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Hereditary urea cycle abnormality

Hereditary urea cycle abnormalities are inherited conditions. They can cause problems with the removal of waste from the body in the urine.

Causes

The urea cycle is a process in which waste (ammonia) is removed from the body. When you eat proteins, the body breaks them down into amino acids. Ammonia is produced from leftover amino acids, and it must be removed from the body.

The liver produces several chemicals (enzymes) that change ammonia into a form called urea, which the body can remove in the urine. If this process is disturbed, ammonia levels begin to rise.

Several inherited conditions can cause problems with this waste-removal process. People with a urea cycle disorder have a defective gene that makes the enzymes needed to break down ammonia in the body.

These diseases include:

- Argininosuccinic aciduria
- Arginase deficiency
- Carbamyl phosphate synthetase (CPS) deficiency
- Citrullinemia
- N-acetylglutamate synthetase (NAGS) deficiency
- Ornithine transcarbamylase (OTC) deficiency

As a group, these disorders occur in 1 in 30,000 newborns. OTC deficiency is the most common of these disorders.

Because this is an X-linked condition, boys are more often affected by OTC deficiency than girls. Girls are rarely affected with OTC. Those girls who are affected have milder symptoms and can develop the disease later in life. Because they are autosomal recessive conditions, the other conditions that cause this problem affect both girls and boys equally.

To get the other types of disorders, you need to receive a non-working copy of the gene from both parents. Sometimes parents don't know they carry a non-working copy of the gene until their child gets the disorder.

Symptoms

Typically, an affected baby begins nursing well and seems normal. However, over time the baby develops poor feeding, vomiting, and sleepiness, which may be so deep that the baby is difficult to awaken. This most often occurs within the first week after birth.

Symptoms include:

- Confusion
- Decreased food intake
- Dislike of foods that contain protein
- Increased sleepiness, difficulty waking up
- Nausea, vomiting

Exams and Tests

The health care provider will often diagnose these disorders when the child is still an infant.

Signs may include:

- Abnormal amino acids in blood and urine
- Abnormal level of orotic acid in blood or urine
- High blood ammonia level
- Normal level of acid in blood

Tests may include:

- Arterial blood gas
- Blood ammonia
- Blood glucose
- Plasma amino acids
- Urine organic acids
- Genetic tests
- Liver biopsy
- MRI or CT scan

Treatment

Limiting protein in the diet can help treat these disorders by reducing the amount of nitrogen waste the body produces. (The waste is in the form of ammonia.) Special low-protein infant and toddler formulas are available.

It is important that a provider guides the baby's protein intake. The provider can balance the amount of protein the baby gets so that it is enough for growth, but not enough to cause symptoms.

It is very important for people with these disorders to avoid fasting.

People with urea cycle abnormalities must also be very careful under times of physical stress, such as when they have infections. Stress, such as a fever, can cause the body to break down its own proteins. These extra proteins can make it hard for the abnormal urea cycle to remove the byproducts.

Develop a plan with your provider for when you are sick to avoid all protein, drink high carbohydrate drinks, and get enough fluids.

Most people with urea cycle disorders will need to stay in the hospital at some point. During such times, they may be treated with medicines that help the body remove nitrogen-containing wastes. Dialysis may help rid the body of excess ammonia during extreme illness. Some people may need a liver transplant.

Support Groups

RareConnect: Urea Cycle Disorder Official Community -- www.rareconnect.org/en/community/urea-cycle-disorders [https://www.rareconnect.org/en/community/urea-cycle-disorders]

Outlook (Prognosis)

How well people do depends on:

- Which urea cycle abnormality they have
- How severe it is
- How early it is discovered
- How closely they follow a protein-restricted diet

Babies diagnosed in the first week of life and put on a protein-restricted diet right away may do well.

Sticking to the diet can lead to normal adult intelligence. Repeatedly not following the diet or having stress-induced symptoms can lead to brain swelling and brain damage.

Major stresses, such as surgery or accidents, can be complicated for people with this condition. Extreme care is needed to avoid problems during such periods.

Possible Complications

Complications can include:

- Coma
- Confusion and eventually disorientation
- Death
- Increase in blood ammonia level
- Swelling of the brain

When to Contact a Medical Professional

Prenatal testing is available. Genetic testing before an embryo is implanted may be available for those using in vitro if the specific genetic cause is known.

A dietician is important to help plan and update a protein-restricted diet as the child grows.

Prevention

As with most inherited diseases, there is no way to prevent these disorders from developing after birth.

Teamwork between parents, the medical team, and the affected child to follow the prescribed diet can help prevent severe illness.

Alternative Names

Abnormality of the urea cycle - hereditary; Urea cycle - hereditary abnormality

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