Pompe Disease

Overview

- Pompe disease, also known as acid maltase deficiency, is a rare genetic lysosomal storage disease with a wide range of clinical phenotypes, presenting in infancy, childhood, or adulthood[1]
- Pompe disease is caused by an absence or deficiency of the lysosomal enzyme acid α-glucosidase (GAA), essential for the degradation of glycogen. Absence or deficiency of the GAA enzyme results in progressive accumulation of lysosomal glycogen that can affect all muscle types[1]
- Pompe disease is classified into Infantile-onset (IOPD) or Late-onset Pompe disease (LOPD)[1]
    - Infantile-onset Pompe disease presents prior to one year of age and is characterized by profound muscle weakness, cardiomegaly, and cardiomyopathy. IOPD is rapidly progressive, typically leading to death by cardiorespiratory failure by two years of age if left unmanaged
    - Late-onset Pompe disease can present in infancy or adulthood with progressive proximal muscle weakness and respiratory insufficiency. Significant morbidity is associated with LOPD, and there is a wide phenotypic range

Incidence

- Overall incidence estimates for the United States for all forms: 1 in 40 000 (based off an ethnically diverse New York population)[2]
- Incidence varies depending on geography, ethnic background, and availability of NBS data[1]

Inheritance

- Autosomal recessive disorder caused by mutations in both copies of the *GAA* gene[1]

Diagnosis

Definitive diagnosis is established by:

- Acid alpha-glucosidase enzyme activity assay: demonstrating deficiency[1]
- *GAA* gene sequencing: demonstrating two pathogenic variants in *trans* (one from each parent)[1]

The following evaluations may support a diagnosis of Pompe disease:

Clinical Findings

- IOPD: muscle weakness, cardiac findings, hypotonia ("floppy baby," head lag), delayed motor milestones, weak suck, feeding and swallowing defects, and failure to thrive[1]
- LOPD: progressive proximal weakness (particularly pelvic girdle) with lack of myotonia; respiratory insufficiency, and feeding/swallowing difficulties[1]

Laboratory Testing

- Creatine kinase: can be normal or up to 15 times the upper limit of normal[1]
- Serum transaminase levels: may be elevated in patients with Pompe disease[1]
- Urine glucose tetrasaccharide (HEX4, Glc4), universally elevated in IOPD, may be normal to elevated in LOPD[1]
- CRIM status (by Western blot (antigenic) or predicted by genotype): IOPD patients can be positive or negative; all LOPD are positive[3]
- Muscle biopsy: When abnormal, typical findings include vacuolated muscle fibers, PAS-positive vacuoles (glycogen storage), and increased acid phosphatase activity in muscle fibers. Normal biopsy does not rule out Pompe[4]

Other

- Electromyography: myotonia, fibrillations, positive sharp waves, and complex repetitive discharges. Findings are most prominent in paraspinal muscles[5]; NCV is typically normal[1]
- Polysomnography: sleep apnea and morning headaches[1]
- Respiratory function: >10% difference in FVC when upright vs supine[1]

Testing Options for Pompe Disease

Sanofi Genzyme does not review or control the content of non-Sanofi Genzyme websites. These listings do not constitute an endorsement by Sanofi Genzyme of information provided by any other organizations. The following is a selection of laboratories offering both GAA enzyme assay (acid α-glucosidase) and *GAA* sequencing. This is not an exhaustive list of labs that offer one or the other, or an endorsement of any one lab. Other testing options can be found at www.concertgenetics.com or www.ncbi.nlm.nih.gov/gtr. Content is current at time of printing and tests may not be available in all states; please contact the laboratory to confirm test availability, sample shipping information, and all other logistics.

