
Newborn Screening for Mucopolysaccharidosis Type I

A Summary of the Evidence and Advisory Committee
Decision

Report Date: 15 March 2015



This summary was prepared under a contract to Duke University from the Maternal and Child Health Bureau of the Health and Resources and Services Administration (Contract Number: HSH250201500002I/HSH25034003T).

EXECUTIVE SUMMARY

This summary reviews the information the federal advisory committee used when deciding whether to recommend adding Mucopolysaccharidosis Type I (MPS I) to the Recommended Uniform Screening Panel (RUSP) in 2015.

About the condition

MPS I is a rare genetic disorder caused by a change in a single human gene. Studies of patients with symptoms suggest that about 1 out of every 100,000 people has MPS I. People with MPS I do not have enough of the IDUA enzyme that helps to break down certain waste products in cells. Babies with MPS I appear normal. There are 2 types of MPS I: the severe type and the attenuated type. Most children with MPS I have the severe type. In this type, MPS I can cause problems with the heart, airways, eyes and ears, muscles, bones, joints, and brain. These problems can worsen quickly and cause early death.

Treatment for MPS I

There is no cure for MPS I. Early diagnosis allows early monitoring and treatment for babies with MPS I. Treatments that can stop MPS I problems from getting worse include enzyme replacement therapy and human stem cell transplantation, also called a “bone marrow transplant.” The treatment a patient receives depends on many factors, including the type of MPS I.

Detecting MPS I in newborns

Newborn screening for MPS I can happen along with routine newborn screening for other conditions during the first few days of life. Newborn screening for MPS I measures IDUA enzyme activity. This process uses the same dried blood spots already collected for screening of other disorders. Newborns with low IDUA activity are at higher risk for MPS I. They need more testing and evaluation to diagnose the condition.

Public health impact

Based on what is known about screening and the risk of being born with MPS I, experts think that screening all newborns in the United States for MPS I would find about 44 babies with the condition each year (about 1.1 out of every 100,000 children born). It would prevent up to 2 deaths before age 5 years due to the disease each year.

Committee decision

The Committee voted in 2015 to recommend adding MPS I to the RUSP. As of 2016, the RUSP recommends that state newborn screening programs include MPS I.

ABOUT THIS SUMMARY

What is newborn screening?

Newborn screening is a public health service that can change a baby's life. Newborn screening involves checking all babies to identify those few who look healthy but who are at risk for one of several serious health conditions that benefit from early treatment.

Certain serious illnesses can be present even when a baby looks healthy. If the baby does not receive screening for these illnesses early in life, a diagnosis may be delayed. Later treatment might not work as well as earlier treatment. Newborn screening programs have saved the lives and improved the health of thousands of babies in the United States (US).

Who decides what screening newborns receive?

In the US, each state decides which conditions to include in its newborn screening program. To help states determine which conditions to include, the US Secretary of Health and Human Services provides a list of conditions recommended for screening. This list is called the Recommended Uniform Screening Panel (RUSP).

Progress in screening and medical treatments can lead to new opportunities for newborn screening. To learn how a condition is added to the RUSP, see **Box A**.

What will this summary tell me?

In 2012, the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) requested an evidence review of newborn screening for Mucopolysaccharidosis Type I (MPS I). This summary presents key review information that the Committee used to make its decision about whether to recommend adding MPS I to the RUSP. It will answer these questions:

- [What is MPS I?](#)
- [How is MPS I treated?](#)
- [How are newborns screened for MPS I?](#)
- [Does early diagnosis or treatment help patients with MPS I?](#)
- [What is the public health impact of newborn MPS I screening in the US?](#)
- [What did the Committee decide about adding MPS I to the RUSP?](#)

Box A: Adding a Condition to the RUSP

A committee, called the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC), makes a recommendation to the US Secretary of Health and Human Services about adding specific conditions to the RUSP. The Committee bases its decision on a review of the condition, the screen, the treatment, and the ability of newborn screening programs to check for the condition. To learn more about the ACHDNC, visit this [website](#).

UNDERSTANDING THE CONDITION

What is MPS I?

MPS I is a rare genetic disorder. People with MPS I have a change in a single gene called IDUA. Normally, this gene makes an IDUA enzyme that breaks down certain normal waste products. In people with MPS I, the enzyme does not work properly. When the enzyme does not work properly, waste products build up in the body and cause serious health problems. These problems can start within the first 2 years of life.

