CONDITION

Inborn errors of metabolism

Inborn errors of metabolism are inherited conditions that disrupt how the body processes nutrients or produces energy.

WHAT IT IS
Group of inherited conditions disrupting body chemistry

BODY SYSTEM
Any organ, often brain, liver, muscles, and heart

MAIN SYMPTOMS
Poor feeding, vomiting, developmental changes, low energy

WHAT CAUSES IT
Inherited genetic changes affecting metabolism

HOW IT IS DIAGNOSED
Blood, urine, enzyme, and genetic tests

MAIN TREATMENT
Special diets, supplements, medicines, and emergency plans

CAN IT BE CURED?
Sometimes - selected conditions have definitive treatments

IS IT AN EMERGENCY?
Sometimes - sudden drowsiness, confusion, or breathing trouble

LONG-TERM OUTLOOK
Early treatment helps, but severe forms can remain serious

Overview

Inborn errors of metabolism are a large group of genetic conditions affecting metabolism. Metabolism is the set of chemical processes your body uses to turn food into energy, build tissues, and remove waste.

Each condition affects a particular enzyme, transport protein, or other part of these processes. An enzyme is a protein that helps a chemical reaction happen. If an enzyme or transporter does not work properly, the body may be unable to break down a substance, make something it needs, or move chemicals into the right cells.

This can cause harmful substances to build up. It can also leave the body short of energy or important compounds. The effects range from mild changes found on a screening test to serious illness affecting the brain, liver, heart, muscles, kidneys, eyes, or other organs.

Examples include phenylketonuria, maple syrup urine disease, urea cycle conditions, fatty acid oxidation conditions, glycogen storage conditions, and some mitochondrial conditions. These are different conditions with different treatments. Advice that is safe for one may be unsuitable for another.

Some are found through newborn screening before symptoms begin. Others appear during infancy, childhood, or adulthood. Early recognition matters because prompt, condition-specific treatment can prevent or reduce complications in some cases.

Symptoms

Symptoms depend on which chemical process is affected and how much function remains. Even people with the same condition may be affected differently.

Possible symptoms in babies and children include:

In teenagers and adults, symptoms may include unexplained confusion, problems with coordination, muscle pain after activity, repeated low blood sugar, liver problems, or a gradual change in thinking or movement.

Some conditions cause ongoing symptoms. Others cause episodes called metabolic crises. During a crisis, body chemistry becomes seriously unbalanced. Episodes may be triggered by an infection, vomiting, dehydration, prolonged fasting, surgery, childbirth, or unusually intense exercise.

Symptoms during a metabolic crisis can include repeated vomiting, severe weakness, rapid breathing, confusion, marked drowsiness, seizures, or loss of consciousness. A person with a diagnosed metabolic condition may have an emergency plan explaining what to do during illness.

Symptoms alone cannot confirm an inborn error of metabolism. Many more common conditions can cause similar problems.

- Poor feeding, repeated vomiting, or difficulty gaining weight
- Unusual sleepiness, low muscle tone, or irritability
- Delayed development or loss of previously gained skills
- Seizures, unusual movements, or problems with balance
- An enlarged liver, jaundice, or unusual body or urine odour
- Muscle weakness, exercise intolerance, or heart problems

Causes and risk factors

Inborn errors of metabolism are caused by changes in genes that provide instructions for metabolic enzymes, transporters, or related proteins.

Most are inherited. Many follow an autosomal recessive pattern. This means a person has received a changed copy of the same gene from each biological parent. The parents are usually healthy carriers and may not know that they carry the change.

Other conditions are X-linked, meaning the altered gene is on the X chromosome. Some mitochondrial conditions are passed through mitochondrial DNA, which is usually inherited from the biological mother. Less often, a condition follows a dominant pattern or results from a new genetic change that was not inherited from either parent.

Having relatives with the same condition, unexplained infant deaths, repeated metabolic crises, or a known gene change can increase the chance of an inherited metabolic condition in a family. Parents who are biological relatives are more likely to carry the same rare recessive gene change, although most related couples do not have an affected child.

These conditions are not caused by parenting, ordinary food choices, or something a person did during pregnancy.

Diagnosis

Some inborn errors of metabolism are first detected through newborn screening. A small blood sample is tested soon after birth for selected conditions. Screening programmes differ by location and do not test for every metabolic condition.

An abnormal screening result is not a diagnosis. Follow-up testing is needed, usually without delay, because screening can produce false-positive results. A false positive means the screening result is abnormal even though the baby does not have the condition.

When symptoms or family history raise concern, testing may include:

Doctors may repeat tests because illness, feeding, medicines, and the timing of the sample can affect results. Genetic testing can confirm many conditions, but results are not always clear. Sometimes biochemical and genetic findings must be considered together.

Close relatives may be offered targeted testing after a diagnosis. A genetic counsellor can explain inheritance, what a result means for relatives, and the options available for future pregnancies.

- Blood tests for glucose, acids, ammonia, amino acids, fats, or other chemical markers

- Urine tests for unusual organic acids or other substances
- Enzyme tests showing whether a particular enzyme works normally
- Genetic testing to identify a relevant gene change
- Occasionally, tests on skin cells, muscle, liver, or another tissue

Treatment and management

Treatment is specific to the exact condition. It is usually coordinated by a specialist metabolic team and may involve dietitians, genetic counsellors, pharmacists, and specialists in the organs affected.

Some conditions are managed with a carefully planned diet. This may limit a nutrient the body cannot process, such as a particular amino acid or type of fat. Other plans prevent long gaps without food. These diets need professional supervision because unnecessary restriction can cause poor growth or nutrient deficiencies.

