VDH VIRGINIA DEPARTMENT OF HEALTH

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

Mucopolysaccharidosis Type-I (MPS-1)

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: MPS-1 is a Lysosomal Storage Disorder (LSD) where the body lacks sufficient activity of the *lysosomal enzyme alpha-L-iduronidase (*IDUA*),* caused by mutations in the *IDUA* gene, and results in accumulation of glycosaminoglycan (GAG) in the lysosomes resulting in swelling, cell damage, and progressive organ dysfunction.

Incidence		1 in every 100,000 newborns.
1st Tier Testing *Screens meeting criteria (critical, multiple abnormal screens) will move to 2nd Tier testing*	Analyte Measured	Enzyme activity: *lysosomal enzyme alpha-L-iduronidase (*IDUA)
	Normal Test Results	*See report for additional information*
	Abnormal Test Results	*See report for additional information*
	Critical Test Results	*See report for additional information*
2nd Tier Testing *(sequencing of IDUA gene at 4p16.3)*	**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*	• Umbilical or inguinal hernia may be present • Valvular heart disease, Cardiac failure • Frequent respiratory infections • Progressive skeletal dysplasia and other abnormalities • Coarse facial features, spinal deformity • Hearing loss • Significant, progressive intellectual or learning difficulties • Death from cardiorespiratory complication within 1st decade if untreated *MPS-1 Attenuated typically has less severe symptoms of above and progresses more slowly*
aNext 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 and Hematopoietic stem cell transplantation (HSCT)
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/* National MPS Society *http://www.mpssociety.org/*

Educational content adapted from www.babysfirsttest.org

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