Newborn Screening for Hemoglobin H Disease

A Summary of the Evidence and Advisory Committee Decision

Report Date: 19 April 2010

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: HHSH250201500002I/HHSH25034003T).

EXECUTIVE SUMMARY

This summary reviews the information the federal advisory committee used when deciding whether to recommend adding Hemoglobin H (HbH) Disease to the Recommended Uniform Screening Panel (RUSP) in 2010.

About the condition

HbH Disease is a disease that affects a protein called hemoglobin. Between 1–21 out of every 100,000 children gets a diagnosis of HbH Disease. People with HbH Disease have problems with key genes for making hemoglobin. Babies with HbH Disease look normal. There are 2 types of HbH Disease: deletional and nondeletional. Most children have the first type. HbH Disease can cause problems with making blood. These problems can affect many parts of the body and lead to death during young adulthood.

Treatment for HbH Disease

Hematopoietic stem cell transplant may cure HbH Disease. Other treatments that may stop symptoms from getting worse include blood transfusions, iron-lowering therapy, and folic acid. Whether and when a child needs treatment depends on many things, like the disease type.

Detecting HbH Disease in newborns

Newborn screening for HbH Disease can happen along with routine newborn screening for other conditions during the first few days of life. Newborn HbH Disease screening measures levels of one type of abnormal hemoglobin in the blood. This process uses the same dried blood spots collected to screen for other disorders. Newborns with high levels of this hemoglobin are at higher risk for HbH Disease. They need more tests to diagnose the disease.

Public health impact

Detailed data on how newborn HbH Disease screening affects public health were not available at the time of the report. However, newborn screening allows diagnosis and monitoring early in life. Without screening, diagnosis can take time after symptoms begin; some babies may never receive a diagnosis. Screening newborns for HbH Disease may prevent problems or delays in diagnosis.

Committee decision

The Committee voted in 2010 to recommend not adding HbH Disease to the RUSP. To add HbH Disease to the RUSP, experts need to know more about how many people have the disease. They also need to know how well early diagnosis and treatment work and how screening affects public health.

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 2009, the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) requested an evidence review of newborn screening for Hemoglobin H (HbH) Disease. This summary presents key review information that the Committee used to make its decision about whether to recommend adding HbH Disease to the RUSP. It will answer these questions:

- What is HbH Disease?
- How is HbH Disease treated?
- How are newborns screened for HbH Disease?
- Does early diagnosis or treatment help patients with HbH Disease?
- What is the public health impact of newborn HbH Disease screening in the US?
- What did the Committee decide about adding HbH Disease 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 HbH Disease?

HbH Disease is a serious form of a genetic condition known as alpha thalassemia. This condition affects a protein called hemoglobin. Normally, hemoglobin helps blood cells carry oxygen from the lungs to other parts of the body. In people with HbH Disease, 3 of the 4 genes for making part of hemoglobin (called alpha globin) are missing or do not work. As a result, the body does not make enough working hemoglobin. This can cause health problems that can start in the first year of life.