Treatment may also include:

Gene-based treatments are available for a small number of conditions and are being studied for others. Their benefits, risks, and availability differ by diagnosis.

Illness management is an important part of care. Infection, vomiting, or reduced food intake can make some metabolic conditions unstable. The emergency plan may include special drinks or feeds, temporary changes in treatment, blood tests, or hospital care. It should be followed rather than replaced with general advice found online.

Routine monitoring may track growth, nutrition, development, blood chemistry, and the health of the liver, heart, kidneys, bones, eyes, or nervous system.

- Special medical formulas or prescribed nutritional supplements
- Vitamins or cofactors that help a partly working enzyme
- Medicines that remove harmful chemicals or reduce their production
- Replacement of a missing enzyme in certain conditions
- Treatment for seizures, heart problems, movement symptoms, or other effects
- Liver, kidney, or stem cell transplantation in selected severe conditions

Complications

Complications occur when harmful substances build up, the body cannot produce enough energy, or an organ is gradually affected.

Depending on the condition, complications may include developmental or learning difficulties, seizures, movement problems, vision or hearing loss, muscle weakness, liver or kidney damage, heart muscle disease, or weakened bones.

Repeated metabolic crises can injure the brain or other organs. However, the risk is not the same for every condition. Some people remain well with treatment, while others have ongoing problems despite careful management.

Treatment itself can also need monitoring. Restrictive diets may affect growth or nutrition, and medicines may have side effects. Regular blood tests and specialist reviews help identify these concerns early.

Prevention

Inherited metabolic conditions generally cannot be prevented after the gene changes have been inherited.

Newborn screening does not prevent the condition, but it can identify some conditions before symptoms develop. Starting treatment early may prevent or reduce complications.

If a gene change is known in a family, genetic counselling can explain the chance of it occurring in another child. Carrier testing, testing during pregnancy, and testing embryos created through in vitro fertilisation may be options for some families. These are personal choices, and availability differs by location.

For someone already diagnosed, following the treatment and emergency plans can reduce the chance of metabolic crises. Recommended vaccinations, prompt attention to illness, and avoiding prolonged fasting may be important for certain conditions, but the correct advice must come from the condition-specific care plan.

Living with it and what to expect

The long-term course is closely linked to the exact diagnosis, when treatment began, and whether the brain or other organs were affected before diagnosis. A single outlook cannot describe this whole group of conditions.

Some people need only regular checks and manageable diet or medicine changes. Others need daily medical foods, several medicines, frequent blood tests, mobility support, or help with

learning and communication. Some progressive conditions worsen over months or years even with treatment.

Children may need support at nursery or school. This can include safe access to prescribed food, help taking medicines, adjustments for fatigue, and a written plan for illness or emergencies. Teenagers usually need gradual support to learn about their condition and take more responsibility for treatment.

Planning matters for travel, surgery, pregnancy, fasting, and strenuous activity. Carrying an emergency letter or medical alert information can help unfamiliar healthcare teams respond appropriately.

Regular follow-up is important even when you feel well. Blood chemistry or organ changes may appear before obvious symptoms. Tell the metabolic team about persistent symptoms, difficulty following the diet, missed treatment, side effects, or changes affecting school, work, or emotional wellbeing.

Many people study, work, form relationships, and take part in family and community life. Daily routines and support needs differ, and they may change over time.

When to get medical help

If you have a diagnosed metabolic condition, follow your personal emergency plan during illness. Contact the metabolic team promptly if you are vomiting, cannot keep prescribed food or fluids down, are eating much less than usual, or have signs of infection. Do not wait for severe symptoms if the plan says to seek help earlier.

Arrange routine follow-up for new but stable concerns such as increasing tiredness, reduced exercise tolerance, changes in movement, difficulty with the prescribed diet, or concerns about growth, learning, or treatment side effects.

Seek urgent medical assessment for repeated vomiting, worsening weakness, unusual behaviour, new confusion, marked drowsiness, or rapid breathing.

Call emergency services for a seizure lasting longer than expected, loss of consciousness, severe breathing difficulty, or if the person cannot be woken normally. Show emergency staff any metabolic emergency letter or medical alert information.

A baby who is difficult to wake, feeds poorly, repeatedly vomits, has breathing changes, or seems seriously unwell also needs urgent medical assessment, whether or not a metabolic condition is known.

Common questions

Are inborn errors of metabolism found only in babies?

No. Severe forms often appear in infancy, and newborn screening finds some conditions early. Milder forms may not become clear until childhood or adulthood, sometimes after an infection, pregnancy, fasting, or heavy exercise.

Does a normal newborn screening result rule them out?

No. Newborn screening covers selected conditions, and the screening panel differs by location. A normal result does not exclude a condition that was not tested for or one that screening did not detect.

Can I have one even if nobody else in my family does?

Yes. Recessive conditions often appear without a known family history because healthy carriers usually have no symptoms. A new gene change can also occur for the first time in one person.

Will I need a special diet for life?

Some people do, but not everyone. The diet depends on the exact metabolic pathway involved and may change with age, health, pregnancy, or new treatments. Major dietary changes should not be started without specialist guidance.

Are inborn errors of metabolism curable?

A few have treatments that can correct or replace the underlying problem, such as selected transplants, enzyme replacement, or gene-based treatment. Many cannot currently be cured but can be managed. Treatment may prevent crises and protect organs without removing the genetic cause.

Can adults be tested for an inherited metabolic condition?

Yes. Testing may be appropriate when symptoms, laboratory findings, or family history suggest a particular condition. The process may include blood and urine studies, enzyme testing, and genetic testing rather than a single broad test.

Sources

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