STAR-G
Screening, Technology and Research in Genetics

Genetic Fact Sheets for Parents

Amino Acid Disorders

Screening, Technology, and Research in Genetics is a multi-state project to improve information about the financial, ethical, legal, and social issues surrounding expanded newborn screening and genetic testing – http:// www.newbornscreening.info

Disorder name: Argininemia / Arginase deficiency
Acronym: ARG 1 deficiency

This fact sheet contains general information about arginase deficiency. 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 with arginase deficiency should be followed by a metabolic doctor in addition to their primary doctor.

What is arginase deficiency?

Arginase deficiency is one type of **amino acid disorder**. People with this condition have problems removing ammonia from the body. Ammonia is a harmful substance. It is made when protein and its building blocks, amino acids, are broken down for use by the body.

Amino Acid Disorders:

Amino acid disorders (AAs) are a group of rare inherited conditions. They are caused by enzymes that do not work properly.

Protein is made up of smaller building blocks called amino acids. A number of different enzymes are needed to process these amino acids for use by the body. Because of missing or non-working enzymes, people with amino acid disorders cannot process certain amino acids. These amino acids, along with other toxic substances, then build up in the body and cause problems.

The symptoms and treatment vary between different amino acid disorders. They can also vary from person to person with the same amino acid disorder. See the fact sheets for each specific amino acid disorder.

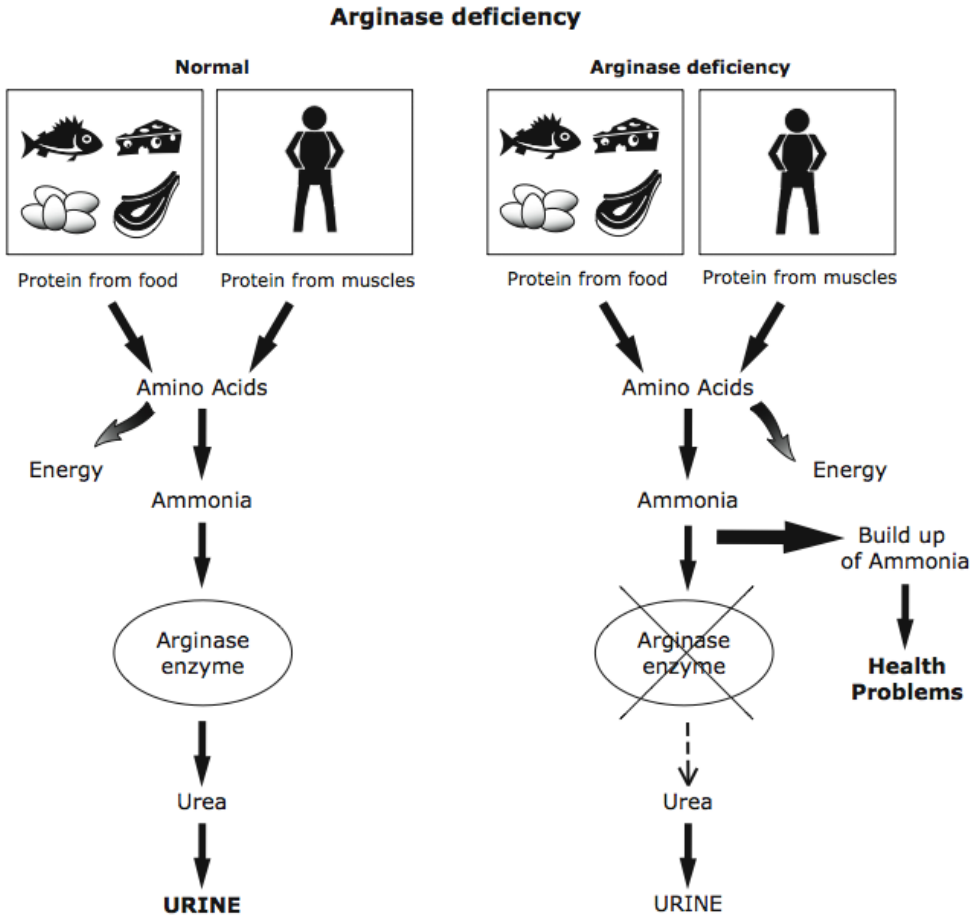
Amino acid disorders are inherited in an autosomal recessive manner and affect both males and females.

What causes arginase deficiency?

This is one of a small number of amino acid disorders called "urea cycle disorders" (UCD).

Arginase deficiency occurs when an enzyme called "arginase" is either missing or not working properly. This enzyme's job is to help break down the amino acid arginine and to help remove ammonia from the body.

When arginase is not working, arginine, along with ammonia, can build up in the blood. This can cause serious effects on growth, learning, and health.



If arginase deficiency is not treated, what problems occur?

