

Lab Facets

Tay-Sachs Disease

What is Tay-Sachs disease?

Tay-Sachs disease (TSD) is a lysosomal storage disorder that causes progressive neurological disease. Patients with TSD have low or absent activity of the enzyme beta-hexosaminidase A.¹ Infantile TSD, the most common form of TSD, presents in the first year of life with loss of developmental milestones and progresses inevitably to death, usually by five years of age. A less common adult onset form of TSD, which presents in adolescence or adulthood, also occurs. There is currently no effective treatment or cure for TSD.

How is Tay-Sachs disease inherited?

TSD is an autosomal recessive disorder. Both parents must be carriers of TSD in order to have affected children. When both parents are carriers, they have a 25% chance with each pregnancy to have an affected child.

Who should be offered Tay-Sachs disease carrier testing?

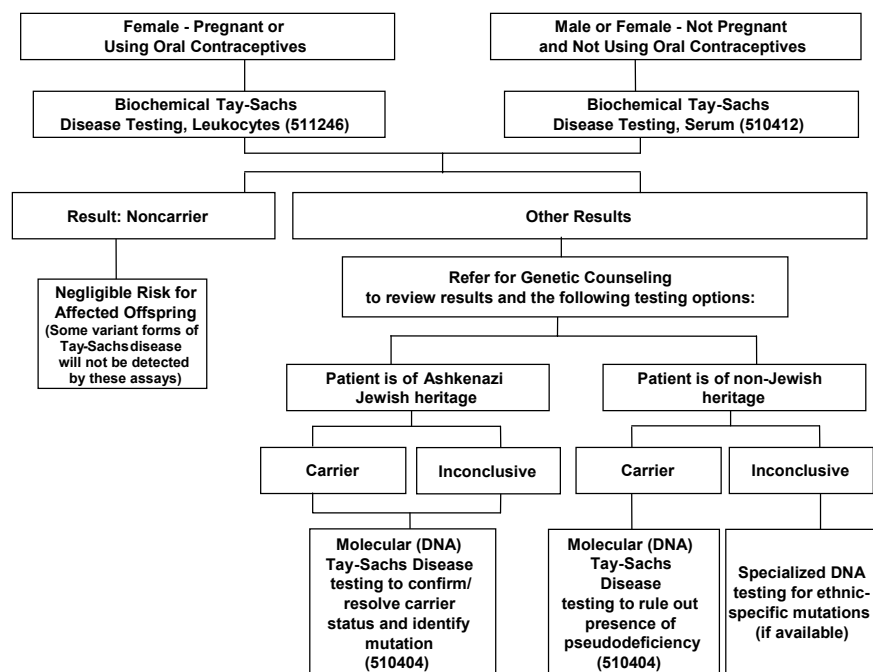
Carriers of TSD are not physically affected by being a carrier and usually do not have a history of the disease in their families. One in 300 individuals in the general population is a TSD carrier,¹ although one in 25 Ashkenazi (eastern European) Jewish individuals is a TSD carrier.² Other ethnic groups with high TSD carrier rates include non-Jewish French Canadians from eastern Quebec and Acadians (Cajuns).¹ Pseudodeficiency mutations, which cause the appearance of reduced enzyme activity but do not cause TSD, can occur in all ethnic groups.

The American College of Obstetricians and Gynecologists (ACOG) recommends TSD carrier testing in couples when one or both members belong to a high-risk population.³ Ideally, testing is performed prior to pregnancy. If only one member of a couple is at high risk, that member can be tested first. If the woman is pregnant at the time of carrier testing, however, it may be advisable to test both members of the couple at the same time. This will avoid delays in determining whether the pregnancy is at risk and ensure that there is still time for options such as prenatal diagnosis.

If both members of a couple are carriers, several options are available. Prenatal diagnosis is available using fetal cells obtained by amniocentesis or chorionic villus sampling (CVS). Couples identified before pregnancy may also consider adoption, sperm or egg donation, or (in some cases) in vitro fertilization with preimplantation diagnosis.

Test options for Tay-Sachs disease

- **Tay-Sachs Disease Biochemical Assay, Serum.** This blood test measures the activity of beta-hexosaminidase A and B in serum. It is mutation-independent, so it is suitable for individuals from any ethnic background. Serum testing is **not** accurate for women who are pregnant or taking oral contraceptives.³
- **Tay-Sachs Disease Molecular (DNA) Assay.** This test examines the patient's DNA for the most common mutations that cause Tay-Sachs disease. The detection rate is approximately 95% in individuals of Ashkenazi (eastern European) Jewish ancestry.¹ The detection rate is 50% or less in other ethnic groups. Molecular testing is not affected by pregnancy or oral contraceptives.
- **Tay-Sachs Disease Biochemical Assay, Leukocytes.** This blood test measures the activity of beta-hexosaminidase A and B in white blood cells. It is mutation-independent, so it is suitable for individuals from any ethnic background. Leukocyte testing is not affected by pregnancy or oral contraceptives.



