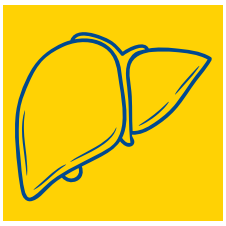


Crigler-Najjar syndrome

A guide for parents, families, carers and healthcare professionals

Children's Liver Disease Foundation
fighting childhood liver disease

What is Crigler-Najjar syndrome?

Crigler-Najjar syndrome (CNS) is a very rare genetic condition. It happens in around 1 in every million births. It affects males and females in equal numbers.

Crigler-Najjar syndrome causes long-term jaundice in newborn babies. It happens when the liver can't get rid of a substance called bilirubin. Bilirubin is made by the body when red blood cells break down. In Crigler-Najjar syndrome, bilirubin collects in the blood. This causes a range of symptoms and complications.

There are two types of Crigler-Najjar syndrome:

Type 1 and Type 2

Each one has a different level of severity.

It is very important to find out if a child has type 1 or type 2 CNS.

What causes Crigler-Najjar syndrome?

Crigler-Najjar syndrome is a genetic condition. This means it is caused by changes in a person's DNA. Genetic conditions are passed from one or both parents to their children.

Crigler Najjar syndrome is an autosomal recessive condition. This means that both parents are carriers of the change (mutation) and can pass it on to their child.

In healthy babies, the liver uses a protein called *UDPGT* to turn bilirubin into bile. The body does this by changing it from unconjugated bilirubin to conjugated bilirubin. Conjugated bilirubin helps the body digest fats and then passes out in the poo.

Unconjugated bilirubin has not been processed by the liver.
It is very toxic to the body.

Conjugated bilirubin has been processed by the liver.
It is not toxic to the body.

Babies with Crigler-Najjar syndrome are missing one or both of the genes that tell the body how to make the *UDPGT* protein. Without the protein, the liver can't process unconjugated bilirubin. It builds up in the body and this is known as hyperbilirubinemia. It causes a range of symptoms and complications. The main symptom is jaundice.

Jaundice is when the skin or the whites of the eyes turn yellow

How is Crigler-Najjar syndrome diagnosed?

Severe jaundice that appears in the first days of life may lead to suspicion of Crigler-Najjar syndrome. Tests used to help confirm the diagnosis may include:

- physical examination
- liver blood tests - this will include a split bilirubin test, which checks the amount of conjugated and unconjugated bilirubin in the body
- wee (urine) test
- genetic testing

A drug called phenobarbital can be used to help find out if a child has type 1 or type 2 Crigler-Najjar syndrome. This drug reduces bilirubin levels in type 2 but makes no difference in type 1.

It is very important to find out if a child has type 1 or type 2 CNS before reading further.

Type 1 Crigler-Najjar is a very serious condition.

You may wish to think carefully about the best time to read this information.

Remember: help and support is available from CLDF.

Our Families and Young People's Teams have a wealth of experience in talking to young people and families who are affected by childhood liver disease.

See details of our support services

Type 1 Crigler-Najjar syndrome

This is the severe form of Crigler-Najjar syndrome. In type 1, babies cannot make any of the *UDPGT* protein. Type 1 Crigler-Najjar syndrome has serious complications. It causes a very fast rise in bilirubin levels in the first week of life. One of the main symptoms is yellowing of the whites of the eyes and skin (jaundice). This gets worse over time and lasts beyond the first three weeks of life.

The rising bilirubin levels put babies at risk of developing a severe complication called kernicterus. This is when high levels of bilirubin build up in the brain and nerve tissues. It is a type of brain damage that is life-threatening, even with treatment.

Kernicterus is also known as bilirubin encephalopathy.

It is a serious complication caused by a build up of bilirubin in the brain.

There is no cure for Crigler-Najjar syndrome. Most children with type 1 CNS who do not receive treatment do not survive past childhood.

