CONDITION

Krabbe disease

Krabbe disease is an inherited condition that damages the protective covering around nerves in the brain and body.

WHAT IT IS
Inherited condition that damages myelin around nerves

BODY SYSTEM
Brain, spinal cord, and peripheral nerves

MAIN SYMPTOMS
Developmental loss, stiffness, feeding difficulty, vision problems

WHAT CAUSES IT
Inherited changes in the GALC gene

HOW IT IS DIAGNOSED
GALC enzyme activity and GALC genetic testing

MAIN TREATMENT
Early stem cell transplant and supportive care

CAN IT BE CURED?
No, transplant may slow progression

IS IT AN EMERGENCY?
Sometimes, with breathing trouble or a prolonged seizure

LONG-TERM OUTLOOK
Often severe; later-onset forms may progress more slowly

Overview

Krabbe disease is a rare inherited condition that affects the nervous system. It is also called globoid cell leukodystrophy or GALC deficiency.

The condition damages myelin , the fatty covering that protects nerves and helps electrical signals travel quickly. Myelin surrounds nerves in the brain, spinal cord, and the rest of the body. When it breaks down, movement, swallowing, vision, learning, and other functions can become more difficult.

Krabbe disease is caused by very low activity of an enzyme called galactocerebrosidase, usually shortened to GALC . This allows harmful substances, especially psychosine, to build up and damage cells that make myelin.

Symptoms most often begin during infancy, but they can first appear in later childhood, adolescence, or adulthood. Earlier-onset forms generally progress faster and are more severe. Later-onset forms may progress more slowly, but they can still cause major disability.

Early recognition matters because a stem cell transplant may slow the condition in carefully selected people, particularly when it is performed before major symptoms or nerve damage develop. It cannot repair damage that has already occurred.

Symptoms

Symptoms differ according to the age at which the condition begins. They usually worsen over time.

In babies, early signs can be difficult to distinguish from more common childhood problems. Possible symptoms include:

As infantile Krabbe disease progresses, a baby may have increasing stiffness followed by severe weakness. Swallowing and breathing can become difficult. The baby may become less responsive to their surroundings.

When symptoms begin later, the pattern can be different. Children, teenagers, or adults may develop walking difficulties, weakness, poor balance, changes in muscle tone, or a decline in vision. Some people have changes in school performance, thinking, speech, or behaviour. Seizures may occur but are not present in everyone.

These symptoms can have many causes. Having one or more of them does not mean that you or your child has Krabbe disease.

- Irritability or frequent unexplained crying
- Feeding difficulty, vomiting, or poor weight gain
- Unusual stiffness or episodes of arching
- Loss of head control or other previously gained skills
- Increased sensitivity to touch, light, or sound
- Muscle weakness
- Vision or hearing problems
- Seizures

Causes and risk factors

Krabbe disease is caused by harmful changes in the GALC gene . This gene provides instructions for making the GALC enzyme. When the enzyme does not work properly, psychosine and related substances build up in the nervous system.

The condition follows an autosomal recessive inheritance pattern. This means a person usually has a harmful GALC gene change in both copies of the gene, one inherited from each biological parent.

Parents who each carry one altered copy are called carriers. Carriers usually do not develop Krabbe disease. For each pregnancy between two carriers, there is:

These chances start again with every pregnancy. They do not change based on the outcome of an earlier pregnancy.

A family history increases the chance of carrying a GALC gene change. However, some families do not know that the change is present until a child is diagnosed or newborn screening identifies a possible concern.

- A 1 in 4 chance that the child will have the condition
- A 1 in 2 chance that the child will be a carrier
- A 1 in 4 chance that the child will inherit neither altered copy

Diagnosis

Some newborn screening programs test for Krabbe disease. Screening is not available everywhere and does not establish a diagnosis by itself. An abnormal result means that prompt follow-up testing is needed.

Diagnosis usually involves measuring GALC enzyme activity in blood cells or cultured skin cells. Very low activity supports the diagnosis. Genetic testing is used to look for harmful changes in both copies of the GALC gene.

Low enzyme activity alone can sometimes be misleading. Some people have pseudodeficiency variants , which lower enzyme activity on a laboratory test without causing Krabbe disease. Results therefore need to be interpreted together with genetic findings, symptoms, and other testing.

A blood test for psychosine may help assess whether the condition is likely to cause early, severe symptoms. This is especially important after an abnormal newborn screen because treatment decisions may need to be made quickly.

Other tests help assess nerve damage but do not usually confirm the condition on their own. They may include:

Testing and interpretation are usually coordinated by a specialist team familiar with inherited metabolic and neurological conditions.

- MRI scans to look at the brain's white matter
- Nerve conduction studies to measure how well peripheral nerves work
- Vision, hearing, swallowing, and developmental assessments
- Examination of muscle tone, reflexes, movement, and coordination

Treatment and management

There is no treatment that can reverse all the nerve damage caused by Krabbe disease. Care aims to slow progression when possible, ease symptoms, protect comfort, and support daily life.

A hematopoietic stem cell transplant may be considered. This procedure supplies blood-forming stem cells from donated umbilical cord blood or bone marrow. The new cells may produce working GALC enzyme and help protect myelin.

Transplant tends to offer the greatest potential benefit when infantile Krabbe disease is identified before symptoms begin. In later-onset disease, it may be considered when symptoms are absent or still mild. It is less likely to help after extensive neurological damage has developed.

A transplant is not a cure. It may slow progression, but some difficulties can continue or emerge afterward. The procedure also carries serious risks, including infection, organ complications, and graft-versus-host disease, in which donated immune cells attack the recipient's tissues. A specialist transplant team weighs these risks against the likely benefits.

