Newborn Screening for Severe Combined Immunodeficiency

A Summary of the Evidence and Advisory Committee Decision

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EXECUTIVE SUMMARY

This summary reviews the information the federal advisory committee used when deciding whether to recommend adding Severe Combined Immunodeficiency (SCID) to the Recommended Uniform Screening Panel (RUSP) in 2010.

About the condition

SCID is the name of a group of serious disorders affecting the immune system. About 1–3 out of every 100,000 babies has SCID. Children with SCID are born with changes in important immune system genes. Because of these changes, children with SCID are missing key cells in the immune system. These changes weaken the immune system and make children with SCID prone to infections. Babies with SCID appear normal. There are many types of SCID, and each can cause problems with the immune system leading to serious infections. This can lead to death within the first year.

Treatment for SCID

Early diagnosis allows early treatment and improves outcomes for babies with SCID. Treatments that help to restore the immune system include hematopoietic stem cell transplantation and enzyme replacement therapy. The treatment a baby receives depends on many things, like the baby's type of SCID.

Detecting SCID in newborns

Newborn screening for SCID can happen along with routine newborn screening for other conditions during the first few days of life. SCID screening measures levels of a T-cell marker. This process uses the same dried blood spots already collected for screening of other disorders. Newborns with low levels of this marker are at higher risk for SCID. They need more testing to diagnose the condition.

Public health impact

Detailed data on how newborn SCID screening would affect public health were not available at the time of the report. However, newborn screening for SCID saves lives by allowing diagnosis and treatment early in life. Without screening, diagnosis can take 7 months or more after symptoms develop; some babies may never receive a diagnosis. Newborn screening allows diagnosis and treatment before symptoms arise.

Committee decision

The Committee voted in 2010 to recommend adding SCID to the RUSP. As of 2010, the RUSP recommends that state newborn screening programs include SCID.

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 2008, the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) requested an evidence review of newborn screening for Severe Combined Immunodeficiency (SCID). This summary presents key review information that the Committee used to make its decision about whether to recommend adding SCID to the RUSP. It will answer these questions:

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

SCID is the name of a group of serious disorders affecting the immune system. Babies with SCID have one of these disorders. Normally, the immune system protects the body against invaders like viruses and bacteria. Children with SCID are born with changes in important immune system genes. Because of these changes, children with SCID are missing key cells in the immune system called T-cells that direct or help with attacks against invaders. Some children may also be missing other cells in the immune system. These changes weaken the immune system and make children with SCID prone to infections of all types. Infections that are minor in most people can be very serious for children with SCID. SCID can cause death within the first year of life.

How common is SCID?

- SCID is rare. As of 2009 (before routine newborn SCID screening), about 1-3 out of every 100,000 children received a diagnosis of SCID.
- This estimate was based on the number of people who developed symptoms and received a diagnosis without newborn screening. Some babies and children with SCID do not receive a diagnosis, so the estimate might be low.
- SCID is much more common in babies of Navajo heritage.

Are there different types of SCID?

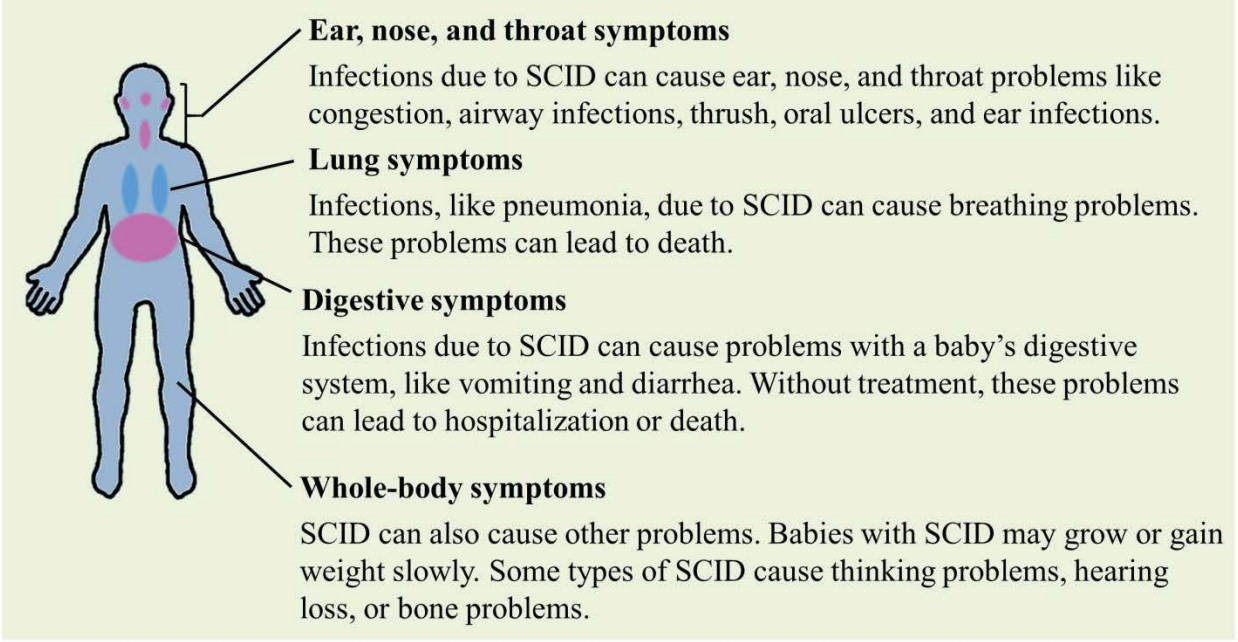
Yes. Doctors classify SCID into types based on the specific problem with the immune system. Each type weakens the immune system in different ways, but most cause similar problems with fighting infection.

