



## ASAS Deficiency (Citrullinemia)

### What is it?

Citrullinemia is one type of amino acid disorder. People with this condition cannot remove ammonia from the body. Ammonia is a harmful substance. It is made when protein and its building blocks (amino acids) are broken down for the body.

### What causes it?

This is one of a small number of conditions called urea cycle disorders (UCD).

This occurs when an enzyme called argininosuccinic acid synthetase (ASAS) is either missing or not working properly. This enzyme's job is to break down certain amino acids and to remove ammonia from the body.

When ASAS is not working, an amino acid called citrulline builds up in the blood. Ammonia and other harmful substances build up. This causes brain damage. If not treated, excess ammonia in the blood can cause death.

### If citrullinemia is not treated, what problems occur?

Normally, the body changes ammonia into a substance called urea. Urea is then safely removed in the urine. If ammonia is not changed to urea, high levels build up in the blood. This can be very harmful. If ammonia levels stay high for too long, severe brain damage can occur.

The symptoms and the age they start vary from person to person. There are two main forms of this condition. The most common is called classic. It usually starts in infancy. There are

also milder forms that start later in infancy or childhood. There is also a rare adult form more common in people of Japanese heritage.

### *Classic Citrullinemia*

Infants who have classic citrullinemia seem healthy at birth but quickly develop symptoms. Within a few days of life, babies will have high ammonia levels. Some of the first symptoms of high ammonia are:

- 1) Poor appetite.
- 2) Extreme sleepiness or lack of energy.
- 3) Irritability.
- 4) Vomiting.

If not treated, high ammonia levels cause:

- 1) Muscle weakness.
- 2) Decreased or increased muscle tone.
- 3) Breathing problems.
- 4) Problems staying warm.
- 5) Seizures.
- 6) Swelling of the brain.
- 7) Coma, and sometimes death.

Other effects of citrullinemia can include:

- 1) Poor growth.
- 2) Enlarged liver.
- 3) Mental retardation.

Without treatment, most babies die within the first few weeks of life.

### *Milder Forms*

In the milder forms, symptoms start later in infancy or childhood. Symptoms can include:

- 1) Poor growth.
- 2) Dry, brittle hair.
- 3) Hyperactivity.

- 4) Behavior problems.
- 5) Learning problems.
- 6) Avoidance of meat and other high-protein foods.
- 7) Episodes of too much ammonia in the blood.

Episodes of excess ammonia often happen:

- 1) After going without food for a long period of time.
- 2) During an illness or infection.
- 3) After high-protein meals.

Some of the first symptoms of excess ammonia in children are:

- 1) Poor appetite.
- 2) Severe headache.
- 3) Vomiting.
- 4) Extreme sleepiness or lack of energy.
- 5) Slurred speech.
- 6) Poor coordination or balance problems.

If not treated, children with high ammonia levels may develop:

- 1) Breathing problems.
- 2) Swelling of the brain.
- 3) Seizures.
- 4) Coma, sometimes leading to death.

If excess ammonia is not treated, it can cause long-term problems:

- 1) Poor growth
- 2) Learning disabilities or mental retardation
- 3) Increased muscle tone

Some people have very mild or no symptoms and are found to be affected only after a brother or sister is diagnosed.

### **What is the treatment for citrullinemia?**

Your baby's primary doctor will work with a metabolic doctor and a dietician to care for your child.

Prompt treatment is needed to prevent the build up of ammonia. You should start treatment as soon as you know your child has the condition.

The following are treatments often recommended for babies and children with citrullinemia.

### ***Low-Protein Diet and/or Special Medical Foods and Formula***

Most children need to eat a diet made up of very low-protein foods, special medical foods and sometimes a special formula. Your dietician will create a food plan that contains the right amount of protein, nutrients and energy to keep your child healthy. A special food plan should be continued throughout your child's life.

### ***Low-Protein Diet***

The most effective treatment for citrullinemia is a low-protein diet. Foods to avoid or strictly limit include:

- 1) Milk, cheese and other dairy products.
- 2) Meat and poultry.
- 3) Fish.
- 4) Eggs.
- 5) Dried beans and legumes.
- 6) Nuts and peanut butter.

