NORTH CAROLINA NEWBORN SCREENING PROGRAM

Mucopolysaccharidosis I Fact Sheet for Providers

What is mucopolysaccharidosis I (MPS I)?

MPS I belongs to a group of inherited lysosomal storage disorders known as mucopolysaccharidoses (MPS). MPS I is caused by the absence or deficiency of a specific enzyme, alpha-L-iduronidase, required to break down glycosaminoglycans (GAGs). Because of this deficiency, GAGs are stored in cells throughout the body, resulting in progressive cellular damage with multisystem involvement.

What are the signs and symptoms MPS I?

Infants with MPS I typically show no symptoms at birth, but they can develop clinical disease in the first 6 to 12 months of life and can benefit from early intervention. MPS I impacts multiple systems, including neurological, respiratory, cardiac, and musculoskeletal; it also affects hearing and vision.

MPS I is a continuous spectrum of disease, with some patients having neurological and physical symptoms (Hurler syndrome) and others having primarily physical symptoms (Hurler-Scheie or Scheie syndromes).

How do I handle an abnormal screen for MPS I?

Newborn screening (NBS) for MPS I uses a two-tier approach measuring iduronidase enzyme activity first, followed by MPS I marker (GAG) analysis if the enzyme level is below the cutoff. A positive NBS is reported when an infant has BOTH deficient enzyme activity and an abnormal MPS I marker value. If you are notified that one of your patients received a positive NBS result for MPS I, immediately contact the Muenzer MPS Center with UNC Pediatric Genetics and Metabolism (919-228-2432) for next steps and prompt referral. Infants with a positive NBS for MPS I require clinical evaluation and confirmatory testing, as early diagnosis is critical for timely treatment initiation to optimize long-term outcomes.

Hurler syndrome

In the severe form of MPS I (Hurler syndrome), developmental delay is evident by the end of the first year, with a plateau during the second year of life followed by a progressive cognitive decline. Language may be limited due to hearing loss and recurrent ear infections. Physical features before the end of the first year can include hernias, skeletal abnormalities (commonly lumbar kyphosis), corneal clouding, coarse facial features, chronic rhinitis, joint stiffness, and hepatosplenomegaly. Without treatment, children with severe MPS I typically die before 10 years of age due to neurological involvement, obstructive upper airway disease, or cardiac complications.

Hurler-Scheie or Scheie syndrome

Children with attenuated forms of MPS I (Hurler-Scheie or Scheie) may range from normal intelligence to mild learning disabilities. Physical features may include obstructive upper airway disease, musculoskeletal involvement with decreased joint range of motion, corneal clouding, and valvular heart disease. Lifespan in individuals with the attenuated form of MPS I can range from teenage years to adulthood.

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How is MPS I identified and diagnosed?

All infants with an abnormal MPS I newborn screening result need a clinical examination and confirmation with urine GAG analysis, enzyme testing, and MPS I gene analysis. The diagnosis of MPS I is based on elevated urine GAGs and deficient alpha-L-iduronidase enzyme activity, with confirmation by DNA analysis. The Muenzer MPS Center will ensure all appropriate testing has been completed and will interpret all labs for diagnostic purposes.

How is MPS I treated?

Current treatment options are available to prevent progression of symptoms and improve quality of life. Treatment can include the following, with supportive care for specific symptoms as necessary:

- For individuals with severe MPS I (Hurler syndrome), hematopoietic stem cell transplantation (HSCT) is the recommended treatment. HSCT replaces the body's bone marrow with healthy blood stem cells capable of producing the missing enzyme. When performed early, ideally prior to 6 to 12 months of age, HSCT has been shown to prevent progression of neurological disease and cognitive impairment in children with the severe form of MPS I. HSCT can also prevent progression of some physical symptoms of MPS I, but bone disease and corneal clouding may not be impacted by HSCT.
- For individuals with attenuated MPS I, intravenous enzyme replacement therapy (IV ERT) can prevent or slow development of some physical symptoms. This treatment is given via weekly intravenous infusion to replace the absent or deficient enzyme (alpha-L-iduronidase). IV ERT is not expected to impact the neurologic disease because the IV administered enzyme does not cross the blood-brain barrier.

Additionally, other promising treatment options are currently under investigation in clinical trials. Treatment options are currently available in North Carolina, and the UNC Muenzer MPS Center providers will discuss all therapeutic approaches with families during their follow-up visits.

Where do I go for more information?

Use your phone's camera to scan the QR codes below.

- UNC Pediatric Genetics and Metabolism
- UNC Health Information and Referrals
- ACMG MPS II ACT Sheet
- Medline Plus

Where do I send parents for information?

Use your phone's camera to scan the QR codes below.

- Muenzer MPS Research and Treatment Center
- Baby's First Test
- National MPS Society
- Project Alive
- Newborn Screening Information Center
- Kennedy Ladd Foundation

NC DEPARTMENT OF HEALTH AND HUMAN SERVICES

State of North Carolina Department of Health and Human Services Division of Public Health

www.ncdhhs.gov

https://slph.dph.ncdhhs.gov/newborn/default.asp

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This fact sheet was supported by the Centers for Disease Control and Prevention of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award totaling $423,900, with 100 percent funded by CDC/HHS. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by CDC/HHS, or the U.S. Government.