Gaucher Disease and ASMD

Incidence of GD

Incidence of GD:
1 in 50,000-100,000 in the general population worldwide,[3] and about 1 in 850 people of Ashkenazi Jewish heritage[3] for GD type 1[3]

Incidence of ASMD

Incidence of ASMD is estimated at 0.5 per 100,000 births[2]

GD Inheritance

Autosomal recessive disease caused by pathogenic variants in both copies of the *GBA* gene[1]

ASMD Inheritance

Autosomal recessive disease caused by pathogenic variants in both copies of the *SMPD1* gene[2]

Overview

Gaucher disease (GD) and Acid Sphingomyelinase Deficiency [(ASMD), historically known as Niemann-Pick disease (NPD) types A, A/B, and B], are rare lysosomal storage diseases with phenotypic overlap.

Gaucher disease is caused by pathogenic variants in *GBA1* which result in a deficiency of the enzyme acid β-glucosidase (also known as glucocerbrosidase or GCase). Deficiency or absence of this enzyme leads to a buildup of glycosylceramide (GL-1) and glucosylsphingosine (lyso-GL-1).[1]

ASMD is caused by pathogenic variants in *SMPD1* which result in deficiency of the enzyme acid sphingomyelinase (ASM) and a subsequent accumulation of sphingomyelin and other lipids.[2]

Both diseases present with similar symptoms: anemia, thrombocytopenia, splenomegaly, and bone involvement due to displacement of normal marrow cells with disease-affected cells resulting in bone pain, osteopenia, and fractures.[1,2] Gaucher disease and ASMD each have a wide phenotypic spectra ranging from severe neuronopathic forms to chronic visceral forms.[1,2]

Some symptoms differ between the two diseases, for example: atherogenic dyslipidemia, liver disease, and pulmonary involvement are more commonly associated with ASMD.[2, 4, 5]

Diagnosis

Definitive diagnosis of GD is established by:

- Acid β-glucosidase enzyme assay: demonstrating deficient activity[3]
- *GBA* gene sequencing: demonstrating two pathogenic variants in *trans* (one from each parent). Though identification of pathogenic alleles is not required for diagnosis, it can provide secondary confirmation and important information related to phenotype.

Definitive diagnosis of ASMD is established by:

- Acid sphingomyelinase enzyme assay: demonstrating deficient activity[6]
    - Should be done in parallel with acid β-glucosidase enzyme assay or reflexed if acid β-glucosidase is normal.[4]
- *SMPD1* gene sequencing: demonstrating two pathogenic variants in *trans* (one from each parent).[2] Though identification of pathogenic alleles is not required for diagnosis, it can provide secondary confirmation and important information related to phenotype.

The following evaluations may support a diagnosis of GD or ASMD:

Laboratory Testing

Gaucher Disease	ASMD
• CBC: Thrombocytopenia, anemia[7] • Lipids: normal LDL, normal triglycerides, low HDL[8] • Hyperferritinemia[9], decreased clotting factors[7] • Bone marrow biopsy*: Gaucher cells (normal biopsy does not rule out Gaucher)[10] • Glucosylsphingosine (lyso-GL-1, glucopsychosine): markedly elevated[11,12]	• CBC: Thrombocytopenia, anemia[4] • Lipids: low HDL, elevated LDL, elevated triglycerides[4] • LFTs: AST, ALT are typically elevated but can be normal[4] • Bone marrow biopsy*: Lipid-laden foam cells (normal biopsy does not rule out ASMD)[4] • Lysosphingomyelin (LSM) may be measured alone or in panel of oxysterols: elevated in ASMD patients[4]

**Bone marrow aspirate/biopsy may have been performed if hematologic malignancy was suspected.*

Other

Gaucher Disease	ASMD

Testing Options for Gaucher Disease and Acid Sphingomyelinase Deficiency

Some of the laboratories offering testing for Gaucher disease enzyme assay acid β-glucosidase, ASM enzyme assay (acid sphingomyelinase), and/or *GBA1* and *SMPD1* sequencing are listed below. There may be other testing appropriate for your patient, and this is not an endorsement of any specific laboratory. Other testing options can be found at www.concertgenetics.com or www.ncbi.nlm.nih.gov/gtr. Consult each laboratory for a full range of options. Content is current at time of publication, and tests may not be available in all states; please call laboratory to confirm test availability, sample shipping information, and all other logistics. Sanofi does not review or control the content of non-Sanofi websites. This listing does not constitute an endorsement by Sanofi of information provided by any other organizations.

