



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](http://www.newbornscreening.info)

Disorder name: Argininosuccinic acid lyase deficiency
Acronym: ASAL deficiency

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This fact sheet contains general information about ASAL 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 this condition should be followed by a metabolic doctor in addition to their primary doctor.

What is ASAL deficiency?

ASAL stands for “argininosuccinic acid lyase.” ASAL deficiency 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 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.

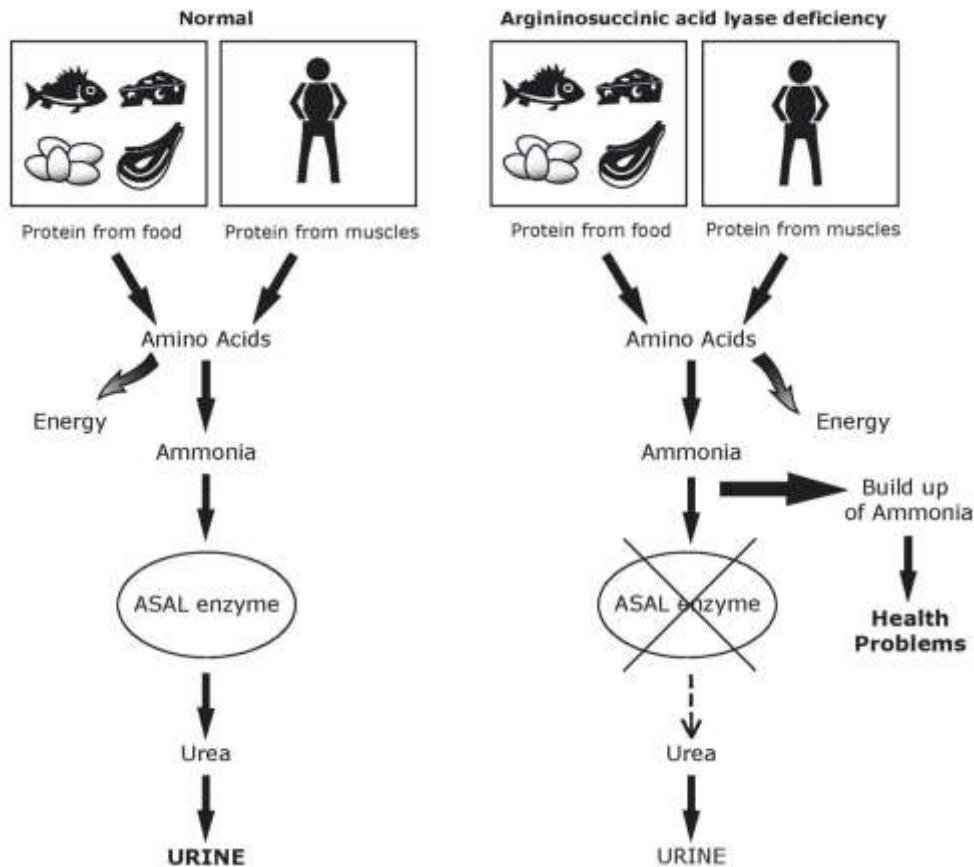
What causes ASAL deficiency?

ASAL deficiency is one of a small number of conditions called "urea cycle disorders" (UCD).

ASAL deficiency is caused by problems with the enzyme "argininosuccinic acid lyase" (ASAL). In people with ASAL deficiency, the ASAL enzyme is either missing or not working properly. This enzyme's job is to help remove ammonia from the body.

When the ASAL enzyme is not working, ammonia and other harmful substances build up in the blood and cause brain damage. If not treated, excess ammonia can cause death.

Argininosuccinic acid lyase deficiency



If ASAL deficiency is not treated, what problems occur?

Normally, the body changes ammonia into a substance called “urea.” Urea is then safely removed in the urine. However, if ammonia is not changed to urea, it begins to build up in the blood, which can be very harmful. If ammonia levels remain high for too long, severe brain damage can occur.

The symptoms of ASAL deficiency and the age they start vary from person to person. There are two types of ASAL deficiency. In the most common type, the symptoms start shortly after birth. There is also a milder type in which symptoms begin in late infancy or early childhood.

