

**Disease Name:**

**ARGINASE DEFICIENCY**  
(ARGINASE DEFICIENCY; HYPERARGININEMIA)

**Classification:** Urea Cycle Defect

**Genetic** **Inheritance:** Autosomal recessive

**Information:** **Population Incidence:** 1:300,000 births

**Ethnic Incidence:** No known population at increased risk

**Gene & Location:** A1 gene on 6q23

**Common Mutation:** None- more than 20 mutations identified

**OMIM #** \*207800

**Disease** **Symptom Onset:** Symptoms begin in first year of life.

**Information:**

**Symptoms:** Infants present with irritability, poor feeding, vomiting and failure to thrive. Typically exhibit neurologic symptoms clumsiness, toe-walking by age 2-3 years, progressing to spastic quadriparesis, seizures, psychomotor retardation, hyperactivity, mental retardation and growth failure. There is considerable genetic heterogeneity. A few cases have presented at birth with cholestatic jaundice, liver failure and death. There may be microcephaly especially if untreated. Growth may be less than the 3<sup>rd</sup> percentile, weight relatively preserved

**Physical Findings:** No dysmorphisms.

**Treatment:** The mainstay is natural protein restriction, arginine-free amino acid supplements and sodium benzoate or phenylbutyrate that generally normalize the arginine levels. As the body makes most of its arginine de novo, dietary restriction must be monitored closely. Phenylbutyrate or benzoate keep ammonia under control and provide an additional nitrogen disposal system.

**Natural History without treatment:** Progressive neurological deterioration with episodes of hyperammonemia and coma.

**Natural History with treatment:** Treatment prior to symptoms in those ascertained because of prior affected siblings have normal development, and those treated early in the course of the disease appear to have some recovery of functioning. For those detected on newborn screening, follow-up data is not available.

**Metabolic Information:**

**Missing Enzyme & Location:**

The enzyme involved is liver arginase. It converts arginine to urea and ornithine in the urea cycle to dispose of excess nitrogen. Ureagenesis continues and severe hyperammonemia seen in other UCD is usually prevented by the up-regulation of the kidney arginase isomer, A11.

**MS/MS profile:**

Arginine- elevated  
Citrulline-elevated

**Prenatal testing:**

Testing by cordocentesis is possible; enzyme analysis is only possible on fetal red blood cells- no affected individuals have been identified in this manner, but it has been done and identified unaffected individuals.

**Miscellaneous Information:**

Prepared for the NW Regional Newborn Screening Program by Sara Copeland MD, Judith Tuerck RN MS and Lorinda Paradise at OHSU in Portland, OR.

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