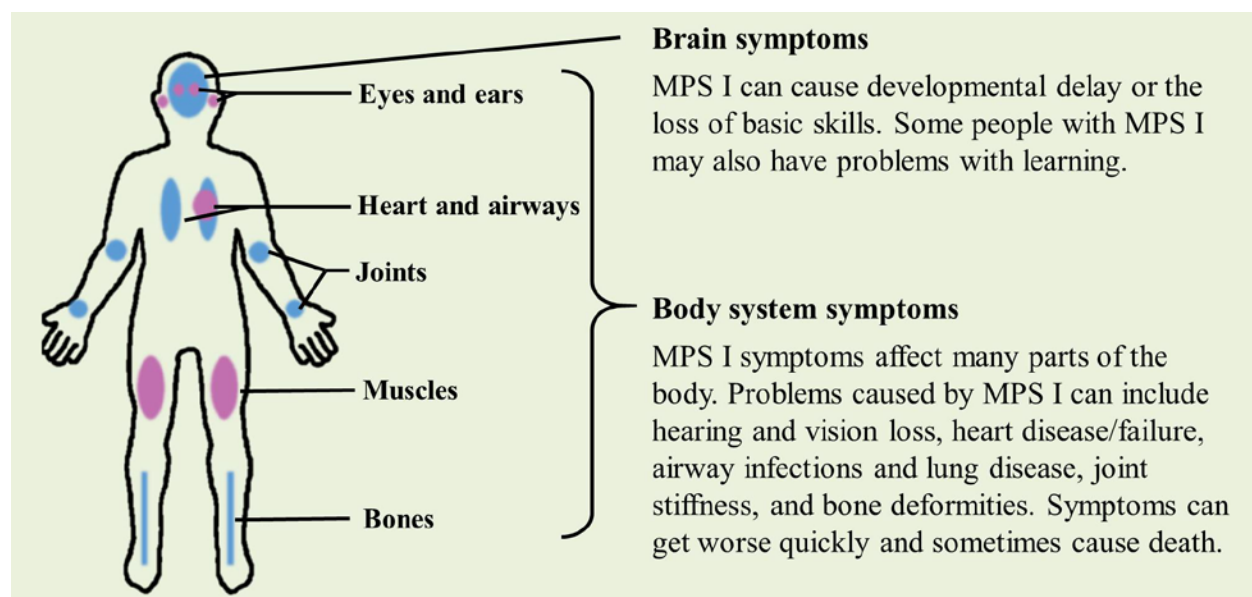
How common is MPS I?

- MPS I is a rare disorder. About 1 out of every 100,000 children receives a diagnosis of MPS I.
- This estimate is based on the number of people who develop symptoms and receive a diagnosis without newborn screening. Not everyone with MPS I is diagnosed, so the estimate might be low.
- MPS I occurs at similar rates in boys and girls. It is more common in babies from certain parts of the world.
- Most children with MPS I have a severe type of the disorder.

What kinds of health problems does MPS I cause?

MPS I can damage many body systems (Figure 1). Most babies with MPS I appear normal, but over time they can develop changes in their appearance.

Figure 1: MPS I Symptoms.



Are there different types of MPS I?

Yes. Doctors classify MPS I into 2 main types based on severity:

- **Severe MPS I:** This is the more severe type of MPS I. It typically causes many symptoms that show early and worsen quickly. People with this type usually have serious health problems. Most people with MPS I have this type.
- **Attenuated MPS I:** This is the less severe type of MPS I. It typically causes problems in fewer body systems than severe MPS I. In this type, symptoms usually develop later and worsen more slowly than in severe MPS I.

When do MPS I symptoms develop?

The timing and type of problems caused by MPS I vary between different people. Table 1 explains when MPS I symptoms may arise.

Table 1: Symptom Timing and Type.

Age	Signs/Symptoms	Details
Birth	No signs	<ul style="list-style-type: none">● MPS I is present at birth. However, most babies with the disorder have no visible signs.● Parents and doctors usually cannot tell just by looking whether a baby has MPS I.
Early childhood	Severe MPS I symptoms	<ul style="list-style-type: none">● Babies with severe MPS I usually show symptoms by age 2.● Without treatment, this type can cause death before age 10.
Childhood	Attenuated MPS I symptoms	<ul style="list-style-type: none">● Children with attenuated MPS I usually show symptoms between ages 2 and 12.● People with this type usually have a normal lifespan.

TREATMENT FOR MPS I

How is MPS I treated?

There is no cure for MPS I. Once a child has symptoms, the child needs treatment for each affected body system.