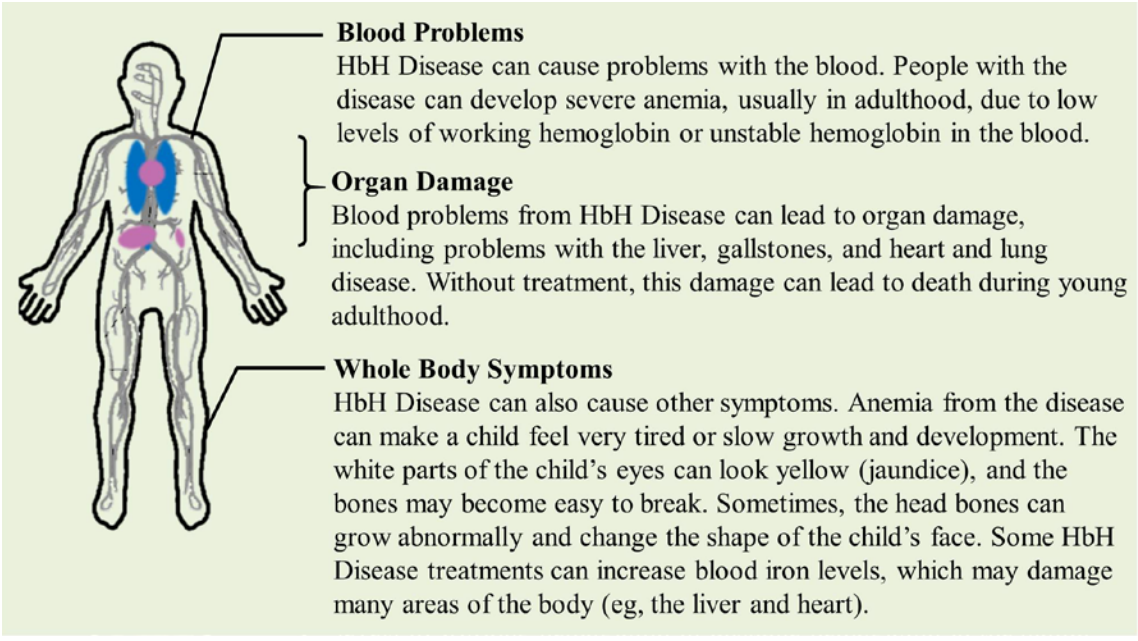
How common is HbH Disease?

- HbH Disease is rare. The number of children with this condition varies across the US. Between 1–21 out of every 100,000 children gets a diagnosis of HbH Disease.
- This range is based on data from the states in the US that screened for the disease at the time of the report.
- HbH Disease is more common in babies of certain heritage, like those with families from Southeast Asia, the Middle East, and the Mediterranean.

What kinds of health problems does HbH Disease cause?

HbH Disease causes problems with the blood that affect many parts of the body (Figure 1).

Figure 1: HbH Disease Symptoms.



Are there different types of HbH Disease?

Yes. Experts classify HbH Disease into 2 main types based on the gene changes that cause the disease:

- Deletional: People with this type are missing 3 alpha-globin genes. In the US, most people with HbH Disease (75%) have this type.
- Non-deletional: People with this type are missing 2 alpha-globin genes and have a third with a specific mutation. In the US, fewer people with HbH Disease (25%) have this type. This type usually causes more severe symptoms. “Constant Spring” is an example of this type of HbH Disease.

When do HbH Disease symptoms develop?

The timing and severity of problems from HbH Disease vary. Table 1 explains when HbH Disease symptoms may arise.

Table 1: Symptom Timing and Type.

Age	Details
Birth	• Babies are born with HbH Disease. • Most babies with the disease have no visible signs or symptoms. Some babies may be pale or have lighter skin than normal. This sign may not be noticed right away. • Most of the time, parents and doctors cannot tell just by looking whether a baby has the disease.
Infancy and Childhood	• When symptoms start varies between different people. • Children can develop anemia or other symptoms in the first year of life. Fevers and infections worsen these symptoms. • Children with the non-deletional type often have more severe anemia and need treatments more often than children with the deletional type.
Adulthood	• Some people with HbH Disease have mild symptoms and need little, if any, treatment. • The effect of the disease on lifespan varies. People with severe HbH Disease can have a shorter lifespan than normal.

TREATMENT FOR HBH DISEASE

How is HbH Disease treated?

Four treatments may stop HbH Disease from getting worse:

- **Hematopoietic stem cell transplantation (HSCT)**

  HSCT is sometimes called a "bone marrow transplant." It works by using cells from a donor who does not have HbH Disease. There are a few ways to get these cells, like umbilical cord blood from a newborn or bone marrow cells from an older donor. When transferred into the blood of a baby with HbH Disease, donor cells grow and develop in the baby's body. They travel to the baby's bone marrow. There, they become normal, blood-forming cells. They make the working hemoglobin that the baby would otherwise be missing. HSCT is the only treatment that may cure HbH Disease at this time.