Early symptoms can include:

- poor feeding
- irritability
- muscles that become floppy, like a rag doll
- extreme tiredness (lethargy)
- a high-pitched cry
- no startle reflex
- being sick (vomiting)
- high temperature (fever)

As kernicterus progresses, further symptoms can include:

- hearing problems
- fits (seizures)
- muscle spasms that cause arching of the back and neck

If significant brain damage occurs before treatment, serious and permanent problems can include:

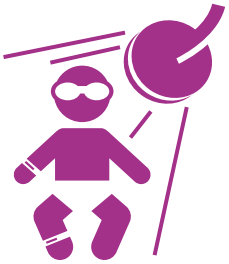
- hearing loss
- cerebral palsy
- learning disabilities

Early treatment is essential in Crigler-Najjar syndrome type 1. The aim is to control bilirubin levels and keep them as low as possible. Treatment will then be ongoing to try and stop high levels of bilirubin building up in the body. The aim is to prevent kernicterus and its complications.

Phototherapy

The main treatment for Crigler-Najjar syndrome type I is phototherapy. During this treatment, a child's bare skin is exposed to intense light. It is similar to a tanning bed. Special eyewear is used to protect the eyes. This treatment helps the body break down and remove bilirubin. But phototherapy is a long process and takes around 12 hours per day. This can significantly impact a child's quality of life. Over time, a child's skin will also thicken as a result of this treatment, so it becomes less effective.

During phototherapy, the levels of bilirubin in the body can still get too high. This is more likely to happen during periods of illness. If bilirubin levels in the body reach toxic levels, other treatments may include:



Intravenous (IV) fluid therapy

This is a way of getting more fluids into the body. A narrow, bendy tube (cannula) is put into a vein using a needle. Fluids and medicines are put into the cannula and go straight into the bloodstream.

Albumin administration

Albumin is a type of protein found in blood plasma (the clear liquid part of the blood). Albumin can be used as a treatment by injecting it into a vein.

Plasmapheresis

This treatment involves separating the liquid part of the blood (plasma) from the blood cells. The plasma is replaced with another liquid (saline or albumin). Or it is treated and returned to the body.

Drug treatments and new therapies

Drug treatments may be used to manage symptoms and complications. Other treatments are also being tested by researchers. This includes hepatocyte transplantation and gene therapies.

Liver Transplant

The only definitive treatment for Crigler-Najjar syndrome type I is a liver transplant. The medical team will carefully consider the best time for a transplant to take place. They will need to weigh up the importance of preventing serious complications with the risks of surgery and immunosuppression.
A transplant is an operation to remove a liver that does not work. It is replaced with a whole or part liver from another person (donor). This could be a deceased or live donor. The new liver provides cells and proteins that can break down bilirubin. If the operation is successful, it can significantly improve a child's quality of life. But it is important to remember that a liver transplant is a major operation.

Type 2 Crigler-Najjar syndrome

Type 2 is a less severe form of Crigler-Najjar syndrome. In type 2, the body produces a small amount of the UDPCT protein. Symptoms are generally milder and children are less likely to develop brain damage (kernicterus). They also respond to some medications, provided they are started early. There is no cure for CNS type 2, but most children are well controlled on medication. Even with some jaundice, they are likely to survive into adulthood. Many will live a relatively normal life.

Symptoms in type 2 Crigler-Najjar syndrome are milder than in type 1. Children may develop yellowing of the whites of the eyes and skin (jaundice). In some children, this may only be triggered at certain times, such as:

- when they are sick
- when they have not eaten for a long period of time
- when they have a general anaesthesia

The main treatment for Crigler-Najjar syndrome type 2 is phenobarbital. This drug helps reduce bilirubin levels in the blood. Bilirubin levels can still rise if a child has another illness, hasn't eaten for some time, or if they experience emotional stress. In such cases, phototherapy and other treatments may be needed.

The only definitive treatment for uncontrollable CNS type 2 is a liver transplant. It will only be considered if the treatments above no longer control the condition. A transplant is an operation to remove a liver that does not work. It is replaced with a whole or part liver from another person (donor). This could be a deceased or live donor. The new liver provides cells and proteins that can break down bilirubin. If the operation is successful, it can significantly improve a child's quality of life. But it is important to remember that a liver transplant is a major operation. It will only be done after the benefits and risks have been carefully weighed up.

Where can I get further help or support?

CLDF can provide you with support and advice whenever you need it.
Contact us on 0121 212 6023 or via email at: families@childliverdisease.org.

This resource was reviewed in December 2024
It is due to be reviewed by December 2027

Trusted Information Creator
Patient Information Forum

View CLDF resources online

Contact us for help and support

Email: info@childliverdisease.org
Website: www.childliverdisease.org