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NEWBORN SCREENING FOR LYSOSOMAL STORAGE DISORDERS

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In recent years, the issue of newborn screening has gained much attention in the popular media. Newborn screening continues to be an important topic of discussion in the Lysosomal Storage Disorder (LSD) space. With many approved LSD therapies NBS is being actively researched. Currently, in the United States, Newborn screening has been approved at the Federal level for MPS I, and the National MPS Society has submitted a nomination for the MPS II condition. Not all states are screening for MPS I, as the states are responsible for funding this initiative.

Historically, the purpose of newborn screening has been to identify and correctly diagnose genetic disorders in the newborn period in an effort to prevent or reduce clinical symptoms with early treatment. Traditionally, conditions considered for newborn screening are those for which the disorder is clearly defined, occurs fairly frequently, and has a clear advantage to early diagnosis. Testing for these conditions needs to be cost effective and accurate. Additionally, the test needs to have a short “turnaround time” with results available quickly so that treatment can be implemented effectively.

At the current time each state chooses the tests that are included in state-specific newborn screening program. Once these diseases are approved on a national level, they are sent to each state to review and add. Currently, there is a growing movement to consider including conditions in newborn screening that do not have traditional treatments. It is now more widely recognized that to many families, information about the diagnosis alone is helpful with the opportunity for genetic counseling, education about additional management options and improved quality of care with early intervention and therapy services.

The consideration to develop newborn screening technology for lysosomal storage disorders continues to develop as LSDs, as a group, are compared against newborn screening principles. Do these conditions have a considerable incidence? Collectively, LSDs occur in about 1/5000 births, which is more frequent than some conditions already included in newborn screening. Does the benefit of testing in the newborn period outweigh the cost? The time and funding for traditional diagnostic evaluation and testing, versus a potential diagnosis in the newborn period, must be considered. Is an effective treatment available? Enzyme replacement therapy (ERT) is now approved or is in development for several LSDs. Transplantation is known to be an effective treatment for a group of lysosomal storage disorders. Now, second generation therapies, such as gene therapy and gene editing are in clinical trials phases for various MPS diseases. Either treatment or future treatment option appears to be more effective if implemented earlier in the disease course.

Considering the potential benefits, the current aim is to develop a test that would allow for these options in the LSD community. To develop a good screening strategy, researchers have identified features common to all LSDs. This is important because the time, finances, and labor to measure each enzyme that is deficient in each LSD, which is the usual method to making a diagnosis, would be unaffordable. So, different methods are being studied. Typically, there is accumulation of material normally broken down within lysosome. The number and size of the lysosomes in a cell increases. Therefore, it is expected that the level of certain lysosomal proteins should also be elevated in the collective group of conditions.

Using these principles, scientists have found some important markers to study. One particular protein that has been identified is the Lysosome Associated Membrane Protein 1 (abbreviated LAMP-1). Studies have been performed looking for levels of this protein in those individuals known to have a LSD, and the levels have been compared to those who are unaffected (controls). In one study, approximately 70% of LSD individuals had LAMP-1 levels that were greater than the levels in 95% of control individuals. Other compounds, called saposins, have also been measured and similar results have been found. One researcher estimated that 85% of LSD individuals could be identified by combining LAMP-1 and saposin screening markers.

With this identification of possible screening markers, some researchers have proposed a tiered, or stepped, screening strategy for LSDs. In this type of system, the first tier of screening, the primary screen, would involve measuring the protein markers to identify an “at risk group.” For the group identified as “at risk,” a second tier test would be performed to identify higher levels of stored materials. A positive result on both assays, both increased protein markers and elevated specific lysosomal compounds, would need to be found before a family is referred for counseling, additional necessary testing, and therapy.

Research regarding Newborn screening for LSDs is increasing. Important questions remain both about the screening process and the testing methods. Controversy will likely continue regarding the appropriateness of screening, especially in the instance of the potential to identify individuals with a condition for which there is no currently available treatment. One may also be concerned about the impact on the parent-child relationship when a newborn is identified with a condition before symptoms of a progressive disorder are visible. The proposed screening strategy would not distinguish between different levels of severity, leaving many questions for families and health care professionals that want to choose the most appropriate treatment***. Additionally, it is important to recognize that newborn screening is a state mandated public health program and may differ significantly from state to state, in terms of available tests and follow up protocols when a positive screen is found.*** As a community, those whose lives have been touched by LSDs will likely continue to become more involved in the potential for newborn screening.

Resources:

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