

Gaucher Disease

Gaucher disease (GD) is a lysosomal storage disease most often affecting individuals of Ashkenazi Jewish (AJ) descent. GD type 1 is the most common form with symptoms ranging from mild to severe. Symptoms include hepatosplenomegaly, anemia, thrombocytopenia, lung disease, and bone abnormalities. Symptoms of type 1 can appear anytime from childhood to adulthood. GD types 2 and 3 are neuronopathic forms differentiated mainly by disease progression and involve the central nervous system with life-threatening problems that typically appear in early infancy. Symptoms of types 2 and 3 also include eye abnormalities, seizures, and damage to the brain. Testing is used for pre-pregnancy carrier screening or for diagnostic testing in individuals suspected of having GD.

Disease Overview

Prevalence

- ~1 in 57,000 to 1 in 75,000^{1,2} in general population
- GD type 1 estimated at 1 in 855 in individuals of AJ descent³

Age of Onset

- Type 1: childhood/adulthood
- Type 2: typically before age 2, with death by age 2-4
- Type 3: typically in childhood, but survival into third or fourth decade

Symptoms

GD affects lysosomal storage and has extreme symptom variability, ranging from perinatal lethality to asymptomatic individuals.

- Type 1
 - Represents 95% of GD; characterized by non-neuronopathic symptoms including bone disease, hepatosplenomegaly, lung disease, and anemia³
- Type 2 (acute neuronopathic)
 - Primary central nervous system (CNS) involvement with rapidly progressive course
- Type 3 (subacute/chronic)
 - Primary CNS involvement with slowly progressive course

Tests to Consider

[Gaucher Disease \(GBA\) Sequencing 3001648](#)

Method: Polymerase Chain Reaction/Sequencing

Carrier screening or diagnostic testing for GD in individuals of non-Ashkenazi Jewish descent

[Gaucher Disease \(GBA\), 8 Variants 0051438](#)

Method: Polymerase Chain Reaction/Fluorescence Monitoring

Carrier screening or diagnostic testing for GD in individuals of Ashkenazi Jewish descent

[Familial Mutation, Targeted Sequencing 2001961](#)

Method: Polymerase Chain Reaction/Sequencing

Useful when pathogenic familial variants identifiable by sequencing are known

Related Tests

[Gaucher Disease \(GBA\), Enzyme Activity in Leukocytes 2014459](#)

Method: Quantitative Fluorometry

Use to diagnose GD only; not accurate for carrier screening

[Ashkenazi Jewish Diseases, 16 Genes 0051415](#)

Method: Polymerase Chain Reaction/Fluorescence Monitoring

- Preferred gene panel for carrier screening in individuals of Ashkenazi Jewish descent
- For test specific information, see [Ashkenazi Jewish Genetic Diseases Panel Test Fact Sheet](#)

Genetics

Gene

GBA

Inheritance

Autosomal recessive

Penetrance

Variable

Test Methodology

- *GBA* sequencing: Long range PCR followed by bidirectional sequencing of all coding regions and intron-exon boundaries of the *GBA* gene
- *GBA* 8 Variants: Polymerase chain reaction (PCR) and fluorescence monitoring
 - Targeted variants: c.115+1G>A; c.84dupG, p.L29Afs; c.1226A>G, p.N409S; c.1263_1317del55; c.1297G>T, p.V433L; c.1342G>C, p.D448H; c.1448T>C, p.L483P; and c.1604G>A, p.R535H

Test Sensitivity and Specificity

Clinical Sensitivity

Sequencing: ~99%³

Targeted variants: 90% in individuals of Ashkenazi Jewish descent; 55% in other ethnicities³

Analytical Sensitivity and Specificity

~99%

Limitations

- Diagnostic errors can occur due to rare sequence variations.
- Regulatory region variants, deep intronic variants, large deletions/duplications/insertions, gene conversion events and complex gene rearrangements may not be detected.

References

1. Meikle PJ, Hopwood JJ, Clague AE, et al. [Prevalence of lysosomal storage disorders](#). JAMA. 1999; 281 (3): 249-54. PubMed

2. Biegstraaten M, van Schaik IN, Aerts JMFG, et al. 'Non-neuronopathic' Gaucher disease reconsidered. Prevalence of neurological manifestations in a Dutch cohort of type I Gaucher disease patients and a systematic review of the literature. *J Inher Metab Dis*. 2008; 31 (3): 337-49. PubMed
3. Pastores GM, Hughes DA. [Gaucher Disease](#). In: Adam MP, Ardinger HH, Pagon RA, et al, editors. GeneReviews, University of Washington; 1993-2020. [Last Update: Jun 2018; Accessed: Feb 2020]

Related Information

Ashkenazi Jewish Genetic Diseases

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