Suggested Algorithm for Tay-Sachs Disease Testing

Note: Rare variants of Tay-Sachs disease, such as the B1 variant and the activator protein deficiency, will not be detected by these assays.

Our board-certified genetic counselors and geneticists are available for consultation regarding these tests. Please call our genetics service department at 800-345-GENE.

References

1. Gravel RA, Clarke JTR, Kaback MM, Mahuran D, Sandhoff K, Suzuki K. The G_{M2} gangliosidosis. In Scriver CR, Beaudet AL, Sly WS, Valle D, eds. *The Metabolic and Molecular Bases of Inherited Disease. II*. 7th ed. New York, NY: McGraw-Hill; 1995: 2839-2879.
2. *What Every Family Should Know*. 4th ed. Newton, Mass: National Tay-Sachs and Allied Diseases Association; 1987.
3. ACOG Committee on Genetics. *Screening for Tay-Sachs Disease*. Washington, DC: American College of Obstetricians and Gynecologists; 1991. Committee Opinion, No. 162.

Tay-Sachs Disease, Biochemical, Serum 510412

CPT 83080

Specimen Serum, frozen

Volume 3 mL

Minimum Volume 1 mL

Container Red-stopper tube

Collection Separate serum from cells within 30 minutes of venipuncture. Transfer specimen to plastic transport tube before freezing. To avoid delays in turnaround time when requesting multiple tests on frozen samples, please submit separate frozen specimens for each test requested.

Storage Instructions Freeze.

Causes for Rejection Quantity not sufficient for analysis; thawed specimen

Use Determine Tay-Sachs disease carriers and affected status. This assay should not be performed on women who are pregnant or who are taking oral contraceptives.

Limitations This assay may not detect patients or carriers of rare variants of Tay-Sachs disease such as the B1 variant or the activator protein deficiency.

Methodology Determination of enzymatic activity using heat inactivation

Contraindications This assay should not be performed on women who are pregnant or who are taking oral contraceptives.

Tay-Sachs Disease, DNA Analysis 510404

CPT 83890; 83892; 83893 (x3); 83894 (x2); 83896 (x6) 83901; 83912

Special Instructions A completed Tay-Sachs Disease Screening Questionnaire must accompany specimens.

Specimen Whole blood or amniotic fluid (submission of maternal blood required for prenatal testing)

Volume 7 mL whole blood or 10 mL amniotic fluid

Minimum Volume 3 mL blood, 5 mL amniotic fluid

Container Lavender-stopper (EDTA) tube or sterile plastic conical tube (amniotic fluid)

Storage Instructions Maintain specimen at room temperature.

Causes for Rejection Frozen or hemolyzed specimen; quantity not sufficient for analysis

Use Pre- and postnatal determination of Tay-Sachs disease carrier status; resolution of pseudodeficiency allele status

Limitations Greater than 95% of the mutant alleles in persons with Ashkenazi Jewish heritage are detected. In persons with non-Ashkenazi heritage, approximately 52% of the mutant alleles are detected.

Methodology Polymerase chain reaction (PCR) and allele-specific oligonucleotide (ASO) and restriction enzyme analyses

Tay-Sachs Disease, Biochemical, Leukocytes 511246

CPT 83080

Special Instructions Collect Monday through Thursday only. Specimens must arrive in lab within 48 hours of collection. A completed Tay-Sachs Disease Screening Questionnaire must accompany specimens.

Specimen Whole blood

Volume 10 mL

Minimum Volume 5 mL

Container Yellow-stopper (ACD whole blood) tube

Collection Refrigerate after collection. Transport to the testing lab using cool pack or LabCorp transport kit. Do not allow sample to freeze. Sample must arrive in the laboratory within 48 hours of collection.

Storage Instructions Refrigerate.

Causes for Rejection Quantity not sufficient for analysis; frozen specimen; specimen not received within 48 hours of collection

Use Identification of Tay-Sachs disease gene carriers and affected individuals

Limitations This assay may not identify patients or carriers of rare variants of Tay-Sachs disease such as the B1 variant or the activator protein deficiency.

Methodology Determination of enzymatic activity using heat inactivation



Results That Matter

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