The effects of this condition vary from person to person. Symptoms can start in infancy or not until later in childhood. Many children have their first symptoms around one year to three years of age. Effects in infants can include:

- poor growth
- learning delays
- spasticity
- poor coordination and balance problems
- fussiness or illness when fed high protein food

Episodes of illness caused by high levels of ammonia in the blood can sometimes occur but are not common. Some of the first symptoms of high blood ammonia are:

- poor appetite
- excessive sleepiness or lack of energy
- irritability
- vomiting

If untreated, other symptoms can follow:

- muscle weakness
- decreased or increased muscle tone
- breathing problems
- problems staying warm
- seizures
- swelling of the brain
- coma, and sometimes death

Often, symptoms of arginase deficiency do not begin until later in infancy or childhood. Common effects in older infants and children include:

- poor growth
- spasticity
- small head size
- hyperactivity
- behavior problems
- learning delays
- avoidance of meat or other high protein foods
- occasional bouts of vomiting and excessive sleepiness

Episodes of high blood ammonia, described above, happen rarely. If they occur, they are more likely to happen:

- after going without food for long periods
- during illness or infection
- after high-protein meals

What is the treatment for arginase deficiency?

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 arginine and 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 arginase deficiency:

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

Low-protein diet

One of the main treatments is a low-protein diet. Foods that are high in protein need to be avoided or limited include:

- milk, cheese, and other dairy products
- meat and poultry
- fish
- eggs
- dried beans and legumes
- nuts and peanut butter

Eating these foods can cause ammonia and arginine to build up, resulting in the symptoms described above. Many vegetables and fruits have only small amounts of protein and can be eaten in carefully measured amounts.

It is important not to remove all protein from your child's 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 child may be given a special formula that contains the correct amount of nutrients and amino acids. Your metabolic doctor and dietician will tell you whether your child should use this formula and how much to use. Some states offer help with payment for this special formula and others require private insurance to pay for the formula and other special medical foods.

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.

2. Medication

There are certain medications that can help the body get rid of excess arginine and ammonia. Your metabolic doctor will decide which medications your child should take.

3. Blood tests

Your child will need to 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.

4. Call your doctor at the start of any illness
Illness or infection can sometimes lead to high arginine and ammonia levels. In order to prevent problems, call your doctor right away when your child has any of the following:

- loss of appetite
- low energy or excessive sleepiness
- vomiting
- fever
- infection or illness
- behavior or personality changes
- difficulty walking or balance problems

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

What happens when arginase deficiency is treated?

With prompt and lifelong treatment, children with arginase deficiency may be able to live healthy lives with typical growth and learning.

Even with treatment, some children still have effects from high blood levels of arginine and ammonia. This can result in permanent learning problems, intellectual disabilities, or spasticity.

What causes the arginase enzyme to be absent or not working correctly?

Genes tell the body to make various enzymes. The ARG1 gene instructs the body to make the arginase enzyme. Everyone has two copies of the ARG1 gene. People with arginase deficiency have changes, also called variants, in both copies of their ARG1 genes that cause them to not work correctly. Because of the variants in the ARG1 genes, the arginase enzyme either does not work properly or is not made at all.

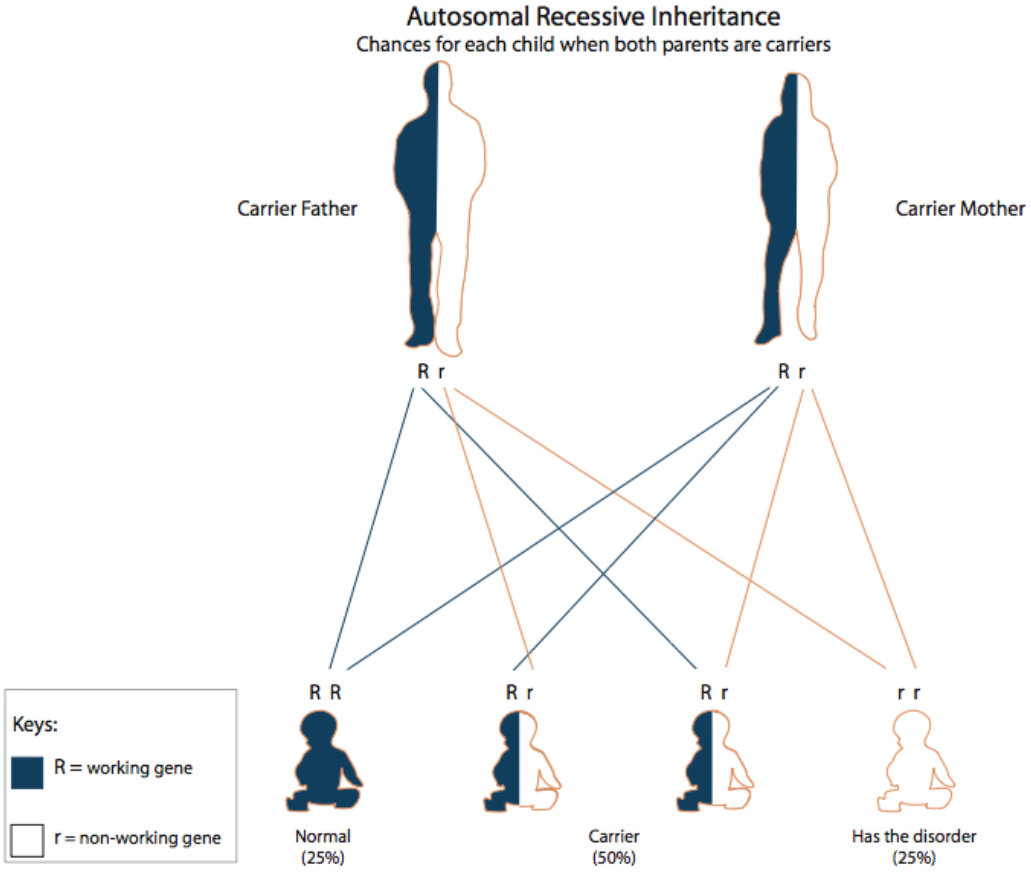
How is arginase deficiency inherited?

