CONDITION

von gierke disease

An inherited condition that prevents the body from releasing enough glucose from glycogen between meals

WHAT IT IS
Inherited disorder affecting glucose release from stored glycogen

BODY SYSTEM
Liver, kidneys, blood, and immune system

MAIN SYMPTOMS
Low blood sugar, enlarged liver, poor growth, tiredness

WHAT CAUSES IT
Inherited changes in G6PC1 or SLC37A4 genes

HOW IT IS DIAGNOSED
Blood tests and confirmatory genetic testing

MAIN TREATMENT
Planned carbohydrate intake, cornstarch, and specialist monitoring

CAN IT BE CURED?
No - genetic changes remain lifelong

IS IT AN EMERGENCY?
Sometimes - severe low blood sugar or inability to eat

LONG-TERM OUTLOOK
Often active lives with lifelong treatment and surveillance

Overview

Von Gierke disease is an inherited condition more formally called glycogen storage disease type I, or GSD I. It affects how the body maintains blood glucose, commonly called blood sugar, between meals.

The body stores extra glucose as glycogen, mainly in the liver. It normally breaks glycogen down and releases glucose when you have not eaten for a while. In GSD I, the final step of this process does not work properly. Glucose becomes trapped inside liver cells instead of entering the blood.

As a result, blood glucose can fall after relatively short periods without food. Glycogen and fat can build up in the liver, causing it to enlarge. Other substances, including lactate, uric acid, and fats called triglycerides, may also rise in the blood.

There are two main forms:

The condition requires lifelong attention to meal timing, nutrition, and medical monitoring. With modern treatment, many people attend school, work, exercise, and take part in family and social life.

- GSD Ia results from changes in the G6PC1 gene
- GSD Ib results from changes in the SLC37A4 gene and can also cause low numbers or poor function of infection-fighting white blood cells

Symptoms

Symptoms often begin in infancy, especially when the time between feeds becomes longer. Their timing and severity are not the same for everyone.

Low blood glucose may cause sweating, shakiness, unusual hunger, paleness, irritability, tiredness, or difficulty concentrating. Babies may be unsettled or difficult to wake. Severe hypoglycaemia can cause confusion, seizures, or loss of consciousness.

An enlarged liver can make the abdomen look rounded or swollen. The kidneys may also enlarge. The spleen is not usually enlarged unless another problem is present.

Other possible features include:

People with GSD Ib may have neutropenia , meaning too few neutrophils, a type of white blood cell that fights bacterial and fungal infections. They may develop repeated infections, mouth ulcers, gum disease, genital or anal sores, or inflammatory bowel disease. Bowel inflammation can cause abdominal pain, diarrhoea, or blood in the stool.

Some people develop complications without obvious early symptoms. Regular monitoring remains important even when day-to-day health feels stable.

- Slow growth or delayed puberty
- Reduced muscle development in the arms and legs
- Frequent nosebleeds or easy bruising
- High blood fats, sometimes causing fatty skin deposits called xanthomas
- Gout-like joint pain from high uric acid
- Reduced exercise tolerance

Causes and risk factors

Von Gierke disease is caused by an inherited gene change. It is not caused by diet, parenting, infection, or anything that happened during pregnancy.

GSD Ia affects an enzyme called glucose-6-phosphatase. GSD Ib affects a transport protein that helps move glucose-6-phosphate inside cells. Both problems prevent the liver from completing the process that releases glucose into the bloodstream.

The condition follows an autosomal recessive inheritance pattern. This means a person usually has a changed copy of the relevant gene from each parent. Parents who each carry one changed copy generally do not have the condition themselves.

When both parents are carriers, each pregnancy has:

These chances start again with every pregnancy. A genetic counsellor can explain what a confirmed diagnosis may mean for siblings and future children.

- A 1 in 4 chance of a child having the condition
- A 1 in 2 chance of a child being an unaffected carrier
- A 1 in 4 chance of a child inheriting neither changed copy

Diagnosis

Doctors may suspect GSD I when a baby or child has low blood glucose after fasting, an enlarged liver, poor growth, or characteristic blood-test results.

Blood tests may show low glucose together with high lactate, triglycerides, cholesterol, or uric acid. Tests may also examine liver and kidney function, blood acidity, and blood-cell counts. In GSD Ib, neutrophil counts may be low or may change over time.

Genetic testing can confirm the diagnosis by finding disease-causing changes in G6PC1 or SLC37A4 . It can also distinguish GSD Ia from GSD Ib, which affects long-term management.

A liver biopsy is not usually needed when genetic testing gives a clear answer. In unusual cases, specialist testing of enzyme activity may be considered.

Once a diagnosis is confirmed, close relatives may be offered targeted genetic testing. If the family's gene changes are known, genetic counselling can also cover testing options before or during a future pregnancy.

Treatment and management

The main goal is to keep blood glucose in a safe range and limit the build-up of lactate, uric

acid, and blood fats. Care is usually coordinated by a specialist metabolic team and a dietitian familiar with glycogen storage conditions.

Treatment commonly involves carefully timed meals and snacks containing complex carbohydrates. Uncooked cornstarch is often used because it releases glucose slowly. Some babies and children need overnight feeding through a tube or another planned source of carbohydrate.

The exact schedule changes with age, growth, activity, illness, and how long a person can safely go without food. It should be planned by the metabolic team rather than adjusted without guidance.

Fructose and galactose enter pathways that cannot be completed normally in GSD I. Foods containing fructose, sucrose, galactose, or lactose may therefore need to be limited. Because these sugars occur in many nutritious foods, restrictions should be supervised to prevent vitamin, mineral, protein, or calorie shortages.

