

# 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 <u>IMMEDIATE</u> 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.

#### Additional Information:

How to Communicate Newborn Screening Results Emergency Protocols (New England Consortium of Metabolic Programs) Gene Reviews Medline Plus Condition Information for Families- HRSA Newborn Screening Clearinghouse ClinGen Actionability Report

Referral (local, state, regional, and national):

Find a Genetics Clinic Directory Genetic Testing Registry

This practice resource is designed primarily as an educational resource for medical geneticists and other clinicians to help them provide quality medical services. Adherence to this practice resource is completely voluntary and does not necessarily assure a successful medical outcome. This practice resource should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. In determining the propriety of any specific procedure or test, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this practice resource. Clinicians also are advised to take notice of the date this practice resource was adopted, and to consider other medical and scientific information that becomes available after that date. It also would be prudent to consider whether intellectual property interests may restrict the performance of certain tests and other procedures.

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## **ACT Sheet**

[Elevated Citrulline] Citrullinemia Types 1 & 2, Argininosuccinic Aciduria, Pyruvate Carboxylase Deficiency

### State and Other Resources

#### State Newborn Screening Program

Newborn Screening, State of Rhode Island Department of Health 401-921-7619, health.ri.gov/newbornscreening/

#### Genetics/Metabolic Consultants

Division of Genetics, Lifespan Physician's Group, Hasbro Children's Hospital 401-444-4000, www.lifespan.org/centers-services/childrens-neurodevelopment-center/genetics-and-dysmorphology

#### Information for Clinicians and Families

Rhode Island Medical Home Portal (see also the Parents & Families section) ri.medicalhomeportal.org/newborn/citrullinemia-type-i

#### Parent/Family Support

National Urea Cycle Disorders Foundation www.nucdf.org/

#### National Resources (with web addresses)

#### **Additional Information**

How to Communicate Newborn Screening Results www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritabledisorders/Resources/achdnc-communication-guide-newborn.pdf

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

Gene Reviews www.ncbi.nlm.nih.gov/books/NBK1458/

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

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

#### Referral (local, state, regional and national)

Find a Genetics Clinic Directory clinics.acmg.net

Genetic Testing Registry www.ncbi.nlm.nih.gov/gtr/

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