This condition is inherited in an autosomal recessive manner. It affects both boys and girls equally.

Everyone has two copies of the ARG1 gene that make the arginase enzyme. In children with arginase deficiency, neither of these genes works correctly. These children inherit one non-working ARG1 gene for the condition from each parent.

Parents of children with arginase deficiency rarely have the condition themselves. Instead, each parent has a single non-working gene for arginase deficiency. They are called carriers. Carriers do not have the condition because their other ARG1 gene is working correctly.

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



Genetic counseling is available to families who have children with this condition. Genetic counselors can answer your questions about how arginase deficiency is inherited, choices during future pregnancies, and how to test other family members. Ask your doctor about a referral to a genetic counselor.

Is genetic testing available?

Genetic testing for arginase deficiency is available. Genetic testing, also called DNA testing, looks for changes in the ARG1 genes that causes the condition.

Talk with your genetic counselor or metabolic doctor about whether DNA testing is possible for your family.

DNA testing is not necessary to diagnose your child. It can be helpful for carrier testing or prenatal diagnosis, discussed below.

What other testing is available?

Special blood and urine tests can be done to confirm if your child has arginase deficiency. Talk to your metabolic doctor or genetic counselor if you have questions about diagnostic testing.

Can you test during a future pregnancy?

If both gene changes (also called variants) have been found in your child with arginase deficiency, DNA testing can be done during future pregnancies. The sample needed for DNA testing is obtained by either CVS or amniocentesis.

If DNA testing is not possible, an enzyme test may be done using a blood sample from the fetus. The sample needed is obtained by a procedure called fetal blood sampling.

Parents may either choose to have testing during pregnancy or wait until birth to have the baby tested. Parents may also choose to use assisted reproductive techniques to decrease the chance that their future children would have Arginase deficiency. A genetic counselor can talk to you about your choices and answer questions about prenatal testing or testing your baby after birth.

Can other members of the family have arginase deficiency or be carriers?

Having arginase deficiency

If they are healthy and growing normally, older brothers and sisters of a baby with arginase deficiency are at low risk of having the condition. However, finding out whether other children in the family have the condition may be important because early treatment can prevent serious health problems. Ask your metabolic doctor whether your other children should be tested.

Arginase deficiency carriers

Brothers and sisters who do not have arginase deficiency still have a chance to be carriers like their parents. Except in special cases, carrier testing should only be done in people over 18 years of age.

If you are a parent of a child with arginase deficiency, your brothers and sisters have a 50% 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 arginase deficiency.

Some states do not offer newborn screening for arginase deficiency. However, expanded newborn screening through private labs is available for babies born in states that do not screen for this condition. Your healthcare provider or genetic counselor can help you obtain expanded newborn screening.

When both 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 arginase deficiency can be tested using blood, urine, or skin samples to see if they also have arginase deficiency.

Carrier testing

If both changes in the ARG1 genes have been found in your child, carrier testing may be available. Your metabolic doctor or genetic counselor can answer your questions about carrier testing.

How many people have arginase deficiency?

About one in every 300,000 babies in the United States is born with this condition.

Does arginase deficiency happen more often in a certain ethnic group?

No, it does not happen more often in any specific race, ethnic group, geographical area, or country.

Does arginase deficiency go by any other names?

Arginase deficiency is sometimes also called:

- Argininemia
- ARG1 deficiency
- Hyperargininemia

Where can I find more information?

Baby's First Test
https://www.babysfirsttest.org/newborn-screening/conditions/argininemia

MedlinePlus
https://ghr.nlm.nih.gov/condition/arginase-deficiency

Metabolic Support UK
https://www.metabolicsupportuk.org

National Urea Cycle Disorders Foundation
http://www.nucdf.org/

Rare Disease Clinical Research Network
https://www.rarediseasesnetwork.org/cms/UCDC

Document Info		
	Created by:	www.newbornscreening.info
	Reviewed by:	HI, CA, OR, and WA metabolic specialists
	Review date:	September 31, 2007 September 28, 2010 May 23, 2013 February 15, 2016 March 9, 2020 March 1, 2023
	Update on:	March 1, 2023

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U.S. Department of Health and Human Services
HRSA
Health Resources and Services Administration
Maternal and Child Health Bureau

This project is supported by a grant from the Maternal and Child Health Bureau, Health Resources and Service Administration, Genetic Services Branch, MCH Project #UH7MC30774-01-00 http://mchb.hrsa.gov