ASAL deficiency in newborns

Infants are healthy at birth but quickly develop symptoms. Within a few days of life, babies have high levels of ammonia in their blood. Some of the first symptoms of high blood ammonia are:

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

If not treated, high ammonia levels can cause:

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

Other effects of ASAL deficiency can include:

- poor growth
- enlarged liver
- delays in learning or intellectual disabilities

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

ASAL deficiency in childhood

In this milder type of ASAL deficiency, symptoms start later in infancy or childhood. Some common symptoms in children who are not treated are:

- poor growth
- dry, brittle hair
- hyperactivity
- behavior problems
- learning or intellectual disabilities
- avoidance of meat and other high protein foods
- enlarged liver
- small head size
- high blood pressure
- episodes of excess ammonia in the blood

Episodes of high blood ammonia often happen:

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

In children, some of the first symptoms of high blood ammonia are:

- poor appetite
- intense headache
- vomiting
- extreme sleepiness or lack of energy
- slurred speech
- poor coordination and balance problems

If not treated, children with high blood ammonia levels can develop:

- breathing problems
- swelling of the brain
- seizures
- coma, sometimes leading to death

Some people have very mild symptoms and are diagnosed with ASAL deficiency after their brother or sister is diagnosed.

What is the treatment for ASAL 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 ammonia. You should start treatment as soon as you know your child has this condition.

The following are treatments often recommended for babies and children with ASAL 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, 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. The food plan should be continued throughout your child's life.

Low-protein diet

The most effective treatment is a diet with low amounts of protein. Foods that are high in protein need to be avoided or strictly limited and include:

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

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

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. Your dietician will help you create the best food plan for your child.

Medical foods and formula

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

Your baby may be given a special formula that contains the correct amount of nutrients and amino acids. Your metabolic doctor and dietician will decide whether your child needs this formula. 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. Any diet changes should be made under the guidance of a dietician familiar with ASAL deficiency.

2. Medication

Most children with ASAL deficiency are given arginine supplements by mouth. Arginine helps the body remove ammonia from the blood. Your doctor will tell you whether your child needs these supplements and how much to take.

There are other medications that can help prevent high ammonia levels. These can either be taken by mouth or by tube feedings. Your metabolic doctor will decide whether your child needs this type of medication.

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

3. Blood tests

Your child will have regular blood tests to measure amino acid and ammonia 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

For some babies and children, even minor illnesses can lead to build up of ammonia. In order to prevent problems, call your doctor right away when your child has any of the following:

- loss of appetite
- low energy or extreme sleepiness
- vomiting
- fever
- infection or illness
- behavior or personality changes
- 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.

5. Liver transplantation

Liver transplant surgery has been tried in some children with ASAL who do not respond to other treatments. Liver transplant in children with ASAL deficiency does not cure the underlying disease and is only done when necessary.

Liver transplant is a major surgical procedure and has some risks. Individuals who have had a liver transplant must take medication for the rest of their lives to prevent their body from rejecting the donor liver. Many factors must be considered before surgery and this option should be discussed thoroughly with your child's doctors.

What happens when ASAL deficiency is treated?

With prompt and lifelong treatment, children with ASAL deficiency may be able to live healthy lives with typical growth and learning. Early treatment can help prevent high ammonia levels which decreases the risk for brain damage and intellectual disabilities.

Even with treatment, some children still have episodes of high ammonia. This can result in brain damage and can cause lifelong learning problems, intellectual disabilities, or spasticity.

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

Genes tell the body how to make various enzymes. The ASL gene instructs the body to make the ASAL enzyme. When the ASL genes do not work correctly, the ASAL enzyme is not made correctly or is not made at all.

How is ASAL deficiency inherited?