Two treatments may help stop MPS I problems from getting worse. These treatments work by making IDUA activity levels closer to normal.

- **Enzyme Replacement Therapy (ERT)**

ERT restores IDUA activity using a man-made version of the missing enzyme. People who need ERT undergo a 4-hour treatment every 1 or 2 weeks. ERT puts the missing enzyme into their blood. It can improve some body system problems caused by MPS I and slow MPS I worsening. Because the enzyme cannot get into the brain, however, it does not help MPS I brain problems. Doctors do not know yet whether ERT helps in severe MPS I.

- **Hematopoietic Stem Cell Transplantation (HSCT)**

HSCT is also called a “bone marrow transplant.” HSCT restores IDUA activity using bone marrow from a donor who does not have MPS I. People with severe MPS I who undergo HSCT get new bone marrow that makes blood cells with a working IDUA enzyme. HSCT can slow or even stop MPS I brain problems. It does not help with all MPS I problems.

Specialists may recommend HSCT when the child is diagnosed with severe MPS I. Children who get HSCT may also need ERT, especially if they must wait for a bone marrow donor.

What are the risks of treatment for MPS I?

Some babies have serious allergies to ERT. Doctors monitor babies closely during treatment. Otherwise, ERT does not have other major risks.

HSCT is a serious medical procedure. It leads to a temporary risk of serious infections and can cause other complications. Risks depend on several different things, like the match between the HSCT ("bone marrow") donor and the person with MPS I. Because of these risks, HSCT can lead to death. Families offered HSCT should talk to specialists about whether this treatment is right for their child.

FINDING NEWBORNS WHO HAVE MPS I

How are newborns screened for MPS I?

Newborn screening for MPS I can happen along with other routine newborn screening in the first few days of life. Most newborn screening begins when a doctor or nurse collects a few drops of blood from a baby's heel and dries them onto a special piece of paper. The hospital sends these "dried blood spots" to the state's newborn screening program. The program uses a laboratory to check the dried blood spots for many disorders.

To screen for MPS I, laboratories use special equipment to measure IDUA enzyme activity in the dried blood spots. Low IDUA activity means a higher risk for MPS I.

When a newborn has low IDUA activity, the baby needs more tests. The newborn screening program works with the baby's doctor when screening results mean that the baby needs other tests or to see a specialist to tell for sure if the baby has MPS I.

How well does screening for MPS I work?

Screening identifies babies with low IDUA activity. After further testing, some of these babies receive a diagnosis of MPS I. Others do not have MPS I. Screening cannot diagnose MPS I, but it can determine which babies should receive more tests or see a specialist.

Experts think that screening detects all babies with MPS I. Experts in the field and newborn screening programs continuously work to make screening better.

What happens if newborn screening indicates a high risk for MPS I?

Doctors refer newborns whose screening results indicate high MPS I risk for more testing. This testing involves blood tests, urine tests, and an exam by a special doctor. The blood tests may look at the baby's IDUA gene. A change in this gene can sometimes explain a baby's low IDUA activity level. Some screening programs use the gene or other blood markers and IDUA activity tests together to find babies at highest risk for MPS I.

MPS I problems may not arise during early infancy, and doctors usually cannot tell at diagnosis which type of MPS I a healthy-looking baby has. Therefore, they monitor these babies to determine when and what type of treatment the baby needs.

What are some of the benefits and risks of newborn MPS I screening?

Table 2 describes the benefits and risks of newborn MPS I screening as of 2015.

Table 2: Benefits and Risks of Screening.

Benefits	Risks
<ul style="list-style-type: none"> ● Earlier identification and evaluation of babies at high risk for MPS I. 	<ul style="list-style-type: none"> ● Many babies identified from newborn screening do not have MPS I. All babies with low IDUA activity need more testing.
<ul style="list-style-type: none"> ● Earlier diagnosis. 	<ul style="list-style-type: none"> ● The timing and type of problems caused by MPS I are hard to predict. ● Doctors usually cannot tell whether a healthy-looking baby with MPS I has the more or less severe type.
<ul style="list-style-type: none"> ● Earlier treatment, which may improve brain development. 	<ul style="list-style-type: none"> ● Earlier exposure to treatment risks.
<ul style="list-style-type: none"> ● More time to plan for the future. 	<ul style="list-style-type: none"> ● More anxiety about the future.
<ul style="list-style-type: none"> ● Health counseling and family planning for family members. 	<ul style="list-style-type: none"> ● Sometimes, people do not want to know genetic risks. Some families do not like sharing health information.
<ul style="list-style-type: none"> ● Reassurance for the families of babies with normal IDUA activity. 	<ul style="list-style-type: none"> ● Unnecessary anxiety for families of babies with low IDUA activity who do not have MPS I.

