VDH VIRGINIA DEPARTMENT OF HEALTH

Division of Child and Family Health- Newborn Screening Follow-Up Program

Pompe Disease

Health Care Professional Fact Sheet

A newborn screening test is a **screen** and not diagnostic testing. An "abnormal" or "critical" result on a newborn screen indicates the baby may be at a higher risk of having a disorder; however, it does not diagnose the baby with the condition. Follow-up testing is **vital** to determine if the baby has the disorder indicated. In the event the condition is diagnosed, timely follow-up testing will result in earlier treatment and better outcomes.

Disorder Indicated: Pompe Disease is a Lysosomal Storage Disorder (LSD) where the body lacks sufficient activity of the *lysosomal enzyme acid alpha-glucosidase* (GAA), caused by mutations in the *GAA* gene, and results in accumulation of glycogen in the lysosomes resulting in swelling, cell damage, and progressive organ dysfunction. There are several forms of Pompe Disease that vary in severity, onset of symptoms, and outcomes.

Incidence		1 in every 40,000 newborns.
1st Tier Testing *Screens meeting criteria (critical, multiple abnormal screens) will move to 2nd Tier testing*	Analyte Measured	Enzyme activity: *lysosomal enzyme acid alpha-glucosidase* (GAA)
	Normal Test Results	*See report for additional information*
	Abnormal Test Results	*See report for additional information*
	Critical Test Results	*See report for additional information* ***(Critical results require immediate evaluation and follow-up)***
2nd Tier Testing *(sequencing of GAA gene at 17q25.3)*	**2nd Tier Potential Results**	**Variant Definition and Recommended Follow-Up**
	Benign/Likely Benign	Not considered to be the cause of the disease, no additional follow-up
	Pseudodeficiency	Low enzyme activity during testing (*in vitro*) but sufficient in infant (*in vivo*), no additional follow-up
	Variant of Unknown Significance (VOUS)	Variant has characteristics of being disease-causing, but insufficient or conflicting evidence exists. **Reported as critical results and referred to Genetics, monitor child for emergence of symptoms.**
	Likely Pathogenic	Variant is considered the probable cause of the disease, should be used cautiously for clinical decision-making and family risk assessment. **Reported as critical results and referred to Genetics, monitor child for emergence of symptoms.**
	Pathogenic	Variant is established as disease-causing and considered the cause of the disease. Variant can be used in clinical judgement and in evaluating risk for family members. **Reported as critical results and referred to Genetics, monitor child for emergence of symptoms**
Note: a combination of variants requiring follow-up (VOUS, Likely Pathogenic, Pathogenic) paired with benign/pseudodeficincy variants will still be reported as a critical result and referred to Genetics		

Signs and Symptoms may include: *Please note: these findings may not be present in young infants or in milder forms of the disease*	**Infantile Onset Pompe Disease (IOPD)** *Generally symptomatic prior to one year*		**Late-Onset Pompe Disease (LOPD)**
	Classic	Non-Classic	
	• Progressive hypotonia • Cardiomyopathy • Failure to thrive • Respiratory infections • Hearing Loss • Most severe	• Hypotonia • Myopathy • Failure to thrive • Respiratory infections • Hearing Loss	• Onset after first year through late adulthood • Progressive weakness • May not be clinically significant until juvenile or adult • Respiratory complications • Premature death • Associated cardiac issues • Significant decrease in quality of life

Next Steps ***may*** include:	**Discuss the next steps of evaluation and *possible* treatment with the regional Geneticist** Provide parental education (see accompanying sheet) Clinical Assessment
Treatment (***if indicated***)	Enzyme Replacement Therapy
Additional Resources	VDH Newborn Screening *http://vdhlivewell.com/newbornscreening* Baby's First Test *www.babysfirsttest.org* American College of Medical Genetics (ACMG) ACT Sheets *www.ACMG.net* Genetics Home Reference *https://ghr.nlm.nih.gov/* International Pompe Association *http://worldpompe.org/*

Educational content adapted from www.babysfirsttest.org

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