Eating foods high in protein can cause ammonia to build up, causing severe illness. Many vegetables and fruits have only small amount of protein and can be eaten in carefully measured amounts.

Do not remove all protein from the diet. Your child still needs a certain amount of protein for normal growth and development. Any changes in the diet should be made under the guidance of a dietician.

### ***Medical Foods and Formula***

There are medical foods such as special low-protein flours, pastas and rice that are made especially for people with amino acid disorders.

Your baby may need to drink a special medical formula that contains the correct amount of amino acids and nutrients. Your metabolic doctor and dietician will decide whether your child needs this treatment.

Your child's exact food plan will depend on many things, such as his or her age, weight and general health. Your dietician will fine-tune your child's diet over time. Any diet changes should be made under the guidance of a dietician.

### ***Medication***

There are certain medications that can help the body get rid of ammonia. These are taken by mouth or by tube feeding to prevent high ammonia levels. Your doctor will decide whether your child needs these medications, which ones, and how much to use.

During episodes of high ammonia, children need to be treated in the hospital. Medications to remove ammonia often are given by IV. Dialysis is sometimes needed to remove ammonia from the blood.

An amino acid called arginine is often given by mouth to help prevent ammonia build up. Your doctor will tell you whether your child needs arginine and how much to use. Do not use any supplements or medications without checking with your doctor

### ***Blood Tests***

Your child will have regular blood tests to measure ammonia and amino acid levels. Your child's diet and medication may need to be adjusted based on blood test results.

### ***Call Your Doctor at the Start of Any Illness***

For some babies and children with citrullinemia, even minor illness can cause high ammonia levels. In order to prevent problems, call your doctor right away when your child has any of the following:

- 1) Loss of appetite
- 2) Low energy or extreme sleepiness
- 3) Vomiting
- 4) Fever
- 5) Infection or illness
- 6) Behavior or personality changes
- 7) Difficulty walking or balance problems

Symptoms of high ammonia often need to be treated in the hospital. Ask your metabolic doctor if you should carry a special travel letter with medical instructions for your child's care.

### **What happens when citrullinemia is treated?**

With prompt and lifelong treatment, children with citrullinemia often can live healthy lives with typical growth and learning. Early treatment can help prevent high ammonia levels.

Even with treatment, some children still have episodes of high ammonia. This can result in brain damage. This can cause lifelong learning problems, mental retardation or increased muscle tone.

### **What causes the ASAS enzyme to be absent or not working correctly?**

Genes tell the body to make enzymes. People with citrullinemia have a pair of genes that do not work correctly. Because of the changes in this pair of genes, the ASAS enzyme does not work properly or is not made at all.

### **Is citrullinemia inherited?**

This condition is inherited. It affects both boys and girls equally.

Everyone has a pair of genes that make the ASAS enzyme. In children with citrullinemia, neither of these genes works correctly. These children inherit one nonworking gene for the condition from each parent.

Parents of a child with citrullinemia rarely have the condition themselves. Instead, each parent has a single nonworking gene for citrullinemia. They are called carriers. Carriers do not have the condition because the other gene of this pair is working correctly.

When both parents are carriers, there is a 25 percent chance in each pregnancy for the child to have citrullinemia. There is a 50 percent chance for the child to be a carrier, just like the parents. And, there is a 25 percent chance for the child to have two working genes.

## **Can other members of the family have citrullinemia or be carriers?**

### ***Having Citrullinemia***

The brothers and sisters of a baby with citrullinemia have a chance of being affected, even if they haven't had symptoms. Finding out whether other children in the family have the condition is important because early treatment can prevent serious health problems. Talk to your metabolic doctor or genetic counselor about testing your other children.

### ***Citrullinemia Carriers***

Brothers and sisters who do not have citrullinemia still have a chance to be carriers like their parents. Except in special cases, carrier testing should be done only in people older than 18.

Each of the parents' brothers and sisters has a 50 percent chance to be a carrier. It is important for other family members to be told that they could be carriers. There is a small chance they are also at risk to have children with citrullinemia.