- **Blood transfusion**

  This treatment involves giving a person with HbH Disease more blood from a healthy donor who has normal hemoglobin levels. It raises hemoglobin levels and lowers the risk of symptoms. Some people with HbH Disease need transfusions once in a while. Others may need them regularly.

- **Iron-lowering therapy**

  This treatment involves taking special medicines to remove extra iron from the body. These medicines can be taken in a few ways, and they prevent iron from damaging the body. Many people with HbH Disease need to take these medicines every day.

- **Folic acid**

  This treatment involves taking a daily folic acid vitamin. The body needs folic acid to make hemoglobin, so people with HbH Disease need a constant supply of it. This treatment helps the body make as much hemoglobin as possible.

Whether and when a child needs treatment depends on many things, like their symptoms and type of HbH Disease. Children with the disease see a blood specialist at least once each year to check their blood and see if they need more treatment.

What are the risks of treatment for HbH disease?

- **HSCT**

  HSCT is a serious procedure. It leads to a short-term risk of serious infections and other problems. Risks depend on a few things, like how well the cells from the donor match those of the baby with HbH Disease. Because of its risks, HSCT can lead to death. Only people with severe HbH Disease need this treatment. Families offered HSCT should talk to specialists about whether it is right for their child.

- **Blood transfusion**

  This is a simple procedure. However, people with HbH Disease who need many transfusions may develop very high iron levels. Iron from the transfusions adds to the high iron from the disease. High iron levels can cause serious problems with the heart, liver, and other organs. Other medicines can help to remove extra iron from the body.

- **Iron-lowering therapy**

  This treatment can cause side effects, like hearing, vision, kidney, or growth problems. Doctors monitor people receiving this therapy to prevent problems.

- **Folic acid**

  This treatment is very safe.

Box B: Where Can I Learn More?

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

- To learn more about HbH Disease, visit the National Institutes of Health Alpha Thalassemia page.
- Visit the Committee's website to learn more about:
  - Nominating conditions to the RUSP.
  - Full HbH Disease evidence report.
  - The ACHDNC recommendation to the Secretary not to add HbH Disease to the RUSP.

FINDING NEWBORNS WHO HAVE HBH DISEASE

How are newborns screened for HbH Disease?

Newborn screening for HbH Disease 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 hemoglobin disorders (including HbH Disease), laboratories measure normal and abnormal hemoglobin in dried blood spots. Higher levels of a certain type of abnormal hemoglobin mean a higher risk for HbH Disease.

When newborns have high levels of this type of hemoglobin, they need more tests to tell if they have HbH Disease. The screening program works with a baby's doctor so that the baby can see a specialist to tell if the baby has HbH Disease.

How well does screening for HbH Disease work?

Screening detects babies with high levels of the abnormal hemoglobin linked to HbH Disease. After more tests, some of these babies get a diagnosis of HbH Disease. Others do not have the disease. Screening cannot diagnose HbH Disease, but it can determine which babies need more tests or to see a specialist.

Experts think that screening detects most babies with HbH Disease. Screening cannot tell apart the types of HbH Disease or predict when symptoms will arise.

What happens if newborn screening indicates a high risk for HbH Disease?

Doctors refer newborns whose screening results indicate high HbH Disease risk for more testing. This testing involves blood and gene tests to check for alpha-globin gene changes. Based on these tests, the baby may be diagnosed with HbH Disease.

Problems from HbH Disease do not always start in early infancy. Most of the time, doctors cannot tell at diagnosis when a healthy-looking baby with the disease will have symptoms. Therefore, they monitor all babies with the disease for problems throughout life to see if they need treatment. Monitoring involves blood tests (to measure blood cells and iron) and regular growth checks. Children with HbH Disease should also avoid certain foods, like those very high in iron, that could make their symptoms worse.

