LSD Info Brief for Providers

Kansas Department of Health and Environment

To protect and improve the health and environment of all Kansans.

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Additional Resources

babysfirsttest.org

rarediseases.org

mpssociety.org

mps1disease.com

unitedpompe.com

pompediseasenews.com

What is the change and when will it take effect?

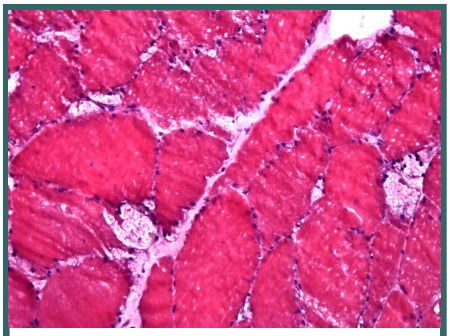
Effective January 2, 2021, the Kansas Newborn Screening Program is adding two lysosomal storage disorders (LSD) to the blood spot screening panel: Pompe disease & Mucopolysaccharidoses-I (MPS-I).

About Lysosomal Storage Disorders, Pompe and Mucopolysaccharidoses-I:

Lysosomal storage disorders (LSDs) are a group of inherited metabolic disorders characterized by lysosomal enzyme deficiencies, preventing cells from breaking down sugars and fats. LSDs are progressive disorders in which sugar or fat molecules cannot be broken down and gradually build up in the body's cells, resulting in tissue damage and a variety of symptoms.

Pompe is associated with mutations in the GAA gene and a deficiency in alpha-glucosidase enzyme. Skeletal and muscle tissues are primarily affected by this disorder. Pompe can present as infantile-onset Pompe disease (IOPD) or late-onset Pompe disease (LOPD). Infantile-onset Pompe disease symptoms develop within the first few months of life. Without treatment, IOPD infants have a life expectancy of less than two years. LOPD patients can develop symptoms anywhere from childhood to adulthood. Earlier onset of symptoms is generally associated with more severe disease and a faster progression.

Mucopolysaccharidoses-I (MPS-I) is one of the most common types of MPS. Depending on severity, it is also known as Hurler, Scheie, or Hurler-Scheie syndrome. It is associated with mutations in the IDUA gene and a deficiency in alpha-L-iduronidase enzyme. MPS-I encompasses a wide range of severity and symptoms. Severe MPS-I commonly presents with developmental delays and impaired motor skills within several months to one year after birth. It is also characterized by coarsening facial features, which are not apparent at birth. Attenuated MPS-I has significant variability in symptom onset and progression.



