CONDITION

Crigler-najjar syndrome

Crigler-Najjar syndrome is an inherited condition that causes bilirubin to build up in the blood.

WHAT IT IS
Inherited failure to process bilirubin

BODY SYSTEM
Liver and nervous system

MAIN SYMPTOMS
Jaundice, yellow eyes, poor feeding, neurologic changes

WHAT CAUSES IT
Inherited UGT1A1 gene changes

HOW IT IS DIAGNOSED
Bilirubin blood tests and UGT1A1 genetic testing

MAIN TREATMENT
Light therapy, bilirubin-lowering medicine, and liver transplantation

CAN IT BE CURED?
Sometimes - liver transplantation restores bilirubin processing

IS IT AN EMERGENCY?
Sometimes - confusion, stiffness, or unusual sleepiness

LONG-TERM OUTLOOK
Good with control; type 1 has greater neurologic risk

Overview

Crigler-Najjar syndrome is a rare inherited condition that affects how the liver processes bilirubin. Bilirubin is a yellow substance made when the body breaks down old red blood cells.

Normally, the liver changes bilirubin into a form that can leave the body in bile and stool. In Crigler-Najjar syndrome, an enzyme needed for this process is missing or does not work well. This causes unconjugated bilirubin, the unprocessed form, to build up in the blood.

The main visible result is jaundice, meaning yellow skin and yellow whites of the eyes. Very high bilirubin levels can enter the brain and damage the nervous system. This is called bilirubin encephalopathy. Long-term brain damage from bilirubin is often called kernicterus.

There are two main forms:

These types are part of a spectrum rather than completely separate conditions. Genetic test results, bilirubin levels, treatment response, and clinical history help specialists understand where someone falls on that spectrum.

- Type 1 causes little or no enzyme activity. It usually appears soon after birth and needs intensive treatment.
- Type 2 leaves some enzyme activity. Bilirubin levels are usually lower, and the condition often responds to medicine.

Symptoms

Jaundice is the main symptom. It often begins during the newborn period in type 1. In type 2, it may be milder or may not be recognised until later in childhood or adulthood.

Symptoms can include:

Unconjugated bilirubin does not usually pass into urine. Dark urine, pale stools, itching, or abdominal swelling are therefore not typical features and may point to another liver or bile-flow problem.

Signs that bilirubin may be affecting the brain can include unusual sleepiness, poor feeding, a high-pitched cry, reduced alertness, stiff or floppy muscles, arching of the neck or back, unsteady movement, slurred speech, or confusion. These need urgent assessment.

Someone with type 2 may feel well apart from jaundice. However, bilirubin can rise during infections, prolonged fasting, surgery, pregnancy, or other physical stress.

- Yellow skin or whites of the eyes
- Jaundice that becomes more noticeable during illness, dehydration, or fasting
- Poor feeding or unusual sleepiness in an affected baby
- Neurologic symptoms when bilirubin reaches the brain

Causes and risk factors

Crigler-Najjar syndrome is caused by changes in the UGT1A1 gene. This gene provides instructions for making an enzyme called bilirubin UDP-glucuronosyltransferase. The enzyme allows the liver to process bilirubin so the body can remove it.

The condition is inherited in an autosomal recessive pattern. This means a person usually inherits one altered copy of the gene from each parent. The parents are often healthy carriers.

When both parents carry a disease-causing UGT1A1 change, each pregnancy has:

These chances apply separately to each pregnancy. They do not change based on what happened in earlier pregnancies.

Having an affected sibling or known UGT1A1 changes in the family increases the chance of the condition. It is not caused by food, parenting, infection, or anything someone did during pregnancy.

- 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

Blood tests measure total bilirubin and its conjugated and unconjugated forms. Crigler-Najjar syndrome causes a persistent rise in unconjugated bilirubin.

Other tests help rule out more common causes of jaundice. These may include a blood count and tests for increased red blood cell breakdown, known as haemolysis. Routine liver tests are often otherwise normal because the liver itself is not inflamed or scarred by the condition.

A UGT1A1 genetic test can confirm the diagnosis by identifying disease-causing changes in the gene. Testing may also help distinguish severe type 1 from forms with some remaining enzyme activity.

Doctors also consider Gilbert syndrome, a common and much milder inherited cause of raised unconjugated bilirubin. Very high or persistent bilirubin levels, especially from infancy, are not typical of Gilbert syndrome.

Response to phenobarbital has historically helped separate the two types. Bilirubin usually falls with this medicine in type 2 because some working enzyme remains. Type 1 generally does not respond. Genetic testing is now an important part of classification.

Treatment and management

Treatment aims to keep unconjugated bilirubin below levels that could affect the brain. The plan is based on age, bilirubin level, remaining enzyme activity, and previous symptoms.

Phototherapy uses a particular wavelength of blue light. The light changes bilirubin in the skin into forms that the body can remove without the missing liver process. This is different from

ordinary household or tanning lights.

People with type 1 may need many hours of phototherapy every day, often beginning shortly after birth. Treatment can become less effective as a child grows because body size increases and the skin becomes thicker. Equipment, eye protection, skin care, hydration, and bilirubin monitoring are managed with a specialist team.

Phenobarbital can increase the activity of the remaining UGT1A1 enzyme in type 2. It is generally ineffective in type 1. Because it can cause sleepiness and interact with other medicines, it requires medical supervision and regular review.