Lab	Available Testing	GD	ASMD	Sample Requirements	Kits	Avg TAT	Mobile Blood Draw	Billing	Contact
ArchimedLife	Enzyme		√	DBS card: 5 circles (min 3); Note: this European lab does not yet have CLIA certification. Results are only reported on a research basis	DBS	10 d	No	No charge*	**E:** eumedicalservices@sanofi.com **W:** http://webportal.archimedlife.com (account required)
	Sequencing		√			2 wks			
	LSM		√			10 d			
ARUP Laboratories	Enzyme	√		WB: 3 ml ACD (yellow), EDTA (lavender) or sodium heparin (green) tube	No	3-10 d	No	Inst	**P:** 800-522-2787 **E:** clientservices@aruplab.com **W:** www.aruplab.com
	Sequencing	√		WB: 3 ml ACD (yellow), EDTA (lavender) tube		2-3 wks			
Centogene	Enzyme	√	√	WB: 5 ml EDTA (lavender) tube; DBS card: 10 circles	Blood, DBS, Saliva	7 d	Yes	Inst, Self-pay, Ins	**P:** 617-580-2102 **E:** customer.support-US@centogene.com **W:** www.centogene.com
	Sequencing (+/- Del/Dup)	√	√	WB: 1 ml EDTA (lavender) tube; DBS card: 10 circles; Saliva; Buccal swab		15 d			
	Lyso-GL-1	√		WB: 1 ml EDTA (lavender) tube; DBS card: 10 circles		7 d			
	LSM-509		√	WB: 1 ml EDTA (lavender) tube; DBS card: 10 circles		7 d			
Greenwood Genetic Center	Enzyme	√	√	WB: 5-10 ml (3-5 ml for ASMD) sodium heparin (green) tube; DBS card: 3 circles	Blood, DBS, Saliva	2 wks	No	Inst, Self-pay, Ins (SC residents)	**P:** 800-473-9411 **E:** labgc@ggc.org **W:** www.ggc.org
	Sequencing	√	√	WB: 5-6 ml EDTA (lavender) tube; DBS card: 3 circles; Saliva		3 wks			
Labcorp	Enzyme	√		WB: 2 x 10 ml EDTA (lavender) tube (peds 1 x 10 ml); Note: Labcorp Test Code: 451780; Integrated Test Code: 370	Blood, Buccal	3-13 d	Yes	Inst Self-Pay, Ins	Labcorp Customers: **P:** 800-345-4363 **W:** www.labcorp.com
	Sequencing	√	√	WB: 7 ml EDTA (lavender) or ACD (yellow) tube Note: For sequencing done via "Inheritest Gene-Specific Sequencing" (test code: 451910). Indicate *GBA* or *SMPD1* gene as needed		9-15 d			
The Lantern Project (PerkinElmer Genomics)	Enzyme	√	√	WB: 2-10 ml sodium heparin (green) tube (volume varies with age); DBS card: 3 circles	Blood, DBS, Saliva	3 d	Yes	No charge*	**P:** 866-354-2910 **E:** genomics@perkinelmer.com **W:** www.LanternProjectDx.com
	Sequencing	√	√	WB: 2-10 ml EDTA (lavender) tube (volume varies with age); DBS card: 3 circles; Saliva		3 wks			
	Lyso-GL-1	√		WB: 2-10 ml EDTA (lavender) tube (volume varies with age); DBS card: 3 circles		3 d			
Mayo Clinic Laboratories	Enzyme	√	√	WB: 6 ml ACD (yellow) tube	DBS, Saliva	5-10 d	Yes	Inst, Ins (can be billed in some cases but account required)	**P:** 800-533-1710 **E:** mcl@mayo.edu **W:** www.mayocliniclabs.com
	Sequencing	√	√	WB: 3 ml EDTA (lavender) or ACD (yellow) tube; DBS card: 2-5 circles		14-20 d			
	Lyso- GL-1	√		WB: 1 ml EDTA (lavender), ACD B (yellow) or sodium heparin (green); Plasma: 0.3 ml; DBS card: 2 circles (Note: Order codes GPSY, GPSYP, or GPSYW)		2-8 d			
	Oxysterols		√	WB: 1 ml EDTA (lavender), ACD B (yellow) or sodium heparin (sodium or lithium) (green) tubes; Frozen plasma: min 0.25 ml; DBS card: 2 circles		2-8 d			

***Testing is performed at no charge. Local charges may apply for sample collection, processing, or shipping.**

Avg TAT = average turnaround time; d = days; DBS = dried blood spot; Del = deletion; Dup = duplication; GPSY = glucopsychosine; Ins = insurance; Inst = institution; min = minimum; WB = whole blood; wks = weeks.

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