

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 (ASA), defects in ASA synthetase and lyase, respectively, in the urea cycle result in hyperammonemia and elevated citrulline.

Conditions associated with this analyte have been identified by the Society of Inherited Metabolic Disorders (SIMD) as critical, and require immediate action.

MEDICAL EMERGENCY - Take the Following IMMEDIATE Actions:

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea).
- Immediate telephone consultation with pediatric metabolic specialist. (See attached list.)
- 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.
- Initial testing: Immediate plasma ammonia, plasma quantitative amino acids, and liver function tests. Consider urine orotic acid test.
- Repeat newborn screen if second screen has not been done.
- 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 quantitative 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 intellectual disability. 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 development and to prevent hyperammonemia.

Additional Information:

American College of Medical Genetics and Genomics (ACMG)

<https://www.acmg.net/StaticContent/ACT/Citrullinemia.pdf>

Genetics Home Reference

<http://ghr.nlm.nih.gov/condition=citrullinemia>

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<http://www.newbornscreening.info/Pro/aminoaciddisorders/ASAS.html>

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

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

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