Illness, dehydration, or an inability to eat can make bilirubin rise. An established sick-day plan may include earlier blood testing, maintaining fluids and nutrition when possible, and contacting the specialist team promptly.

If bilirubin reaches a dangerous level, hospital treatment may be needed. Plasma exchange or exchange transfusion can lower bilirubin quickly, but these are temporary measures used in specific situations.

A liver transplant provides liver cells with working UGT1A1 enzyme and can cure the bilirubin-processing problem. It is the definitive treatment for type 1, although the timing is individual. Transplantation is major surgery and requires lifelong medicines to prevent rejection, so its benefits and risks need careful discussion.

Gene-based treatments are being studied, but their availability and role continue to develop.

Complications

The most serious complication is bilirubin encephalopathy. Unconjugated bilirubin can cross into the brain, where it is toxic to nerve cells.

Permanent injury, called kernicterus, can cause movement disorders, hearing loss, problems with eye movement, dental enamel changes, and developmental disability. The risk is highest in type 1, particularly when treatment is interrupted or bilirubin rises during illness.

Type 2 carries a lower risk, but neurologic injury can still occur. Severe infection, prolonged fasting, dehydration, surgery, or certain medicines may increase bilirubin or make it easier for bilirubin to enter the brain.

Long daily phototherapy can also affect sleep, school, work, travel, and family life. Liver transplantation brings separate risks, including rejection, infection, and side effects from anti-rejection medicines. Transplant teams monitor for these complications over the long term.

Prevention

Crigler-Najjar syndrome cannot be prevented because it is inherited.

Genetic counselling can help people understand how the condition may be passed on. If the specific family gene changes are known, carrier testing and reproductive testing options may be available.

Complications can often be reduced through regular bilirubin monitoring, consistent treatment, and early planning for illness or surgery. Avoiding prolonged fasting and dehydration may help prevent sudden bilirubin rises. Medicines and supplements should be reviewed because some can affect bilirubin handling or interact with treatment.

Living with it and what to expect

The course differs greatly between type 1 and type 2.

Type 1 usually requires intensive daily management from infancy. Phototherapy can control bilirubin, but treatment may take many hours and often becomes harder to maintain as the body grows. Many people are assessed for liver transplantation before bilirubin becomes difficult to control or neurologic injury occurs.

Type 2 is usually less intensive. Jaundice may remain visible or become stronger during illness, fasting, or stress. Many people can attend school, work, exercise, and have families, although they still need follow-up and a plan for situations that may raise bilirubin.

Routine care may include bilirubin blood tests, medicine reviews, hearing or neurologic assessment when indicated, and discussion of treatment effectiveness. Follow-up is usually coordinated by a liver or metabolic specialist.

Pregnancy, surgery, and serious illness require advance planning because bilirubin levels can change. The relevant teams need to know about the condition before procedures or new medicines are started.

Emotional and practical effects matter as well. Visible jaundice may attract unwanted comments, while daily phototherapy can affect sleep and independence. Support from family, specialist nurses, rare-condition organisations, and others living with the condition may help with these challenges.

When to get medical help

Arrange routine medical advice if jaundice becomes more noticeable, treatment is becoming difficult to maintain, or side effects are interfering with daily life. Contact the specialist team before planned surgery, pregnancy, prolonged fasting, or starting a new medicine or supplement.

Seek prompt medical advice during an illness if the affected person cannot drink, is vomiting repeatedly, has signs of dehydration, or cannot continue usual treatment.

Get emergency medical help for:

These symptoms do not prove that bilirubin is affecting the brain, but they need immediate assessment. Bring information about the diagnosis and usual treatment if it is readily available, without delaying emergency care.

- New confusion or reduced alertness
- Unusual or extreme sleepiness
- Poor feeding in a baby
- A high-pitched cry
- New stiffness, floppiness, or arching
- Slurred speech or unsteady movement
- Seizures or loss of consciousness

Common questions

Is Crigler-Najjar syndrome the same as Gilbert syndrome?

No. Both involve the UGT1A1 gene and raise unconjugated bilirubin, but Gilbert syndrome is much milder and usually does not need treatment. Crigler-Najjar syndrome can produce far higher bilirubin levels and may threaten the nervous system.

Can Crigler-Najjar syndrome appear in adults?

The genetic condition is present from birth. Type 1 almost always becomes clear during infancy. Type 2 may be diagnosed later if jaundice is mild or was previously mistaken for another condition.

Does the jaundice ever go away?

Bilirubin levels can rise and fall, so jaundice may become more or less visible. The underlying enzyme problem remains unless a successful liver transplant restores bilirubin processing.

Why does blue-light treatment help?

Blue-light phototherapy changes bilirubin in the skin into forms that can leave the body without first being processed by the missing liver enzyme. The effect is temporary, so regular treatment may be needed.

Is Crigler-Najjar syndrome contagious?

No. It is caused by inherited gene changes and cannot spread between people.

Can someone with Crigler-Najjar syndrome have children?

Yes. The condition does not automatically prevent someone from having children. Genetic counselling can explain inheritance, testing options, and the chance of passing a UGT1A1 change to a child. Pregnancy should be planned with specialist care because bilirubin may need closer monitoring.

Sources

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