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# Newborn Screening for Krabbe Disease

A Summary of the Evidence and Advisory Committee  
Decision

Report Date: 21 December 2009



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## EXECUTIVE SUMMARY

This summary reviews the information the federal advisory committee used when deciding whether to recommend adding Krabbe Disease to the Recommended Uniform Screening Panel (RUSP) in 2009.

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### About the condition

Krabbe Disease is a rare disorder that affects the nervous system. About 1 out of every 100,000 babies has Krabbe Disease. People with Krabbe Disease do not have enough of the GALC enzyme that helps the body break down fats in the nervous system. Babies with Krabbe Disease appear normal. There are 4 types of Krabbe Disease: early infantile, late infantile, juvenile, and adult. Most children have the infantile types. Krabbe Disease can cause problems with development, movement, and other symptoms that can worsen quickly and cause death by age 2.

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### Treatment for Krabbe Disease

There is no cure for Krabbe Disease. Early diagnosis allows early treatment, which could improve outcomes for some babies with the disease. Hematopoietic stem cell transplant, also called a “bone marrow transplant,” is a treatment that might stop symptoms from getting worse. Whether and when a baby needs this treatment depends on many things, like the type of Krabbe Disease.

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### Detecting Krabbe Disease in newborns

Newborn screening for Krabbe Disease can happen along with routine newborn screening for other conditions during the first few days of life. Newborn Krabbe Disease screening measures GALC enzyme levels and looks for changes in the GALC gene. This process uses the same dried blood spots already collected for screening of other disorders. Newborns with low GALC enzyme levels and changes in the GALC gene are at higher risk for Krabbe Disease. They need more testing to diagnose the condition.

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### Public health impact

Detailed data on how newborn Krabbe Disease screening would affect public health were not available at the time of the report. However, newborn screening for the disease allows diagnosis and monitoring early in life. Without screening, diagnosing the disease can take 5 months or longer after symptoms begin. Newborn screening allows diagnosis and treatment before severe symptoms start.

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### Committee decision

The Committee voted in 2009 to recommend not adding Krabbe Disease to the RUSP. To add Krabbe Disease to the RUSP, experts need to know more about how to define disease types, the best screening method, and how well treatment works.

## 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 Krabbe Disease. This summary presents key review information that the Committee used to make its decision about whether to recommend adding Krabbe Disease to the RUSP. It will answer these questions:

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

Krabbe (pronounced crab-AY) Disease is a rare genetic disorder affecting the nervous system. People with Krabbe Disease are born with a change in a single gene called GALC. Normally, this gene makes a GALC enzyme that helps break down fats in the nervous system. In people with Krabbe Disease, the GALC enzyme does not work properly. As a result, certain fats build up and damage the protective coating around nerve cells. Without this coating, nerves do not work properly. These changes cause symptoms that can lead to death in early childhood.

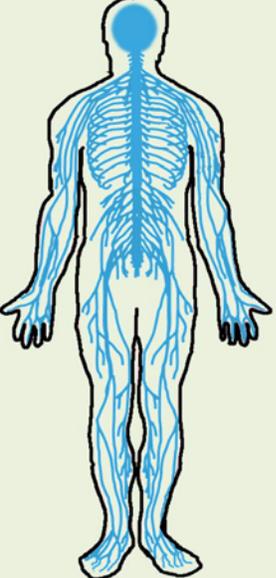
### How common is Krabbe Disease?

- Krabbe Disease is a rare disorder. About 1 out of every 100,000 children receives a diagnosis of Krabbe Disease.
- This estimate is based on the number of people who develop symptoms and get a diagnosis without newborn screening. Not everyone with Krabbe Disease is diagnosed, so the real number of people affected may be higher.
- Krabbe Disease may be more common in babies from families with Arab heritage from some locations.

### What kinds of health problems does Krabbe Disease cause?

Krabbe Disease causes problems with the nervous system that affect development, movement, and other related symptoms (Figure 1).

#### Figure 1: Krabbe Disease Symptoms.



The diagram shows a human silhouette with a blue-tinted nervous system highlighted. The brain, spinal cord, and peripheral nerves are visible, illustrating the areas affected by the disease.

**Developmental symptoms**  
Damage to the nervous system from Krabbe Disease can cause symptoms affecting development. Some babies and children with the disease have slowed mental or physical development.

**Movement symptoms**  
Damage to the nervous system from Krabbe Disease can cause symptoms affecting movement. Some people with Krabbe Disease develop muscle weakness and stiffness that cause problems with things like moving, chewing, swallowing, and breathing. These problems can lead to death.

