ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

ACT Sheet

Newborn Screening ACT Sheet

[Elevated Citrulline]

Amino Acidemia/Urea Cycle Disorder

Differential Diagnosis: Citrullinemia type I, argininosuccinic aciduria, citrullinemia type II. Other rarer cause: pyruvate carboxylase deficiency

Condition Description: Elevated citrulline results from one of several defects affecting the urea cycle, the pathway that converts ammonia to urea. In addition to elevated citrulline, these conditions are associated with hyperammonemia which may be severe and life-threatening.

You Should Take the Following IMMEDIATE Actions:

- Inform family of the newborn screening result.
- Ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea).
- Consult with the pediatric metabolic specialist the same day.
- Evaluate the newborn (poor feeding, vomiting, lethargy, hypotonia, tachypnea, seizures, signs of liver disease). If any of these signs are present or if the newborn is ill, transport to the hospital for further treatment in consultation with the metabolic specialist.
- Initiate confirmatory/diagnostic testing and management, as recommended by the specialist.
- Provide family with basic information about the possible diagnoses and their management.
- Report final diagnostic outcome to newborn screening program.

Diagnostic Evaluation: Plasma ammonia: is markedly elevated in citrullinemia type I and is less pronounced in the other conditions. Plasma amino acids: Citrulline is usually markedly elevated in citrullinemia type I. Citrulline and other amino acids including tyrosine are elevated in citrullinemia type II. Citrulline and argininosuccinic acid are elevated in argininosuccinic aciduria. Urine amino acids: Argininosuccinic acid is more readily detected in urine than plasma and is elevated in argininosuccinic aciduria. Molecular genetic or enzyme testing may be required to differentiate the various disorders and establish the diagnosis.

Clinical Considerations: Citrullinemia and argininosuccinic aciduria can present acutely in the newborn period with hyperammonemia, seizures, failure to thrive, lethargy, and coma. Later signs include developmental delay and hepatic dysfunction. Although treatment with a low protein diet to prevent hyperammonemia helps optimize growth and development, the outcome can be variable. Citrin deficiency may present with cholestatic liver disease in the neonate. Pyruvate carboxylase deficiency produces coma, seizures, and life-threatening ketolacticacidosis.

Local Referral Site:

UAB Department of Genetics
VHL108B 1670 University Blvd
Birmingham, AL 35233
Phone: 205-996-6983
Fax: 205-975-6389

Alabama Newborn Screening Program
1-866-928-6755

Additional Information:

Emergency Protocols (New England Consortium of Metabolic Programs)
https://www.newenglandconsortium.org/argininosuccinic-acid-synthetase-deficiency-citrullinemia-as

Medline Plus
https://medlineplus.gov/genetics/condition/citrullinemia/

Condition Information for Families-HRSA Newborn Screening Clearinghouse
https://newbornscreening.hrsa.gov/conditions/citrullinemia-type-i