sachs disease carrier identification. Mol Genet Metab.

2006;87(2):122-127
4. Toro C, Shirvan L, Tifft C. *HEXA* disorders. In: Adam MP, Feldman J, Mirzaa GM, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 1999. Updated October 1, 2020. Accessed August 31, 2026. Available at www.ncbi.nlm.nih.gov/books/NBK1218/
5. Neudorfer O, Pastores GM, Zeng BJ, Gianutsos J, Zaroff CM, Kolodny EH. Late-onset Tay-Sachs disease: phenotypic characterization and genotypic correlations in 21 affected patients. Genet Med. 2005;7(2):119-123
6. Sutton VR. Tay-Sachs disease screening and counseling families at risk for metabolic disease. Obstet Gynecol Clin North Am. 2002;29(2):287-296
7. Gravel RA, Kaback MM, Proia RL, Sandhoff K, Suzuki K, Suzuki K. The GM2 gangliosidoses. In: Valle D, Antonarakis S, Ballabio A, Beaudet A, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill. Accessed August 31, 2026 Available at http://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225547784
8. D'Souza G, McCann CL, Hedrick J, et al. Tay-Sachs disease carrier screening: a 21-year experience. Genet Test. 2000;4(3):257-263. doi:10.1089/10906570050501470

Performance

Method Description

Leukocyte hexosaminidase A and total hexosaminidase are estimated using a semiautomated modification of the method of O'Brien, et al (1970) with further specific recommendations on specimen preparation as outlined by the International Tay-Sachs Disease Testing Quality Control and Data Collection Center.(O'Brien JS, Okada S, Chen A, Fillerup DL. Tay-Sachs disease: detection of heterozygotes and homozygotes by hexosaminidase assay. N Engl J Med. 1970;283[1]:15-20; Cowan T, Pasquali M. Laboratory investigations of inborn errors of metabolism. In: Sarafoglou K, Hoffman GF, Roth KS, eds. Pediatric Endocrinology and Inborn Errors of Metabolism. 2nd ed. McGraw-Hill; 2017:1139-1158)

Next-generation sequencing (NGS) and/or Sanger sequencing are performed to test for the presence of variants in coding regions and intron/exon boundaries of the gene analyzed, as well as some other regions that have known disease-causing variants. The human genome reference GRCh37/hg19 build was used for sequence read alignment. At least 99% of the bases are covered at a read depth over 30X. Sensitivity is estimated at above 99% for single nucleotide variants, above 94% for deletion-insertions (delins) less than 40 base pairs (bp), above 95% for deletions up to 75 bp and insertions up to 47 bp. NGS and/or a polymerase chain reaction-based quantitative method is performed to test for the presence of deletions and duplications in the gene analyzed.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed
Preanalytical processing: Monday through Friday, Sunday
Assay is performed: Friday

Report Available
2 to 8 days

Specimen Retention Time
White blood cell homogenate: 1 month

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

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
83080 x2
81406 (if appropriate)
81479 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
NAGR	Hexosaminidase A and Tot, WBC/Mole	87543-5

Result ID	Test Result Name	Result LOINC® Value
8775	Hexosaminidase Total, WBC	24075-4
2294	Hexosaminidase Percent A, WBC	23825-3
2284	Interpretation (NAGW)	59462-2
35029	Reviewed By	18771-6