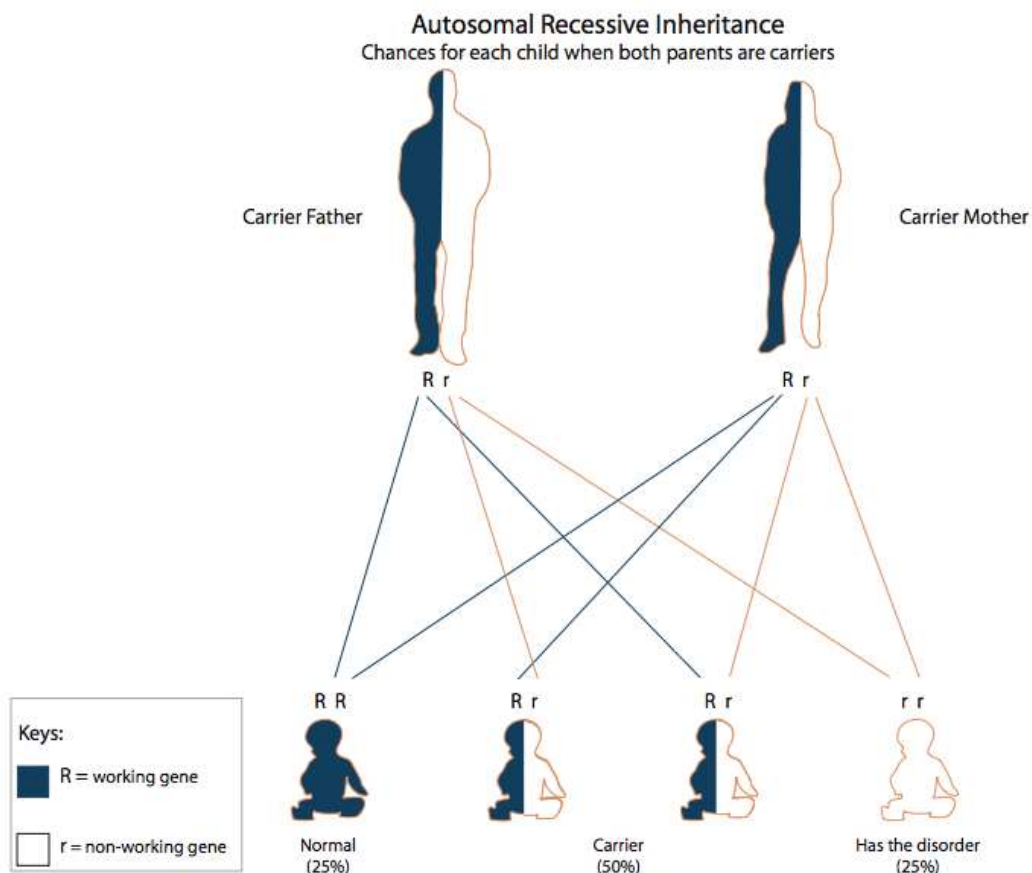
This condition is inherited in an autosomal recessive manner. It affects both boys and girls equally.

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

Parents of children with ASAL deficiency rarely have the condition themselves. Instead, each parent has a single non-working ASL gene. They are called

carriers. Carriers do not have the condition because their other ASL gene is working correctly.

When both parents are carriers, there is a 25% chance in each pregnancy for the child to have ASAL 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 ASAL deficiency. Genetic counselors can answer your questions about how the condition 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 ASAL deficiency is available. Genetic testing, also called DNA testing, looks for changes called variants, in the ASL genes. Ask your metabolic doctor or genetic counselor whether DNA testing is available to 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 tests on blood, urine, or skin samples can be done to confirm if your child has ASAL deficiency. Talk to your metabolic doctor or genetic counselor if you have questions about this type of testing.

Can you test during a future pregnancy?

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

If DNA testing would not be helpful, an enzyme test can be done on cells from the fetus. Again, the sample needed for this test is obtained by either CVS or amniocentesis.

Parents may 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 ASAL 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 ASAL deficiency or be carriers?

Having ASAL deficiency

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

ASAL deficiency carriers

Brothers and sisters who do not have the condition 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 ASAL 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 chance they are also at risk to have children with ASAL deficiency.

All states offer newborn screening for ASAL. However, 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 ASAL deficiency can be tested using blood, urine, or skin samples to see if they also have this disorder.

Carrier testing

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

If the gene changes cannot be found, DNA testing would not be helpful for carrier testing. However, other methods of carrier testing may be available. Your metabolic doctor or genetic counselor can answer your questions about carrier testing.

How many people have ASAL deficiency?

This is a rare condition. About one in every 70,000 babies in the United States is born with ASAL deficiency.

Does ASAL deficiency happen more frequently in a certain ethnic group?

ASAL deficiency does not happen more often in any specific race, ethnic group, geographical area, or country.

Does ASAL deficiency go by any other names?

ASAL deficiency is sometimes also called:

- Argininosuccinase deficiency
- Argininosuccinic aciduria
- Argininosuccinic acidemia
- Argininosuccinic acid lyase deficiency
- ASL deficiency
- ASA
- Arginine succinate lyase deficiency

Where can I find more information?

National Urea Cycle Disorders Foundation

<http://www.nucdf.org/>

Metabolic Support UK

<https://www.metabolicsupportuk.org>

Baby's First Test

<http://www.babysfirsttest.org>

Urea Cycle Disorders Consortium Registry

<https://www.rarediseasesnetwork.org/cms/ucdc>

Genetic Home Reference

<https://ghr.nlm.nih.gov/condition/argininosuccinic-aciduria>

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