Does early diagnosis or treatment help patients with MPS I?

Early diagnosis allows **early monitoring and treatment** – which may improve outcomes for people with MPS I. Getting treatment early may help with brain development and other symptoms. Researchers need more data to know how much it might improve lives of babies with MPS I.

Box B: Where Can I Learn More?

Follow the links below to learn more about information from this summary.

- To learn more about MPS I, visit the [National Institutes of Health MPS I](#) website.
- Visit the Committee’s website to learn more about:
 - [Nominating conditions to the RUSP](#).
 - [Full MPS I evidence report](#).
 - [The ACHDNC recommendation to the Secretary to add MPS I to the RUSP](#).

PUBLIC HEALTH IMPACT

How would newborn MPS I screening affect the health of the country?

Based on what is known about screening and the risk of being born with MPS I, experts think that screening all newborns in the US for MPS I would do the following:

- Find about 44 babies with MPS I each year (about 1.1 out of every 100,000 children born).
- Prevent between 0 and 2 deaths by age 5 due to MPS I each year.

Without screening, diagnosing severe MPS I can take 6 months or longer after a baby develops symptoms. For attenuated MPS I, diagnosis can take 2 to 4 years after symptoms develop. Sometimes, the diagnosis is never made. Newborn screening for MPS I allows diagnosis early in life before symptoms arise.

What is the status of newborn MPS I screening in the US?

- At the time of the report, one state (Missouri) screened newborns for MPS I. Two more (Illinois and New Jersey) had requirements to start.
- Most states estimated that newborn MPS I screening could begin 1 to 3 years after funding became available.

ADVISORY COMMITTEE DECISION

What did the Committee recommend?

The ACHDNC voted in 2015 to recommend adding MPS I to the RUSP. The Committee based its decision on the ability of screening to find babies with MPS I and early treatment being better than later treatment. In 2016, the US Secretary of Health and Human Services recommended that all newborns receive MPS I screening.

To screen for any condition, states must be prepared. They must have the right equipment and procedures. There must also be specialists who can work with families to determine whether a baby has the condition and, if so, the best treatment.

HELPFUL INFORMATION

Glossary

Term	Definition
ACHDNC	<u>A</u> dvisory <u>C</u> ommittee on <u>H</u> eritable <u>D</u> isorders in <u>N</u> ewborns and <u>C</u> hildren. The committee that oversees the RUSP.
Attenuated MPS I	The less severe type of MPS I. It causes problems in fewer systems that develop later and worsen more slowly than in severe MPS I.
Dried blood spot	A drop of blood that is collected from a baby's heel, dried onto a special piece of paper, and used to screen for many disorders.
ERT	<u>E</u> nzyme <u>r</u> eplacement <u>t</u> herapy. A treatment for MPS I that supplies a man-made version of the missing IDUA enzyme.
HSCT	<u>H</u> ematopoietic <u>s</u> tem <u>c</u> ell <u>t</u> ransplantation. A treatment for MPS I that provides the body with a working copy of the IDUA gene. Also called a bone marrow transplant.
IDUA gene	The gene responsible for causing MPS I.
IDUA enzyme	An enzyme from the IDUA gene that normally breaks down certain waste products.
MPS I	<u>M</u> ucopolysaccharidosis <u>T</u> ype <u>I</u> . A rare genetic disorder causing problems with the heart, airways, eyes and ears, muscles, bones, joints, and brain.
RUSP	<u>R</u> ecommended <u>U</u> niform <u>S</u> creening <u>P</u> anel. The list of conditions recommended for newborn screening.
Secretary of Health and Human Services	The head of the US Department of Health and Human Services. This person decides whether to add conditions to the RUSP.
Severe MPS I	The more severe type of MPS I. This type causes many symptoms that show early and worsen quickly.
Specialist	A doctor with expertise in a specific area of medicine.

Source

The information in this summary comes from the report *Newborn Screening for Mucopolysaccharidosis Type I (MPS I): A Systematic Review of Evidence* (16 March 2015), commissioned by the ACHDNC. The report reviewed evidence on MPS I screening and treatments in children through January 2015. It included both published and unpublished research. To see a copy of the report, visit this [page](#).