**Other symptoms**  
Damage to the nervous system from Krabbe Disease can cause other symptoms. Some babies with the disease may develop vision loss, seizures, excessive crying, or poor feeding.

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## Are there different types of Krabbe Disease?

Yes. Doctors classify the disease into 4 types based on when symptoms start. The Krabbe Disease types are early infantile, late infantile, juvenile, and adult. Most people with the disease have the early or late infantile types.

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## When do Krabbe Disease symptoms develop?

The timing and type of problems caused by Krabbe Disease vary. Table 1 explains when Krabbe Disease symptoms may arise. Symptoms are usually more severe when they affect babies and young children.

**Table 1: Symptom Timing and Type.**

Age	Disease Type	Details
Birth	All types	<ul style="list-style-type: none"><li>● Babies are born with Krabbe Disease. However, most babies with the disease have no visible signs or symptoms.</li><li>● Parents and doctors usually cannot tell just by looking whether a baby has Krabbe Disease.</li></ul>
Infancy	Early infantile	<ul style="list-style-type: none"><li>● Brain and nervous system changes begin before babies show symptoms.</li><li>● Babies with this type of Krabbe Disease usually have symptoms before 6 months of age.</li><li>● Without treatment, this type usually causes death before age 2 years.</li></ul>
Childhood through adulthood	Late infantile, juvenile, and adult	<ul style="list-style-type: none"><li>● People with later-onset disease usually have milder symptoms.</li><li>● When symptoms start and the effect of the disease on lifespan vary between different people.</li><li>● Some people with the gene change causing Krabbe Disease may never have symptoms.</li></ul>

## TREATMENT FOR KRABBE DISEASE

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### How is Krabbe Disease treated?

There is no cure for Krabbe Disease. However, hematopoietic stem cell transplantation (HSCT) may stop Krabbe Disease symptoms from getting worse.

HSCT is sometimes called a “bone marrow transplant.” A bone marrow transplant works by using cells from a donor who does not have Krabbe Disease. There are a few different ways to get these cells from a donor, like umbilical cord blood from a newborn or bone marrow cells from an older donor. When transfused (transferred) into the blood of a baby with Krabbe Disease, these donor cells grow and develop within the baby's body. They travel to the baby's bone marrow. There, they become normal, blood-forming cells. They make the GALC enzyme that the baby would otherwise be missing.

HSCT may improve the chance of survival for some babies with Krabbe Disease. Doctors need more data to know:

- How much the treatment will help each baby with the disease.
- How to improve the effects of treatment.

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### What are the risks of treatment for Krabbe disease?

HSCT is a serious procedure. It leads to a short-term risk of serious infections and other complications. Risks depend on a few different things, like how well bone marrow cells from the donor match those of the baby with Krabbe Disease. Because of its risks, HSCT can lead to death. The risks of HSCT often outweigh the benefits until the disease type is known. Families offered HSCT should talk to specialists about whether this treatment is right for their child.

## FINDING NEWBORNS WHO HAVE KRABBE DISEASE

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### How are newborns screened for Krabbe Disease?

Newborn screening for Krabbe 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 Krabbe Disease, some laboratories use a machine called a tandem mass spectrometer to measure the GALC enzyme in the dried blood spots. Low levels of the GALC enzyme mean a higher risk for Krabbe Disease. Babies with low levels need a second screening step. This step uses DNA testing to look for one or more changes in the baby's GALC gene. The type and number of changes can help to predict disease severity.

When newborns have low levels of the GALC enzyme and changes in the GALC gene, they need more tests and monitoring to determine if they have Krabbe Disease. The newborn screening program works with a baby's doctor so that the baby can see a specialist to tell if the baby has Krabbe Disease.

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### How well does screening for Krabbe Disease work?

Screening detects babies with low levels of the GALC enzyme and changes in the GALC gene. After more tests, some of these babies receive a diagnosis of Krabbe Disease. Others do not have Krabbe Disease. Screening cannot diagnose Krabbe Disease, but it can determine which babies need more tests or to see a specialist.

Experts think that screening detects most babies with Krabbe Disease. Screening cannot tell apart the disease types or predict when, if ever, symptoms will arise. Experts in the field and newborn screening programs are working to make screening better.

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

Doctors refer newborns whose screening results indicate high risk of Krabbe Disease for more testing. This testing involves a doctor's exam and blood or skin tests to check how well the baby's GALC enzyme works. Doctors also check for specific changes in the GALC gene.