All types of SCID can cause serious health problems and require treatment early in life. Early detection is crucial for all types of SCID.

What kinds of health problems does SCID cause?

SCID causes problems with the immune system that lead to infections of all types. SCID can also affect other parts of the body (Figure 1).

Figure 1: SCID Symptoms.



When do SCID symptoms develop?

Table 1 explains when SCID symptoms typically occur.

Table 1: Symptom Timing and Type.

Age	Symptom	Details
Birth	None	• Babies are born with SCID. However, most babies with SCID have no visible signs. • Parents and doctors usually cannot tell just by looking whether a baby has SCID.
Early infancy	Infections	• Babies with SCID get repeated infections in the first few months of life. These infections cause symptoms affecting many parts of the body.
Early childhood	Death	• Without treatment, SCID causes death within the first few years of life from infection.

TREATMENT FOR SCID

How is SCID treated?

Babies with SCID get frequent infections and need treatment for them. Treating and preventing infections can prolong life.

Babies with SCID also need special treatments to strengthen the immune system. These treatments can improve the chance of survival and sometimes cure the disease. They work best before babies develop serious infections. These treatments include:

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

  HSCT is sometimes called a bone marrow transplant. A bone marrow transplant strengthens the immune system using cells from a donor who does not have SCID. There are a few ways to get these cells from a donor, like umbilical cord blood from a newborn or bone marrow cells from an older donor. After these cells are put into the blood of a baby with SCID, they grow in the baby's bone marrow. These cells make cells in the immune system that would otherwise be missing in babies with SCID. HSCT works best when certain markers from the donor and baby match.

  HSCT greatly improves the chance of survival for babies with all types of SCID. About 95% of babies treated with HSCT as newborns survive and develop working immune systems. Babies who get HSCT in the first few months of life, before any infections, benefit most.

- **Enzyme Replacement Therapy (ERT)**

  Babies with some types of SCID, who are missing one specific immune system enzyme, may receive ERT. ERT replaces the baby's missing enzyme with a man-made version. People who receive ERT need treatments throughout their lives. ERT can improve the chance of survival for some babies with SCID.

The treatment a baby receives depends on many things, like the baby's type of SCID.

What are the risks of treatment for SCID?

Like any treatment, each type of treatment for SCID has risks.

- **HSCT**

  HSCT is a serious procedure. Risks depend on several different things, like the match between the HSCT donor and the baby with SCID. Because of these risks, HSCT can lead to death. The risks of HSCT go up as a baby gets older, and the risks of delayed HSCT may outweigh its benefits. Families offered HSCT should talk to specialists about whether this treatment is right for their child.

- **ERT**

  ERT is relatively safe. Some babies have serious allergies to ERT, so doctors monitor babies closely during treatment. Because ERT only works for some types of SCID, babies without these types do not benefit from ERT. Otherwise, ERT does not have other major risks.

Box B: Where Can I Learn More?

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

- To learn more about SCID, visit the National Institute of Allergy and Infectious Diseases SCID website.
- Visit the Committee's website to learn more about:
  - Nominating conditions to the RUSP.
  - Full SCID evidence report.
  - The ACHDNC recommendation to the Secretary to add SCID to the RUSP.

