Disease Name	**Argininosuccinic Acidemia**
Alternate name(s)	Argininosuccinase deficiency, Argininosuccinic aciduria, Argininosuccinic acid lyase deficiency, ASL deficiency, Agininosuccinyl-CoA lyase deficiency
Acronym	ASAL
Disease Classification	Amino Acid Disorder
Variants	Yes
Variant name	Late onset form
Symptom onset	Neonatal onset is typical, although later-onset may occur.
Symptoms	Anorexia, vomiting, lethargy, seizures and coma possibly leading to death.
Natural history without treatment	Mental and physical delays due to hyperammonemia, cyclic vomiting, seizures, cerebral edema and trichorrhexis nodosa. Coma and death possible.
Natural history with treatment	Normal mental and physical development is possible if treatment is initiated before hyperammonemic crisis.
Treatment	Protein restricted diet, arginine supplementation to help complete the urea cycle, essential amino acid supplementation, ammonia scavenging drugs in some cases and supplemental carnitine if patient has a secondary deficiency.
Other	Enzyme is genetically heterogeneous and patients may present in infancy/childhood with MR or seizures.
Physical phenotype	Trichorrhexis nodosa (short, dry, brittle hair) in older patients.
Inheritance	Autosomal recessive
General population incidence	1:70,000
Ethnic differences	No
Population	N/A
Ethnic incidence	N/A
Enzyme location	Erythrocytes, liver and fibroblasts
Enzyme Function	Catalyzes the conversion of argininosuccinate to fumurate and arginine as part of the urea cycle.
Missing Enzyme	Argininosuccinate lyase
Metabolite changes	Hyperammonemia
Prenatal testing	Enzyme assay in cultured amniocytes. DNA possible if mutations known. Analyte testing of amniocytes.
MS/MS Profile	Citrulline is elevated, may show elevated argininosuccinic peak.
OMIM Link	http://www.ncbi.nlm.nih.gov/omim/207900
Genetests Link	www.genetests.org
Support Group	National Urea Cycle Disorders Foundation http://www.nucdf.org/ National Coalition for PKU and Allied Disorders http://www.pku-allieddisorders.org/ Children Living with Inherited Metabolic Diseases http://www.climb.org.uk/

Newborn Screening ACT Sheet
[Increased Citrulline]
Amino Aciduria/Urea Cycle Disorder

Differential Diagnosis: Citrullinemia I, argininosuccinic acidemia, citrullinemia II (citrin deficiency), pyruvate carboxylase deficiency.

Condition Description: The urea cycle is the enzyme cycle whereby ammonia is converted to urea. In citrullinemia and in argininosuccinic acidemia, defects in argininosuccinic acid (ASA) synthetase and lyase, respectively, in the urea cycle result in hyperammonemia and elevated citrulline

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YOU SHOULD TAKE THE FOLLOWING ACTIONS:

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea).
- Immediate consult with pediatric metabolic specialist.
- Evaluate the newborn (poor feeding, vomiting, lethargy, hypotonia, tachypnea, seizures, and signs of liver disease). Measure blood ammonia. If any sign is present or infant is ill initiate emergency treatment for hyperammonemia in consultation with metabolic specialist.
- Transport to hospital for further treatment in consultation with metabolic specialist.
- Initiate timely confirmatory/diagnostic testing and management, as recommended by specialist.
- Provide family with basic information about hyperammonemia.
- Report findings to newborn screening program.

Diagnostic Evaluation: Plasma **ammonia** to determine presence of hyperammonemia. In citrullinemia, plasma amino acid analysis will show increased **citrulline** whereas in argininosuccinic acidemia, **argininosuccinic acid** will also be present. **Orotic acid**, which may be detected by urine organic analysis, may be increased in both disorders. **Note:** "Urine organic analysis" may not identify orotic acid in some laboratories because of the tests employed. In citrin deficiency, liver enzymes, lactic acid and bilirubin may be elevated. Blood lactate and pyruvate will be elevated in pyruvate carboxylase deficiency.

Clinical Considerations: Citrullinemia and argininosuccinic acidemia can present acutely in the newborn period with hyperammonemia, seizures, failure to thrive, lethargy, and coma. Later signs include mental retardation. Citrin deficiency may present with cholestatic liver disease in the newborn period. Pyruvate carboxylase deficiency produces coma seizures and life-threatening ketoacidosis. Treatment for ASA and citrullinemia is to promote normal growth and developmental and to prevent hyperammonemia.

Additional Information:

Gene Reviews
Genetics Home Reference

Referral (local, state, regional and national):

Testing
Clinical Services