Krabbe Disease problems do not always start during early infancy, and doctors usually cannot tell when or if a healthy-looking baby with Krabbe Disease will develop symptoms. Therefore, doctors monitor all babies with the disease for problems to see when or if they need treatment. Monitoring involves testing to check how the brain responds to sounds or patterns and how quickly nerves carry brain messages. Doctors may also take pictures of the brain with special scanners or test the blood and brain for specific problems.

Babies at the highest risk for Krabbe Disease need monitoring more often than those at lower risk.

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

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

**Table 2: Benefits and Risks of Screening.**

Benefits	Risks
<ul style="list-style-type: none"><li>● Earlier identification and evaluation of babies at risk for Krabbe Disease.</li></ul>	<ul style="list-style-type: none"><li>● Some babies identified from newborn screening do not have Krabbe Disease. All babies with low levels of the GALC enzyme and changes in the GALC gene need more testing.</li></ul>
<ul style="list-style-type: none"><li>● Earlier symptom monitoring.</li></ul>	<ul style="list-style-type: none"><li>● The need for monitoring can cause anxiety about the future.</li></ul>
<ul style="list-style-type: none"><li>● Earlier diagnosis and treatment, which may improve the chance of survival.</li></ul>	<ul style="list-style-type: none"><li>● Earlier exposure to treatment risks.</li><li>● Some babies at risk for Krabbe Disease do not need treatment. Doctors cannot tell which babies with the disease need treatment right away.</li><li>● Experts do not yet know whether treatment will relieve or prolong symptoms in Krabbe Disease.</li></ul>

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## Do early diagnosis and treatment help patients with Krabbe Disease?

Maybe.

Experts have some evidence that the answer to this question is “yes.” For example, they know that:

- Diagnosis before severe symptoms develop allows earlier monitoring and treatment.
- For babies with infantile Krabbe Disease, receiving treatment before severe symptoms arise may improve certain outcomes or lower the risk of death.

However, early diagnosis and treatment may not always help in Krabbe Disease. For example, experts also know that:

- Even with treatment, many children with infantile Krabbe Disease can still develop nervous system symptoms.
- For babies with later-onset disease, doctors cannot predict when (if ever) symptoms will arise. The risks of HSCT for these babies often outweigh the benefits until the disease type is known.

Experts need to learn more about Krabbe Disease to say for sure whether early diagnosis and treatment help patients with the disease.

### **Box B: Where Can I Learn More?**

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

- To learn more about Krabbe Disease, visit the [National Institutes of Health Krabbe Disease](#) website.
- Visit the Committee’s website to learn more about:
  - [Nominating conditions to the RUSP.](#)
  - [Full Krabbe Disease evidence report.](#)
  - [The ACHDNC recommendation to the nominator not to add Krabbe Disease to the RUSP.](#)

## PUBLIC HEALTH IMPACT

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

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

However, newborn screening for Krabbe Disease allows diagnosis and monitoring early in life. Without screening, diagnosing Krabbe Disease can take more than 5 months after a baby develops symptoms; some babies never receive a diagnosis. Newborn screening allows diagnosis and treatment before severe symptoms arise.

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

- At the time of the report, one state (New York) screened newborns for Krabbe Disease.
- Data on state readiness to begin newborn Krabbe Disease screening were not available at the time of the report.

## ADVISORY COMMITTEE DECISION

What did the Committee recommend?

The ACHDNC voted in 2009 to recommend that Krabbe 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 doctors define the disease types, the best screening method, and how well treatment works. The ACHDNC will reconsider adding Krabbe Disease to the RUSP once these data are available.

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.
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.
GALC gene	Problems with this gene cause Krabbe Disease.
GALC enzyme	An enzyme that helps break down fats in the nervous system.
HSCT	<u>H</u> ematopoietic <u>s</u> tem <u>c</u> ell <u>t</u> ransplantation. A treatment for Krabbe Disease that provides the body with the GALC enzyme that would otherwise be missing. Also called a “bone marrow transplant.”
Krabbe Disease	A rare genetic disorder causing problems with the nervous system.
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.
Specialist	A doctor with expertise in a specific area of medicine.
Tandem mass spectrometer	A machine that measures markers in dried blood spots.
Transfused	Transferred into the blood.

### Source

The data in this summary come from the report *Evidence Review: Krabbe Disease* (21 December 2009), commissioned by the ACHDNC. The report reviewed data on Krabbe Disease screening and treatments in children through July 2009. It included both published and unpublished research. To see a copy of the report, visit this [page](#).