Blood glucose may be checked at home, especially around sleep, exercise, illness, or treatment changes. Some people use continuous glucose monitoring, although results still need to be interpreted alongside symptoms and confirmatory checks.

Additional treatment may be used for high uric acid, abnormal blood fats, kidney problems, or high blood pressure. People with GSD Ib may need treatment for neutropenia, infections, mouth disease, or bowel inflammation. Specialist centres may use medicines that improve neutrophil numbers and function, but these require careful monitoring.

Liver transplantation may be considered for selected people with severe metabolic problems, difficult-to-manage liver tumours, or other major complications. It is not routine treatment and does not remove the inherited gene change from the rest of the body. Gene-based treatments remain under study.

Complications

Repeated or severe low blood glucose can cause seizures and may injure the brain. Consistent prevention and prompt treatment are therefore central to care.

Over years, possible complications include kidney disease, high blood pressure, gout, reduced bone strength, anaemia, and pancreatitis linked to very high triglycerides. Rarely, high pressure can develop in the blood vessels of the lungs.

Noncancerous liver growths called hepatic adenomas may appear, often during adolescence or adulthood. Many remain stable, but they can bleed, grow, or occasionally develop cancerous changes. Regular liver imaging helps find changes before they cause symptoms.

GSD Ib can cause repeated infections and ongoing bowel inflammation. Chronic diarrhoea or poor absorption may affect nutrition and growth.

Not everyone develops these problems. Risk is influenced by the type of GSD I, metabolic control, age, and individual health history.

Prevention

Von Gierke disease cannot be prevented through food, exercise, vaccination, or lifestyle because it is inherited.

Complications can often be reduced through reliable carbohydrate intake, avoidance of unplanned fasting, prompt illness management, and regular specialist follow-up.

When the family's gene changes are known, genetic counselling can explain carrier testing, testing during pregnancy, and embryo testing with in vitro fertilisation. These are personal choices rather than required steps.

Living with it and what to expect

Management is usually most intensive in infancy and childhood, when frequent feeds and growth changes make glucose needs less predictable. Plans need to be reviewed as a child grows, starts school, becomes more active, or enters puberty.

Over months and years, follow-up usually includes checks of glucose control, lactate, uric acid, blood fats, kidney function, blood pressure, growth, and nutrition. Urine tests can look for early kidney changes. Liver ultrasound or other imaging is used to monitor liver size and adenomas. People with GSD Ib also need blood counts and assessment for infections or bowel inflammation.

Illness, vomiting, travel, exercise, and disrupted sleep can interfere with normal meal timing. A written emergency plan should explain when extra carbohydrate is needed and when hospital treatment with intravenous glucose may be required. Schools, workplaces, and regular caregivers should know where this plan and emergency supplies are kept.

Teenagers gradually take on more of their own treatment. This transition may involve learning to prepare cornstarch, read food labels, monitor glucose, order supplies, and explain the condition to others. Moving from paediatric to adult metabolic care should be planned rather than abrupt.

Adults may need advice about alcohol, shift work, fasting for procedures, contraception, and

pregnancy. Pregnancy is possible, but glucose needs can change substantially. Specialist metabolic and obstetric care is important before and throughout pregnancy.

Most people need treatment and surveillance for life. Good metabolic control can support growth and reduce complications, but it does not remove every long-term risk.

When to get medical help

Follow the personal emergency plan whenever food or cornstarch cannot be kept down. Vomiting or diarrhoea can become urgent quickly because the body cannot rely on stored glycogen in the usual way.

Seek emergency help for:

Do not give food or drink to someone who is unconscious or unable to swallow safely. Standard glucagon rescue may not work normally in GSD I because the liver cannot complete glucose release. Use the person's specialist emergency instructions and tell emergency staff that intravenous glucose may be needed.

Contact the metabolic team promptly for repeated low readings, a change in usual fasting tolerance, persistent vomiting, or problems with feeding equipment.

People with GSD Ib should seek prompt advice for fever, spreading skin redness, worsening mouth sores, severe abdominal pain, or bloody diarrhoea because neutropenia can make infections more significant.

Routine appointments are the right place to discuss growth, puberty, diet, exercise, medication effects, or gradual changes in liver or kidney tests.

- A seizure, loss of consciousness, or severe confusion
- Low blood glucose that does not improve as directed
- Inability to take or keep down the planned carbohydrate
- Extreme drowsiness, unusual behaviour, or difficulty waking
- Rapid or deep breathing with worsening illness

Common questions

Is von Gierke disease the same as glycogen storage disease type I?

Yes. Von Gierke disease is the older name for glycogen storage disease type I. GSD Ia and GSD Ib affect related parts of the pathway used to release glucose from the liver.

Can someone with GSD I ever fast?

Safe fasting time is usually shorter than for someone without the condition. How long is safe changes with age, treatment, illness, and individual glucose response. Planned fasting for blood tests, surgery, or religious practice requires advance instructions from the metabolic team.

Why is uncooked cornstarch used?

Uncooked cornstarch is digested slowly, so it can provide a steadier source of glucose between meals or overnight. Cooking changes how it is digested. The amount, timing, and preparation need to be individually planned.

Can people with von Gierke disease exercise?

Many people can be active, but exercise uses glucose and may increase the risk of hypoglycaemia. Activity plans may include glucose checks and planned carbohydrate before, during, or after exercise. Sudden changes in activity should be discussed with the metabolic team.

Does a liver transplant cure GSD I?

A transplant can correct the liver's inability to release glucose and may treat serious liver complications. It does not change the genes in other organs, requires lifelong transplant care, and is reserved for selected situations.

Will my other children have it?

If both biological parents carry a disease-causing change in the same GSD I gene, each pregnancy has a 1 in 4 chance of being affected. Genetic testing and counselling can clarify the pattern in a particular family.

Sources

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