CONDITION

Rabson-mendenhall syndrome

Rabson-mendenhall syndrome is an inherited condition in which the body responds very poorly to insulin.

WHAT IT IS
Rare condition causing extreme insulin resistance

BODY SYSTEM
Hormones, growth, skin, and metabolism

MAIN SYMPTOMS
Poor growth, dark thick skin, excess hair, high blood sugar

WHAT CAUSES IT
Inherited changes affecting the insulin receptor

HOW IT IS DIAGNOSED
Blood tests and genetic testing

MAIN TREATMENT
Specialist diabetes care and growth support

CAN IT BE CURED?
No - the genetic change remains

IS IT AN EMERGENCY?
Sometimes - diabetic ketoacidosis needs emergency treatment

LONG-TERM OUTLOOK
Lifelong, with serious complications and often shortened lifespan

Overview

Rabson-mendenhall syndrome is a very rare inherited condition that causes severe insulin resistance. Insulin is a hormone made by the pancreas. It helps glucose, a type of sugar, move from the blood into cells for energy.

In this condition, insulin cannot signal normally because the insulin receptor does not work properly. A receptor is a protein on the surface of a cell that receives a chemical message. The pancreas may produce extremely large amounts of insulin to compensate, but this often becomes insufficient to control blood glucose.

The condition can affect growth, appearance, skin, teeth, genital development, and the way the body stores fat. Diabetes may develop during childhood or adolescence and can be difficult to manage.

Rabson-mendenhall syndrome is part of a group called insulin receptor-related severe insulin resistance syndromes. It is usually more severe than type A insulin resistance syndrome but less severe than Donohue syndrome. The boundaries between these conditions are not always clear.

Because it is so rare and complex, care is usually coordinated by a specialist children's or adult hormone team. The medical term for this specialty is endocrinology.

Symptoms

Features may be noticeable before birth, during infancy, or later in childhood. They differ between people, even within the same family.

Poor growth is common. A baby may be smaller than expected before birth, and a child may gain weight or height slowly. There may be relatively little fat beneath the skin, which can make muscles appear prominent.

The body may produce very high insulin levels before blood glucose becomes consistently high. Over time, the pancreas may no longer be able to compensate, leading to diabetes.

Common features include:

Acanthosis nigricans often appears around the neck, armpits, groin, or other skin folds. It is related to very high insulin levels and is not caused by poor washing.

Symptoms of high blood glucose can include thirst, frequent urination, tiredness, blurred vision, and unplanned weight loss. However, a person can have worsening glucose control before these symptoms become obvious.

Some people have enlargement of the pineal gland, a small gland in the brain involved in sleep timing. This finding may be seen on a scan, but it does not usually cause the main health problems associated with the condition.

- Dark, thick, velvety skin, called acanthosis nigricans
- Increased body or facial hair, called hypertrichosis
- Poor growth and reduced fat beneath the skin
- Enlarged or crowded teeth and dental problems
- Thick or fast-growing nails
- Prominent eyes, a broad nose, or other distinctive facial features
- Enlarged external genital tissues

- Irregular periods or enlarged ovaries in some girls and women

Causes and risk factors

Rabson-mendenhall syndrome is caused by harmful changes in the INSR gene. This gene provides instructions for making the insulin receptor. When the receptor cannot respond normally, glucose control and several aspects of growth and development are affected.

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

Parents who each carry one altered copy usually do not have Rabson-mendenhall syndrome. For every pregnancy between two carriers, there is a chance that the child will inherit both altered copies. A genetics professional can explain the specific chances for a family.

The condition affects people of any sex. It is not caused by food, weight, parenting, or anything that happened during pregnancy. Having biological parents who are closely related increases the chance that both carry the same rare gene change, but the condition can occur without known family relatedness.

Diagnosis

Diagnosis begins with the person's growth, skin findings, physical features, family history, and blood test results. Because the condition is rare, several tests may be needed to distinguish it from other causes of severe insulin resistance.

Blood tests usually measure glucose and insulin. Insulin levels can be extremely high, including when glucose is still near the usual range. Tests such as fasting glucose, glycated haemoglobin, or an oral glucose tolerance test may be used to assess how the body handles glucose. Glycated haemoglobin, often called HbA1c, estimates average glucose over the previous two to three months.

Genetic testing that identifies harmful changes in both copies of the INSR gene can confirm the diagnosis. Testing the biological parents may clarify how the gene changes were inherited and help with family testing.

Other assessments may include blood fats, liver and kidney tests, hormone tests, dental examinations, and checks of growth and puberty. Imaging may be used for a particular concern, but a pineal gland finding alone does not confirm the condition.

Doctors may also consider Donohue syndrome, type A insulin resistance syndrome, inherited conditions affecting body fat, and other uncommon causes of severe insulin resistance.

Treatment and management

There is no treatment that repairs the underlying gene change. Management aims to improve glucose control, support growth and nutrition, identify complications early, and help the person take part in everyday life.

Treatment is challenging because ordinary amounts of insulin may have little effect. Options are selected by a specialist team and may change as glucose control changes.

Medicines that improve the body's response to insulin may be tried. Insulin treatment may also be needed, sometimes in much larger amounts than are used for more common forms of diabetes. The balance can be difficult because glucose may remain high while treatment can still occasionally cause low blood glucose.

Some specialist centres use insulin-like growth factor 1, or IGF-1. This laboratory-made hormone can send growth and glucose-related signals through a pathway that partly bypasses the insulin receptor. Evidence comes mainly from small studies and individual cases, so it is not suitable or available for everyone. It requires close monitoring for adverse effects, including low blood glucose.

