Kansas
Department of Health and Environment

Argininosuccinic Acidemia
Information for Health Professionals

Argininosuccinic acidemia is a urea cycle disorder in which the argininosuccinic acid lyase (ASAL) enzyme deficiency causes severe hyperammonemia.

✓ Clinical Symptoms

Hyperammonemia causes symptoms within the first few days of life which may include: feeding problems, lethargy, vomiting, and irritability. If untreated, high ammonia levels can cause muscle weakness, hypotonia, breathing problems, problems regulating body temperature, poor growth, enlarged liver, learning delays or intellectual disabilities, seizures, swelling of the brain, and coma. Death typically occurs within the first few days/weeks of life if untreated.

✓ Incidence

Argininosuccinic acidemia occurs in less than 1 out of every 100,000 births with no increased incidence based on sex, race, or ethnicity.

✓ Genetics of argininosuccinic acidemia

Mutations in the ASL gene cause argininosuccinic acidemia. Mutations in this gene reduce or eliminate the activity of the enzyme argininosuccinic acid lyase, which is necessary in the urea cycle for the conversion of argininosuccinic acid into arginine. Mutations ultimately lead to an accumulation of ammonia in the blood causing the symptoms of this condition.

✓ How do people inherit argininosuccinic acidemia?

Argininosuccinic acidemia is inherited in an autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition. Each pregnancy between carrier parents has a 25% chance of producing a child affected with argininosuccinic acidemia, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Immediate diagnosis and treatment of argininosuccinic academia in the neonatal period is critical to normal development and survival. Treatment is usually effective if started before ammonia levels are excessive. Hyperammonemia is a medical emergency that may require dialysis. Individuals should follow a life-long low-protein diet, which may require medical formulas and foods. Certain medications, such as sodium benzoate and/or sodium phenylacetate, as well as supplementation of arginine, may help prevent ammonia build-up. Episodes of high ammonia levels may require medications via IV or dialysis.

✓ Screening Methodology

Primary newborn screening for argininosuccinic acidemia utilizes tandem mass spectrometry to determine the level of citrulline. Individuals with a positive screen will have elevated levels of citrulline. False positive and false negative results are possible with this screening.

✓ What to do After Receiving Presumptive Positive ASA Screening Results

1) **The clinician should immediately check on the clinical status of the baby.**
2) **Consultation with a metabolic specialist is essential.**
3) **The specialist may request confirmatory lab tests on the baby.**
4) **Call KS Newborn Screening Program at 785-291-3363 with questions about results.**
5) **Report Clinical Findings to Newborn Screening Program at 785-291-3363.**
6) **Same birth siblings (twins, triplets) of infant diagnosed with argininosuccinic acidemia should be re-screened; addition testing of these siblings may be indicated.**
7) **Consider testing older siblings of affected individuals. Some people with mild or no symptoms may go undiagnosed.**

✓ Confirmation of Diagnosis

The diagnosis of argininosuccinic acidemia can be confirmed by performing quantitative plasma ammonia and plasma and urine amino acid analysis. Individuals will have the presence of argininosuccinic acid in both blood and urine. Levels of orotic acid may be elevated in urine. Symptomatic individuals will have significantly elevated blood ammonia levels.

✓ Communication of Results to Parents

If a baby has a presumptive positive argininosuccinic acidemia newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If the baby is diagnosed with argininosuccinic acidemia, the following points should be conveyed to parents:

- ***Parents should understand that treatment for argininosuccinic acidemia will be life-long.***
- ***Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring, and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include the following specialties: pediatrics, metabolic disease specialist, and dieticians. Regular blood analysis is needed.***
- ***Genetic counseling services may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation, contact:

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