When both test parents are carriers, newborn screening results are not sufficient to rule out the condition in a newborn baby. In this case, special diagnostic testing should be done in addition to newborn screening.

## **Can other family members be tested?**

### ***Diagnostic Testing***

Brothers and sisters of a child with citrullinemia can be tested using blood, urine or skin samples.

### ***Carrier Testing***

If both gene changes have been found in your child, other family members can have genetic testing to see if they are carriers.

If DNA testing is not helpful, other methods of carrier testing may be available. If you have questions about carrier testing, ask your genetic counselor or metabolic doctor.

## **How may people have citrullinemia?**

About one in 57,000 babies in the United States is born with citrullinemia. No known population is at increased risk.

## **Does citrullinemia happen more frequently in a certain ethnic group?**

The classic form of citrullinemia occurs in all ethnic groups around the world. The adult-onset form of citrullinemia is more common among people of Japanese descent.

## **Does citrullinemia go by any other names?**

Citrullinemia is sometimes also called:

- 1) Citrullinemia, type 1 (classic form).
- 2) Argininosuccinate synthetase deficiency.
- 3) Argininosuccinate acid synthetase deficiency.
- 4) AS deficiency.
- 5) ASS deficiency.
- 6) Citrullinuria.

The adult-onset form of citrullinemia is also called:

- 1) Citrullinemia, type 2.
- 2) Late-onset citrullinemia.

## **Where can I find more information?**

National Urea Cycle Disorders Foundation  
[www.nucdf.org](http://www.nucdf.org)

Children Living with Inherited Metabolic Diseases (CLIMB)  
[www.climb.org.uk](http://www.climb.org.uk)

National Coalition for PKU and Allied Disorders  
[www.pku-allieddisorders.org](http://www.pku-allieddisorders.org)

Genetic Alliance  
[www.geneticalliance.org](http://www.geneticalliance.org)

### Children's Special Health Services (CSHS)

State Capitol Judicial Wing  
600 E. Boulevard Ave., Department 301  
Bismarck, ND 58505-0269  
Toll Free: 800.755.2714  
701.328.2436  
Relay TDD: 701.328.3975  
CSHS website: [www.ndhealth.gov/CSHS](http://www.ndhealth.gov/CSHS)  
North Dakota Department of Health website:  
[www.ndhealth.gov](http://www.ndhealth.gov)

#### Family support resources available from CSHS:

- Guidelines of Care Info
- Family Support Packet
- Financial Help Packet
- Insurance Fact Sheet

#### *Family Resources*

Family to Family Network  
Center for Rural Health  
University of North Dakota  
School of Medicine and Health Sciences  
P.O. Box 9037  
Grand Forks, ND 58202-9037  
Toll Free: 888 434.7436  
701.777.2359  
Fax: 701.777.2353  
E-mail: [NDF2F@medicine.nodak.edu](mailto:NDF2F@medicine.nodak.edu)  
[www.medicine.nodak.edu/crh](http://www.medicine.nodak.edu/crh)

Pathfinder Services of ND  
Pathfinder Family Center  
1600 2<sup>nd</sup> Ave. SW, Ste. 19  
Minot, ND 58701  
Toll Free: 800.245.5840  
701.837.7500  
Relay TDD: 701.837.7501  
E-mail: [ndpath01@ndak.net](mailto:ndpath01@ndak.net)  
[www.pathfinder.minot.com](http://www.pathfinder.minot.com)

Family Voices of North Dakota, Inc.  
P.O. Box 163  
Edgeley, ND 58433  
Toll Free: 888.522.9654  
701.493.2634  
Fax: 701.493.2635  
[www.geocities.com/ndfv](http://www.geocities.com/ndfv)

\*\*This fact sheet has general information. Every child is different and some of these facts may not apply to your child specifically. Certain treatments may be recommended for some children but not others. All children should be followed by a metabolic doctor in addition to their primary-care provider.

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#### **Disclaimer**

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[www.ndhealth.gov/familyhealth](http://www.ndhealth.gov/familyhealth)