Ongoing care may involve:

A diabetes team can explain glucose targets and how to use any prescribed monitoring equipment. Major dietary restrictions should not be started without specialist advice, particularly when a child is already growing slowly.

- Regular glucose and HbA1c monitoring
- Individual nutrition and growth support
- Monitoring of kidneys, eyes, nerves, blood pressure, and blood fats
- Dental care for large, crowded, or early-erupting teeth
- Assessment of puberty, periods, and ovarian changes
- A plan for illness, ketone testing, and low blood glucose
- Psychological, school, and social support

Complications

The main long-term concern is diabetes that is difficult to control. Persistently high glucose can damage small blood vessels and nerves. This may lead to kidney disease, vision problems, reduced sensation, and slow healing.

Diabetic ketoacidosis, or DKA, can occur when there is not enough effective insulin. The body then produces acidic chemicals called ketones. DKA is an emergency.

Very high insulin levels can contribute to progressive acanthosis nigricans, ovarian enlargement, excess hair growth, and changes in genital tissues. Problems with teeth and gums may affect eating or require specialist dental treatment.

Growth may remain below the expected range. Some people develop complications involving the heart, liver, or kidneys, although the exact pattern is not the same for everyone.

Treatment itself can cause problems. Insulin and IGF-1 can lower glucose too far, causing hypoglycaemia. Symptoms may include shaking, sweating, hunger, confusion, unusual behaviour, or loss of consciousness.

Prevention

Rabson-mendenhall syndrome cannot be prevented through diet, exercise, pregnancy care, or lifestyle choices. It results from inherited gene changes.

If the gene changes in a family are known, genetic counselling can explain carrier testing and reproductive options. These may include testing during pregnancy or testing embryos created through in vitro fertilisation. These are personal choices, and availability differs by location.

The condition itself cannot be reversed, but regular monitoring and treatment may reduce the effect of some diabetes-related complications. Prompt care during illness is especially important because glucose and ketone levels can change quickly.

Living with it and what to expect

Rabson-mendenhall syndrome is lifelong. Its course is influenced by how much insulin receptor function remains, how glucose control changes, and whether complications develop.

During early childhood, very high insulin levels may keep glucose from rising continuously. As the child grows, especially around puberty, insulin resistance may become harder to manage. Diabetes can then become more apparent or more difficult to control.

Care often involves frequent blood tests, glucose checks, medicines, dental appointments, and visits to several specialists. A written care plan can help relatives, schools, and other caregivers

understand glucose monitoring, low blood glucose treatment, and when to seek help.

Growth and physical differences may affect confidence or social experiences. Age-appropriate explanations, school support, and contact with rare-condition or diabetes communities can help reduce isolation. Mental health support may also be useful for the affected person and family.

People may attend school, build relationships, and take part in many everyday activities, but treatment can be demanding. Serious diabetes complications can occur at a young age, and lifespan is often shortened. Individual outcomes cannot be predicted from the diagnosis alone, and some people live into adulthood with sustained specialist care.

Transition from children's to adult services should be planned rather than delayed until care is interrupted. Adults may need advice about sexual health, periods, fertility, pregnancy risks, and genetic counselling.

When to get medical help

Keep routine appointments with the endocrinology and diabetes teams, even when the person feels well. Insulin resistance and organ complications can worsen without causing early symptoms.

Contact the care team promptly about persistent glucose readings outside the agreed range, repeated low glucose episodes, new thirst or urination, unexplained weight loss, vomiting, worsening skin problems, changes in vision, or concerns about growth and puberty.

Seek urgent medical advice during an infection or other illness if glucose remains high, ketones are present, or the person cannot keep fluids down. Follow the individual sick-day plan if one has been provided.

Call emergency services for possible diabetic ketoacidosis, including:

Severe low blood glucose is also an emergency if the person has a seizure, becomes unconscious, cannot swallow safely, or does not recover after the prescribed emergency treatment.

- Vomiting with abdominal pain or dehydration
- Deep or unusually rapid breathing
- Fruity-smelling breath
- Increasing sleepiness, confusion, or difficulty waking
- High glucose with moderate or high ketones

Common questions

Is Rabson-mendenhall syndrome the same as diabetes?

No. It is a genetic insulin receptor condition that causes extreme insulin resistance. Diabetes is one major consequence, but the condition also affects growth, skin, teeth, body hair, and development.

Can Rabson-mendenhall syndrome be cured?

There is currently no cure that corrects the gene change or restores normal insulin receptor function. Treatment focuses on glucose control, growth, symptoms, and prevention or early treatment of complications.

Is it contagious?

No. It cannot spread through contact, food, blood, or shared living spaces. It is usually inherited when a child receives an altered INSR gene copy from each biological parent.

Why does the skin become dark and thick?

Extremely high insulin levels stimulate skin cells and related growth pathways. This produces acanthosis nigricans, especially in skin folds. It is not dirt and usually cannot be scrubbed away.

How is it different from Donohue syndrome?

Both result from serious problems with the insulin receptor. Donohue syndrome is generally more severe, begins around birth, and often causes life-threatening problems in infancy. Rabson-mendenhall syndrome usually allows longer survival, although it can still cause serious early complications.

Can someone with this condition have children?

Some adults may be able to have children, but insulin resistance, ovarian changes, and other health complications may affect fertility or pregnancy safety. Pre-pregnancy assessment and genetic counselling are important because reproductive risks are specific to the person and family.

Sources

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