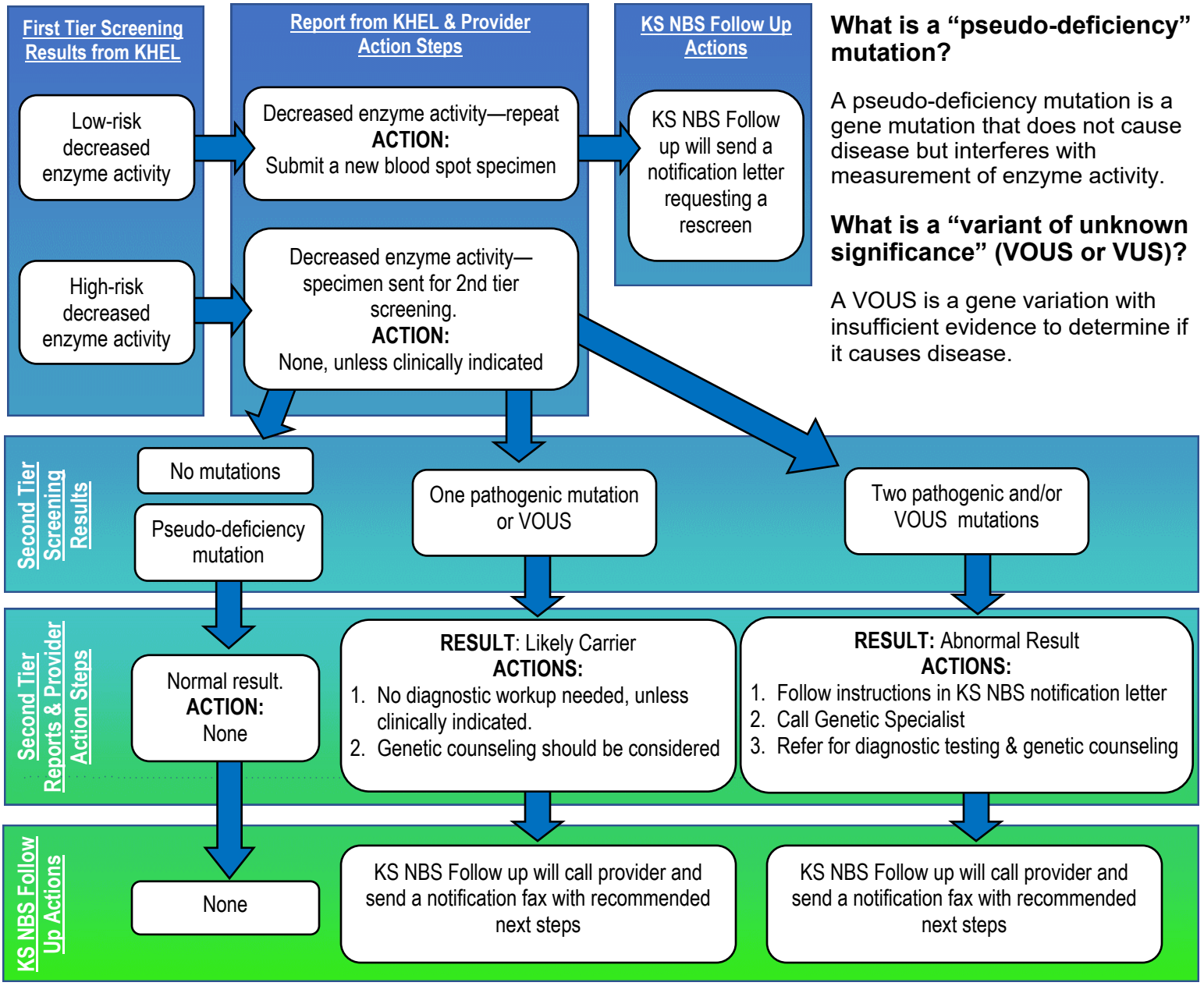
Muscle biopsy showing large vacuoles in a case of Pompe disease.

Why is this important?

Symptoms of LSD disorders do not appear until after the disease progresses significantly. As with all other conditions on Kansas' panel, early detection of these conditions allows families and providers to begin treatment *before* symptoms begin. Early treatment prevents severe disability, early death, and helps babies have the best possible quality of life. With the addition of these two disorders, Kansas will now screen for 34 of the 35 conditions on the Recommended Uniform Screening Panel (RUSP) and will be one of only 23 states that routinely screen for Pompe and Mucopolysaccharidoses-I.

How do we screen for Pompe and MPS-I and what should you expect after screening?

The Kansas NBS program takes a punch from the blood spot card for first tier screening and conducts a digital microfluidics enzyme analysis. Specimens with decreased enzyme activity are classified as low-risk or high-risk. Low-risk specimens require a repeat blood spot screening to determine whether the enzyme activity values normalize. We expect most low-risk specimens will normalize with a second screening. High-risk specimens are sent for both targeted Next Generation Sequencing (tNGS) and enzyme-based second tier screening. Abnormal results from both second tier screenings will be sent to submitting facilities and the provider of record on the blood spot screening submission forms. Second tier screening results include normal, pseudo-deficiency, likely carrier, and abnormal. Review the chart below for a summary of the screening process.



What is a "pseudo-deficiency" mutation?

A pseudo-deficiency mutation is a gene mutation that does not cause disease but interferes with measurement of enzyme activity.

What is a "variant of unknown significance" (VOUS or VUS)?

A VOUS is a gene variation with insufficient evidence to determine if it causes disease.

Sources:

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