Supportive treatment is important at every stage. Depending on a person's needs, it may include:

Palliative care can be provided alongside other treatment. It is not limited to the final stage of illness.

Gene-based and other experimental treatments are being studied, but they are not established cures. Families considering research participation should receive a clear explanation of possible risks, uncertain benefits, and alternatives.

- Physical and occupational therapy for movement, positioning, and equipment
- Speech and communication support
- Feeding assessment and nutrition support

- Treatment for pain, stiffness, reflux, or seizures
- Respiratory care and help clearing mucus
- Vision and hearing services
- Palliative care to manage symptoms and support quality of life

Complications

Krabbe disease can affect many functions because myelin is important throughout the nervous system.

Possible complications include loss of movement, severe muscle stiffness, weakness, contractures, and difficulty maintaining a comfortable position. A contracture is permanent tightening around a joint that limits movement.

Swallowing problems can cause poor nutrition, dehydration, or food and liquid entering the lungs. This is called aspiration and can lead to chest infections. Weak breathing muscles and reduced ability to clear mucus may also increase respiratory problems.

Other complications can include seizures, loss of vision or hearing, communication difficulties, chronic pain, and reduced awareness of the surroundings. People who receive a stem cell transplant can also develop treatment-related complications and need long-term monitoring.

Not everyone develops every complication. The pattern is influenced by the age at onset, the specific gene changes, the amount of remaining enzyme activity, and whether treatment began before major nerve damage.

Prevention

Krabbe disease cannot be prevented through lifestyle changes because it is inherited.

If the condition or a GALC gene change is known in your family, genetic counselling can explain inheritance and testing options. Carrier testing may be available for adult relatives. Reproductive options can include prenatal testing or testing embryos created through in vitro fertilisation. These are personal choices, and counselling should be non-directive.

Newborn screening does not prevent Krabbe disease. Where it is available, it may identify some affected babies before symptoms begin, when stem cell transplant has the best chance of helping.

Living with it and what to expect

The course of Krabbe disease is closely linked to the age at which symptoms begin.

Infantile disease usually progresses rapidly. Development may stop and previously gained abilities can be lost over months. Feeding, movement, vision, swallowing, and breathing often require increasing support. The outlook is poor when severe symptoms begin in infancy, although the exact course cannot be predicted for one child.

Later-onset forms may develop over years rather than months. Some people remain independent for a period, while others gradually need mobility aids, communication support, help with daily activities, or full-time care. Symptoms and speed of progression can differ even between relatives with the same condition.

After a stem cell transplant, long-term follow-up remains necessary. Transplant may preserve some abilities or slow further decline, but it does not guarantee typical development or prevent every future symptom. Rehabilitation and educational support may still be needed.

Regular care may involve neurology, metabolic medicine, rehabilitation, nutrition, respiratory care, ophthalmology, audiology, and transplant specialists. Routine reviews monitor growth, comfort, movement, swallowing, breathing, seizures, vision, hearing, and equipment needs.

Krabbe disease also affects family life. Caregivers may need practical help, respite care, psychological support, and guidance with education or disability services. A care plan can help families communicate the person's needs across home, school, hospital, and emergency settings.

When to get medical help

Arrange a routine medical assessment if you notice persistent changes in development, movement, feeding, vision, hearing, or behaviour. This is particularly important if Krabbe disease is already present in the family.

Contact the specialist team promptly if a person with Krabbe disease develops new swallowing problems, more frequent choking, worsening stiffness, new weakness, possible seizures, reduced alertness, or a clear loss of abilities. These changes may require an earlier review rather than waiting for the next routine appointment.

Seek urgent medical help for:

If a baby has an abnormal newborn screening result for Krabbe disease, follow-up testing should be arranged without delay. This is time-sensitive, but a positive screen does not by itself confirm the condition.

- Breathing that is difficult, unusually slow, or interrupted
- Blue, grey, or very pale lips or skin
- A seizure lasting longer than advised in the person's emergency plan
- Repeated seizures without recovery between them
- Severe choking or suspected food or liquid inhalation
- Marked difficulty waking or a sudden major change in responsiveness

Common questions

Is Krabbe disease the same as multiple sclerosis?

No. Both conditions damage myelin, but their causes are different. Krabbe disease is an inherited enzyme condition. Multiple sclerosis is an immune-mediated condition and usually begins later in life.

Can adults get Krabbe disease?

Yes. Although symptoms most often begin in infancy, Krabbe disease can first appear in childhood, adolescence, or adulthood. Adult-onset disease often progresses more slowly than infantile disease.

Can someone carry the gene without having symptoms?

Yes. A person with one harmful GALC gene change is usually a healthy carrier. Krabbe disease generally develops when harmful changes are present in both copies of the gene.

Does a positive newborn screen mean my baby has Krabbe disease?

No. Newborn screening identifies babies who need further testing. GALC enzyme testing, genetic testing, psychosine measurement, and specialist assessment help determine whether the baby has the condition and how urgently treatment should be considered.

Does a stem cell transplant cure Krabbe disease?

No. A transplant may slow progression, especially before symptoms begin, but it cannot reliably repair established nerve damage. It also has significant risks and requires specialist assessment.

Is Krabbe disease painful?

It can cause discomfort or pain from muscle stiffness, nerve irritation, reflux, contractures, or positioning difficulties. Pain may be difficult to recognise in someone who cannot communicate verbally, so changes in sleep, expression, movement, or behaviour should be

assessed.

Sources

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