CONDITION

Homocystinuria

Homocystinuria is an inherited condition that causes homocysteine to build up and can affect the eyes, bones, brain, and blood vessels.

WHAT IT IS
Inherited condition causing abnormal homocysteine buildup

BODY SYSTEM
Eyes, bones, brain, and blood circulation

MAIN SYMPTOMS
Lens problems, learning difficulties, fragile bones, blood clots

WHAT CAUSES IT
Inherited changes affecting amino acid processing

HOW IT IS DIAGNOSED
Blood amino acid tests, genetic testing, sometimes enzyme testing

MAIN TREATMENT
Dietary therapy, vitamins, betaine, and specialist monitoring

CAN IT BE CURED?
No - inherited enzyme changes remain lifelong

IS IT AN EMERGENCY?
Sometimes - clot, stroke, or breathing symptoms

LONG-TERM OUTLOOK
Early lifelong treatment greatly reduces complications

Overview

Homocystinuria is a group of rare inherited conditions in which the body cannot process an amino acid called homocysteine normally. Amino acids are chemicals used to make proteins and carry out other important tasks.

The most common form is called classic homocystinuria . It is caused by reduced activity of an enzyme called cystathionine beta-synthase, or CBS. Enzymes are proteins that help chemical reactions happen in the body.

When CBS does not work properly, homocysteine and related chemicals build up. This can affect the eyes, skeleton, learning and development, and blood vessels. High homocysteine can increase the risk of a blood clot in a vein or artery.

Other forms of homocystinuria affect how homocysteine is changed back into another amino acid called methionine. These are known as remethylation conditions . Their symptoms, blood test patterns, and treatments can differ from classic homocystinuria.

Some babies are identified through newborn screening. Others are diagnosed later after symptoms develop or because another family member has the condition. Early treatment matters because it can lower homocysteine and reduce the risk of complications.

Symptoms

Symptoms differ widely. Some people develop signs in infancy or childhood, while others have few noticeable problems until adolescence or adulthood. A blood clot may occasionally be the first sign.

Possible features of classic homocystinuria include:

A displaced lens is called ectopia lentis . It can cause blurred vision, glare, or rapidly changing glasses prescriptions. Eye complications such as glaucoma or retinal detachment can also occur.

Some skeletal features may resemble Marfan syndrome, another inherited condition. However, homocystinuria and Marfan syndrome have different causes and risks.

Remethylation forms may cause poor feeding, slow growth, low muscle tone, developmental delay, seizures, unusual tiredness, or problems with movement and balance. Certain forms can also affect the spinal cord, nerves, blood cells, or kidneys.

Not everyone has every symptom. The severity is influenced by the specific genetic change, how much enzyme activity remains, whether vitamin B6 helps, and how early treatment begins.

- The lens inside the eye moving out of its normal position
- Severe short-sightedness or other vision problems
- Long arms, legs, fingers, or toes
- Curvature of the spine or changes in the breastbone
- Low bone density and an increased risk of fractures
- Delayed development or learning difficulties
- Behavioural, emotional, or mental health symptoms
- Blood clots in the legs, lungs, brain, or other organs

Causes and risk factors

Homocystinuria is caused by a change in a gene involved in processing homocysteine. Classic homocystinuria usually involves the CBS gene. Remethylation forms can involve several other genes or problems with vitamin B12 processing.

These conditions are usually inherited in an autosomal recessive pattern. This means a child must inherit one altered copy of the relevant gene from each biological parent.

Parents who each carry one altered copy usually do not have the condition. For each pregnancy between two carriers, there is a chance that the child will inherit both altered copies. Genetic counselling can explain these chances for a particular family without assuming that every family has the same genetic result.

Homocystinuria is not caused by something a person ate, did, or was exposed to. Diet can affect homocysteine levels after the condition develops, but it does not cause the inherited enzyme problem.

Diagnosis

Newborn screening may detect classic homocystinuria by measuring methionine in a dried blood spot. However, screening methods differ by location, and screening may miss some affected babies. A normal newborn screening result does not completely exclude the condition if symptoms or family history later raise concern.

Diagnosis usually begins with blood tests that measure:

Classic homocystinuria usually causes very high total homocysteine together with raised methionine. Remethylation conditions often cause high homocysteine with low or normal methionine. These patterns guide further testing but are not enough on their own to identify every form.

Genetic testing can confirm the responsible gene changes. In some situations, enzyme testing in cells or additional metabolic tests may be needed.

Once the condition is identified, assessment may include an eye examination, checks of growth and bone health, developmental or learning assessments, and evaluation for previous blood clots. Close relatives may be offered testing because diagnosis before symptoms begin can allow earlier treatment.

- Total homocysteine
- Methionine and other amino acids

- Vitamin B12 and folate when relevant
- Other markers that help distinguish between different forms

Treatment and management

Treatment aims to keep total homocysteine as close as possible to the target set by the specialist metabolic team. Management is lifelong and is tailored to the specific type of homocystinuria.

Some people with classic homocystinuria respond to pyridoxine , a form of vitamin B6 that helps the CBS enzyme work. A supervised response test is usually used to find out whether it lowers homocysteine enough. High-dose vitamin B6 can damage nerves, so it should not be started or changed without specialist guidance.