FINDING NEWBORNS WHO HAVE SCID

How are newborns screened for SCID?

Newborn screening for SCID 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 SCID, laboratories use special equipment to measure a T-cell marker in the dried blood spots. Low levels of the T-cell marker mean a higher risk for SCID.

When a newborn has low levels of the T-cell marker, the baby needs more tests to tell if the baby has SCID. The newborn screening program works with the baby's doctor so that the baby can see a specialist and have tests to tell for sure if the baby has SCID.

How well does screening for SCID work?

Screening detects babies with low levels of a T-cell marker. Most babies of these babies have a problem with the immune system. After more tests, a specialist can determine whether a baby has SCID or another serious problem. Screening cannot diagnose SCID, but it can determine which babies need to see a specialist for more tests.

Experts think that screening detects most babies with SCID. Screening cannot tell apart the types of SCID. Experts in the field and newborn screening programs work to make screening better.

What happens if newborn screening indicates a high risk for SCID?

Doctors refer newborns whose screening results indicate high SCID risk for more testing. This testing involves blood tests to see if the immune system has all the cells it needs to work properly. Doctors may also check for a change in important immune system genes. Knowing the gene change that causes SCID can sometimes help with planning the best treatment.

What are some of the benefits and risks of newborn SCID screening?

Table 2 describes the benefits and risks of newborn SCID screening as of 2009.

Table 2: Benefits and Risks of Screening.

Benefits	Risks
• Earlier identification and evaluation of babies at high risk for SCID.	• Some babies found from newborn screening do not have SCID. All babies with low levels of the T-cell marker need more testing. • Follow-up tests can be burdensome for families and disrupt parent/child bonding.
• Earlier use of protective measures to prevent infections.	• The need for monitoring could cause families to have anxiety about the future.
• Earlier diagnosis and treatment, which greatly improve the chance of survival.	• There is a very small chance that screening could miss a child with a treatable type of SCID.

Do early diagnosis and treatment help patients with SCID?

Yes. **Early diagnosis** before symptoms develop allows **early treatment**, which greatly improves a baby's chance of survival.

- Babies with SCID diagnosed during the newborn period are more likely than those diagnosed later to get treatment for their frequent infections. Treating and prevent infections can prolong life.
- Early HSCT in the first few months of life lowers the risk of death or disability due to SCID. About 95% of newborns with SCID who receive HSCT survive and develop working immune systems. Later HSCT does not work as well.
- Children who receive SCID treatment before, rather than after, getting serious infections have a better chance of survival.

PUBLIC HEALTH IMPACT

How would newborn SCID screening affect the health of the country?

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

However, newborn screening for SCID saves lives by allowing diagnosis and treatment early in life. Without screening, diagnosing SCID can take 7 months or longer after a baby develops symptoms; some babies with SCID never receive a diagnosis. Newborn screening allows SCID diagnosis and treatment before symptoms arise.

What is the status of newborn SCID screening in the US?

- At the time of the report, 2 states (Massachusetts and Wisconsin) screened newborns for SCID.
- Data on state readiness to begin newborn SCID 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 adding SCID to the RUSP. The Committee based its decision on the ability of screening to find babies with SCID and early treatment being better than later treatment. In 2010, the US Secretary of Health and Human Services recommended that all newborns receive SCID 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	Advisory Committee on Heritable Disorders in Newborns and Children. The committee that oversees the RUSP.
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	Enzyme replacement therapy. A treatment for SCID that supplies a man-made version of a missing immune system enzyme.
HSCT	Hematopoietic stem cell transplantation. A treatment for SCID that provides the body with cells in the immune system that would otherwise be missing. The most common type of HSCT is a bone marrow transplant.
SCID	Severe Combined Immunodeficiency. A group of serious disorders that affect the immune system.
RUSP	Recommended Uniform Screening Panel. The list of conditions recommended for newborn screening.
T-cell	A type of immune system cell missing in people with SCID. T-cells direct or help with immune system attacks against invaders.
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.
Specialist	A doctor with expertise in a specific area of medicine.

Source

The information in this summary comes from the report *Evidence Review: Severe Combined Immunodeficiency (SCID)* (29 April 2009), commissioned by the ACHDNC. The original report reviewed data on SCID screening and treatments in children through October 2008. It included both published and unpublished research. Parts of the report were updated in 2009 after newborn screening identified a child in the US with SCID. To see a copy of the report, visit this page.