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# Argininosuccinic Acidemia (ASA) – Amino Acid Disorder

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## What are amino acid disorders?

The amino acid disorders are a class of inherited metabolic conditions that occur when certain amino acids either cannot be broken down or cannot be produced by the body, resulting in the toxic accumulation of some substances and the deficiency of other substances.

## What is ASA?

Argininosuccinic Acidemia (ASA) is a urea cycle defect. The urea cycle is the body's system for getting rid of waste nitrogen and for synthesizing urea and the amino acid arginine. Hyperammonemia, a toxic build-up of ammonia in the blood, results when one of the enzymes in the urea cycle is not functioning properly.

## What is its incidence?

ASA affects about 1 in every 70,000 babies born in Ontario.

## What causes the disease?

Mutations in the gene for argininosuccinate lyase, one of the six enzymes in the urea cycle, result in enzyme that is not working well or is deficient.

## What are the clinical features of the disease?

Although babies with ASA may appear normal at birth, without treatment they may soon start to have symptoms of hyperammonemia, which can lead to coma and death. Symptoms of hyperammonemia can include lethargy, vomiting, poor appetite, seizures, hypotonia and muscle weakness, and breathing problems. Episodes of hyper-ammonemia may occur after a high-protein or large meal or after a prolonged

period without food – such as during an illness – because the body begins to break down the protein found in muscle tissue.

There is also a milder form of ASA with a later age of onset; the presentation is variable.

## How is the diagnosis confirmed?

The diagnosis is confirmed by measuring amino acid levels in blood and urine. Argininosuccinic acid and orotic acid levels will be elevated in the urine. Citrulline levels will be elevated in the blood while arginine levels will be low. Enzyme studies may also be helpful in confirming the diagnosis. Diagnostic testing is arranged by specialists at your regional treatment centre.

## What is the treatment of the disease?

A low protein diet and a special medical formula are often recommended in children with ASA. Dietary supplementation with arginine is also recommended. A medication called sodium phenylbutyrate may be considered. Children with ASA should also avoid going long periods without food. This special diet can prevent hyperammonemic episodes and their sequelae. In an acute symptomatic episode, IV glucose and fluids can be given, along with other medications that can help the body to get rid of harmful substances and to decrease the level of ammonia in the blood. Treatment is coordinated by specialists at your regional treatment centre.

## What is the outcome of treatment?

Babies who have a prolonged period of hyperammonemia may suffer from brain damage. Children who begin treatment before any symptoms of ASA occur may develop normally, however, some children may have some neurological impairment despite treatment.

## Can a family have more than one child with ASA?

Argininosuccinic acidemia is inherited as an autosomal recessive disease. Parents of a child with ASA are assumed to be carriers for the disease and have a 1 in 4 (25%) chance, in each pregnancy, of having another child with this condition. Prenatal testing for ASA can be done as early as 10-12 weeks of pregnancy. Genetic counselling to discuss the benefits of prenatal testing options in more detail is recommended.

Unaffected siblings of a child with ASA have a 2/3 chance of being carriers. ASA carriers are healthy and do not have symptoms of the disease.

### Resources

<http://www.newbornscreening.info/Parents/aminoaciddisorders/ASAL.html>

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

<http://www.geneclinics.org>