People who do not respond fully to vitamin B6 may need a diet that limits methionine. Because methionine is present in protein, this usually involves carefully controlled amounts of ordinary high-protein foods and a special amino acid formula. The goal is not simply to avoid all protein. Children and adults still need enough nutrients for growth, muscles, bones, and general health.

A metabolic dietitian can help plan meals, monitor nutrition, and adjust treatment during growth, illness, pregnancy, or changes in activity.

Betaine may be used to help the body convert homocysteine back into methionine. Folate or vitamin B12 may also be used when appropriate. Remethylation forms often require specific vitamin treatments, including special forms of vitamin B12, so their management is not the same as treatment for CBS deficiency.

Regular monitoring may include blood amino acid levels, nutritional tests, growth, bone health, eye examinations, and review of development or mental health. Treatment plans may need adjustment if homocysteine remains above target.

People facing surgery, prolonged immobility, dehydration, or pregnancy need advance planning because these situations may increase clot risk. The metabolic and surgical or maternity teams can coordinate precautions.

Complications

The most serious complication is a blood clot. A clot can form in a deep vein, travel to the lungs, or block blood flow to the brain, heart, or another organ. This risk can occur at a young age, especially when homocysteine remains high.

Other possible complications include:

Some complications cannot be fully reversed once they have occurred. Lowering homocysteine and maintaining treatment can reduce the chance of new problems, even when diagnosis happens later.

- Permanent vision loss from severe eye problems
- Osteoporosis, meaning weak or less dense bones
- Repeated fractures or spinal curvature
- Developmental, educational, or movement difficulties
- Seizures
- Mental health or behavioural symptoms
- Nutritional deficiencies if a restricted diet is poorly balanced

Prevention

The inherited genetic changes that cause homocystinuria cannot currently be prevented through diet, exercise, or actions during pregnancy.

Newborn screening and family testing can identify some people before symptoms appear. Early, consistent treatment can prevent or reduce many complications, particularly blood clots, eye damage, and developmental problems.

People who have homocystinuria or carry a related gene change may choose genetic counselling when planning a pregnancy. Counselling provides information about inheritance, testing options, and reproductive choices without directing a family toward one decision.

Living with it and what to expect

Homocystinuria remains present throughout life, but its effects can change over time. Treatment is usually most intensive during childhood growth, illness, pregnancy, and other periods when nutritional or metabolic needs change.

People diagnosed through newborn screening and treated early may develop normally and avoid many major complications. Others may continue to have learning, vision, bone, or movement difficulties, especially if these began before treatment. Starting treatment later can still lower clot risk and help prevent further harm.

Daily life may involve special foods or formula, medicines or vitamins, blood tests, and regular

appointments. Children may need support at school for vision or learning needs. Adults may need practical planning for work, travel, prescriptions, and access to suitable food.

Following a restricted diet can become harder during adolescence or when living independently. A metabolic dietitian can help make the plan more practical rather than relying on unnecessary food avoidance.

Routine follow-up remains important even when you feel well. High homocysteine does not usually cause a sensation, and complications can develop without obvious warning. With ongoing treatment and monitoring, many people study, work, have relationships, and take part in everyday activities.

When to get medical help

Arrange routine medical advice if you develop new blurred vision, rapidly changing eyesight, bone pain, repeated fractures, worsening balance, seizures, or changes in learning, behaviour, or mood. These symptoms need assessment but are not always emergencies.

Contact your metabolic team promptly if you cannot take your usual treatment, have repeated vomiting or diarrhoea, become dehydrated, or expect to have surgery. Planning is also important before pregnancy and during long journeys or periods of reduced movement.

Seek emergency help for possible signs of a blood clot or stroke, including:

These symptoms can have several causes, but they require urgent assessment.

- Sudden weakness, numbness, facial drooping, or difficulty speaking
- Sudden loss of vision or a severe new neurological symptom
- New chest pain, coughing up blood, or unexplained shortness of breath
- Painful swelling, warmth, or redness in one leg
- Collapse, severe confusion, or a seizure lasting longer than usual

Common questions

Is homocystinuria the same as having high homocysteine?

No. Homocystinuria is an inherited metabolic condition that can cause very high homocysteine. Mild or moderate increases can also occur for other reasons, including vitamin deficiencies, kidney problems, certain medicines, or other health conditions.

Can homocystinuria be cured?

There is no routine cure that removes the inherited cause. Treatment can lower homocysteine and greatly reduce the risk of complications, but it generally needs to continue for life.

Can I eat normal protein?

Some people can, particularly when their condition responds well to vitamin B6. Others need a carefully controlled low-methionine diet and special amino acid formula. Protein should not be restricted without a metabolic dietitian because inadequate intake can harm growth and nutrition.

Why do I need treatment if I feel well?

High homocysteine often causes no day-to-day symptoms before a complication occurs. Treatment reduces the buildup and helps protect blood vessels, eyes, bones, and the nervous system.

Can people with homocystinuria have children?

Many can. Pregnancy may increase the risk of blood clots and can change nutritional needs, so care should be planned with metabolic and maternity specialists. Genetic counselling can explain the chance of passing on a gene change.

Is homocystinuria related to Marfan syndrome?

They are separate inherited conditions. Both can cause long limbs and eye lens problems, but their genetic causes, blood test findings, and medical risks are different.

Sources

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