What are some of the benefits and risks of newborn HbH Disease screening?

Table 2 describes the benefits and risks of newborn HbH Disease screening as of 2010.

Table 2: Benefits and Risks of Screening.

Benefits	Risks
• Earlier detection and evaluation of babies at risk for HbH Disease.	• Some babies found from newborn screening do not have HbH Disease. All babies with high levels of abnormal hemoglobin need more testing.
• Earlier diagnosis and treatment.	• Earlier exposure to treatment risks. • Some babies and young children with HbH Disease do not need treatment. • Experts do not know if early diagnosis and treatment improve long-term health.
• Earlier symptom monitoring.	• Monitoring can cause families to have anxiety about the future. • Experts do not know if early monitoring improves long-term health.

Do early diagnosis and treatment help patients with HbH Disease?

At the time of the report, experts did not know if screening newborns for HbH Disease improved health outcomes. No studies had examined how early diagnosis and treatment affect patients with the disease.

Experts must learn more to say for sure whether early diagnosis and treatment help patients with HbH Disease.

PUBLIC HEALTH IMPACT

How would newborn HbH Disease screening affect the health of the country?

Detailed data on how newborn HbH Disease screening would affect public health in the US were not available at the time of the report.

However, newborn screening allows diagnosis and monitoring early in life. Without screening, diagnosing the disease can take time after symptoms develop; some babies with the disease may never receive a diagnosis. Screening newborns for HbH Disease may help to avoid problems or delays in diagnosis.

What is the status of newborn HbH Disease screening in the US?

- At the time of the report, 5 states (California, Hawaii, Iowa, Missouri, and Washington) screened all newborns for HbH Disease.
- Data on state readiness to begin newborn HbH Disease screening were not available at the time of the report.

ADVISORY COMMITTEE DECISION

What did the Committee recommend?

The ACHDNC voted in 2010 to recommend that HbH Disease not be added to the RUSP. The Committee based its decision on gaps in what is known about the disease. The Committee wanted to know more about:

- How many people in the US have the disease.
- Whether early diagnosis and treatment help in the disease.
- The public health impact of newborn HbH Disease screening.

The ACHDNC may reconsider adding it to the RUSP once these data are available.

HELPFUL INFORMATION

Glossary

Term	Definition
ACHDNC	Advisory Committee on Heritable Disorders in Newborns and Children. The committee that oversees the RUSP.
Alpha-globin genes	Genes for making a part of hemoglobin. Some of these genes are missing or do not work in HbH Disease.
Alpha thalassemia	A genetic condition affecting hemoglobin.
Anemia	A condition in which people have a low levels of normal hemoglobin.
Blood transfusion	A treatment that gives a person with HbH Disease more blood from a healthy donor who has normal hemoglobin levels.
Deletional	The most common type of HbH Disease. People with this type are missing 3 alpha-globin genes.
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.
Folic acid	A vitamin the body needs to make hemoglobin.
Hemoglobin	A protein in the blood that helps to carry oxygen.
HbH Disease	Hemoglobin H Disease. A rare genetic disease that causes problems with making hemoglobin.
HSCT	Hematopoietic stem cell transplantation. A treatment for HbH Disease that provides the body with blood cells making normal hemoglobin.
Jaundice	Yellowing of the skin or eyes.
Non-deletional	The less common type of HbH Disease. People with this type are missing 2 alpha-globin genes and have a third with a specific mutation.
RUSP	Recommended Uniform Screening Panel. The list of conditions recommended for newborn screening.
Secretary of Health & Human Services	The head of the US Department of Health and Human Services. This person decides whether to add conditions to the RUSP.
Specialist	A doctor with expertise in a specific area of medicine.

Source

The information in this summary comes from the report *Evidence Review: Hemoglobin H Disease* (19 April 2010), commissioned by the ACHDNC. The report reviewed data on HbH Disease screening and treatments in children through March 2010. It included both published and unpublished research. To see a copy of the report, visit this page.