Lab	Available Testing	Sample Requirements	Kits	Avg TAT	Mobile Blood Draw	Billing	Contact
Centogene	Enzyme	WB: 1ml 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	WB: 1ml EDTA (lavender) tube; DBS card: 10 circles; Saliva; Buccal swab		15-25 d			
	Del/Dup	WB: 1ml EDTA (lavender) tube; DBS card: 10 circles; Saliva; Buccal swab		15 d			
Duke University	Enzyme	WB: 2-4 ml EDTA (lavender) tube; DBS card: 5 circles; Muscle (call to discuss)	No	15 d	No	Inst	**P:** 919-613-8400 **E:** clientservices@dm.duke.edu **W:** https://testcatalog.duke.edu
	Sequencing	WB: >2 ml EDTA (lavender) tube		28 d			
	Urine HEX4	Dried urine spots		15 d			
EGL/Eurofins	Enzyme	WB: 3-5 ml sodium heparin (green) tube	Blood, DBS, Saliva	7-10 d	No	Inst, Ins, Self-pay	**P:** 855-831-7447 **E:** eglcs@egl-eurofins.com **W:** www.egl-eurofins.com
	Sequencing	WB: 2-10 ml EDTA (lavender) tube (volume varies with age); Saliva (per Oragene kit)		4 wks			
	Del/Dup	WB: 2-10 ml EDTA (lavender) tube (volume varies with age); Saliva (per Oragene kit)		2 wks			
Greenwood Genetic Center	Enzyme	WB: 5-10 ml sodium heparin (green) tube; DBS card: 3 circles	Blood, DBS, Saliva	2 wks	No	Inst, Ins (SC residents only), Self-pay	**P:** 800-473-9411 **E:** labgc@ggc.org **W:** www.ggc.org
	Sequencing	WB: 2-6 ml EDTA (lavender) tube; DBS card: 3 circles; Saliva		3 wks			
	Del/Dup	WB: 5-7 ml EDTA (lavender) tube		26 d			
	Urine HEX4	3 ml random urine		10 d			
LabCorp/ Integrated Genetics	Enzyme	WB: 2-3 ml EDTA (lavender) tube; DBS card: 6 circles (performed at Integrated Genetics)	Blood, DBS, Buccal (Mouth-wash)	7-14 d	Yes	Inst, Ins, Self-pay	**LabCorp Customers:** **P:** 888-522-2677 **W:** www.labcorp.com **Integrated Customers:** **P:** 800-848-4436 **E:** asklGclientservices@integratedgenetics.com **W:** www.integratedgenetics.com
	Sequencing	WB: 8.5 ml EDTA (lavender) tube or ACD (yellow) tube (performed at Integrated Genetics)		2-3 wks			
The Lantern Project (performed at PerkinElmer Genomics)	Enzyme	WB: 2-10 ml EDTA (lavender) 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 (includes Del/Dup)	WB: 2-10 ml EDTA (lavender) tube (volume varies with age); DBS card: 3 circles, Saliva: (per Oragene kit)		3 wks			
Mayo Clinic Laboratories	Enzyme	WB: 6ml ACD (yellow) tube; DBS card: 3 circles	DBS (in some cases), Saliva	5-10 d	Yes	Inst (ins can be billed in some cases, Inst acct 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			
	Urine HEX4	3 ml random urine		7-14 d			
Seattle Children's Hospital	Enzyme	WB: 2 ml sodium heparin (green) or ACD (yellow) tube; DBS card: 3 circles	DBS (in some cases), Saliva	7-10 d	No	Inst, Ins (Medicaid: WA, AK, ID, MT only), Self-pay	**P:** 206-987-2617 **E:** labGC@seattlechildrens.org **W:** https://seattlechildrenslab.testcatalog.org
	Sequencing	WB: 3 ml EDTA (lavender) tube or ACD (yellow) tube		2-3 wks			
Sema4	Enzyme	WB: 5-10 ml ACD (yellow) (preferred), EDTA (lavender), or sodium heparin (green) tubes. Minimum of 3 ml.	Blood, Saliva	7 d	Yes	Inst, Ins, Self-pay	**P:** 800-298-6470 **E:** clientservices@sema4.com **W:** www.sema4.com
	Sequencing (includes Del/Dup)	WB: 5-10 ml ACD (yellow) AND 2 x 5-10 ml EDTA (lavender); Saliva		2-3 wks			

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

acct = account; avg TAT = average turnaround time; d = days; DBS = dried blood spot; del = deletion; dup = duplication; Ins = insurance; Inst = institution; WB = whole blood; wks = weeks.

References: 1. American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM). *Muscle Nerve.* 2009;40:149-160. **2.** Martiniuk F, et al. *Am J Med Genet.* 1998;79:69-72. **3.** Kronn DF, et al. *Pediatrics.* 2017;140(Suppl 1):S24-S45. **4.** Werneck LC, et al. *Arq Neuropsiquiatr.* 2013;71:284-289. **5.** Hobson-Webb LD, et al. *Clin Neurophysiol.* 2011;122:2312-2317.

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