Cystinosis: An overview for patients and families

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Introduction

Cystinosis is a rare inherited disorder which is estimated to affect 1 in 100,000 to 200,000 people. Cystinosis is characterised by the accumulation of an amino acid called cystine within the lysosomes of the body. Lysosomes are a compartment within the cell that digest and recycle materials such as proteins.

Cystine is an amino acid which is a building block of protein and is essential to life. Protein is broken down inside the lysosomes into several amino acids (including Cystine). In a patient without cystinosis cystine is allowed to leave the lysosome to be used again by the body.

In patients living with cystinosis there is no transport system available to carry cystine out of the lysosomes therefore causing cystine to accumulate within the cell.

The accumulating cystine will eventually form into crystals within your cells and start to affect various organs such as the kidneys, eyes, muscle, pancreas and the brain.

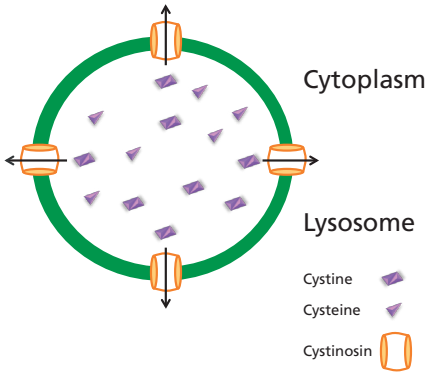


Diagram A: Normal Lysosome with Cystine (purple) passing freely through the lysosome.

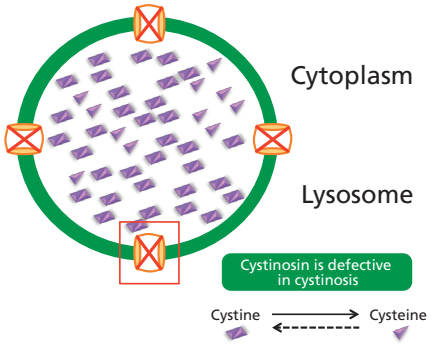


Diagram B: Cystinotic lysosome showing the accumulation of Cystine due to no transport system.

Types of cystinosis

Early onset: *Infantile cystinosis*

This is the most common form of cystinosis. The first symptoms generally appear several months after birth. Without treatment renal failure may develop between the age of 8 and 12 years.

Symptoms may occur within the first year or two of life. These include:

- Poor growth and development
- Poor appetite
- Excessive thirst
- Excessive urination
- Dehydration
- Ricketts

These symptoms are caused by the damage done to the kidneys. The kidney is unable to concentrate the urine and allows important electrolytes such as sodium, potassium, phosphorus and bicarbonate to be wasted into the urine. This is often referred to as Fanconi Syndrome.

Cystine crystals in the eye can be seen with a slit lamp eye test (a small strip of light shone in the eye) between 12 and 16 months of age. This can lead to pain and discomfort from bright lights (photophobia).

Late onset: *Juvenile cystinosis*

This is a rare form of cystinosis. The symptoms are comparable to those of infantile cystinosis but with later onset, usually in adolescence or early adult life. Renal failure can develop between the ages of 20 and 30 years.

Non-nephropathic cystinosis

This form is sometimes described as ocular cystinosis. It is usually discovered at adult age through performing other routine

examinations such as an eye test. Patients with this form rarely report any symptoms and damage to other organs generally does not occur.

Child (Infantile cystinosis)

- Failure to thrive
- Photophobia
- Ricketts
- Vomiting
- Dehydration
- Excessive urination
- Developmental delay
- Corneal crystals
- Kidney damage from the age of 2
- Low potassium
- Low phosphate
- Too much acid in the blood

Late onset cystinosis

- Symptoms same as infantile
- Presents from the age of 10 up to early adulthood
- Will reach end stage renal failure between 15 and 25 years of age

Adult (Benign cystinosis)

- Corneal crystals
- Photophobia
- No other organ damage

Treatment

Symptomatic treatment (before kidney failure develops)

It is possible to relieve some of the kidney symptoms by ensuring that you drink an adequate amount of water to replace the excessive fluid loss.

Taking supplements will replace the sodium, bicarbonate and potassium being leaked by the kidneys. The amount of supplements you take may vary according to your blood results. Vitamin D and phosphorus supplements will heal and prevent bone diseases.

Cystinosis specific treatment

There is currently no complete cure for cystinosis. The aim of specific treatment is to reduce the amount of cystine within the cells. Cysteamine is a cystine-depleting drug which reduces the level of cystine within the lysosomes.

Cysteamine is most effective when taken four times a day at six hourly intervals. This medication is a life-long treatment and must be taken every day

Cysteamine treatment reduces the progression towards kidney failure. It is not an easy medicine as it has a smell that some people find unpleasant and has to be taken regularly in the long term.

Cysteamine is still effective even after kidney failure has developed. It prevents other organs in the body being damaged and can prevent further damage to the pancreas and liver.

Eye drops containing cysteamine can prevent damage to the eye and can help with photophobia (discomfort in bright light). These need to be applied several times a day to prevent cystine crystals forming.

Treatment monitoring

It is possible to measure the effectiveness of treatment by taking a white blood cell (WBC) cystine level. This is a blood test that allows us

to measure the amount of cystine accumulating in the cells and should be checked every 3-4 months. To prevent damage to your organs the level should be kept below 1.0. Blood samples should be taken 5-6 hours after taking cysteamine. It is important to let your healthcare professional know if you are missing any doses of cysteamine.

How do you get cystinosis?

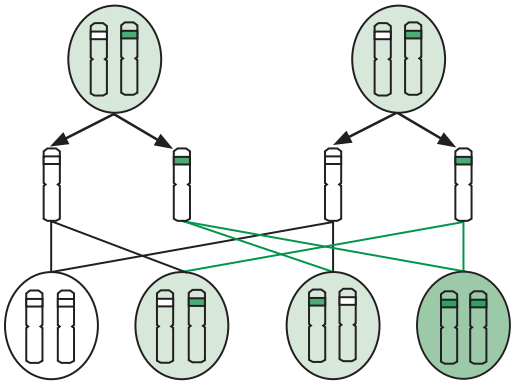
Cystinosis is a genetic inherited disease and is not infectious, contagious or brought on by lifestyle.

We have thousands of genes, each carrying their own set of instructions. When a gene is altered it can result in a genetic condition or disease. We all have two copies of each gene. One inherited from our mother and one inherited from our father.

Cystinosis is inherited in a way that is called recessive. This means that individuals must inherit two copies of the altered gene to be affected by cystinosis. Individuals who inherit one copy of the altered gene are completely healthy and are known as carriers.

When both parents are carriers of the same altered gene there are four possible outcomes for each pregnancy (see diagram below).

Autosomal recessive inheritance: both parents are carriers



Each child of parents who both carry the cystinosis gene has a 25% chance of inheriting a changed gene from both parents and being

affected by cystinosis.

There is a 50% chance that the child will inherit just one copy of the cystinosis gene. This means they will be healthy carriers like their parents.

There is a 25% chance that the child will inherit both normal copies of the gene and will not have cystinosis or be a carrier of cystinosis.