

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

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.
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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 development and to prevent hyperammonemia.

Additional Information:

[Gene Reviews](#)

[Genetics Home Reference](#)

Referral (local, state, regional and national):

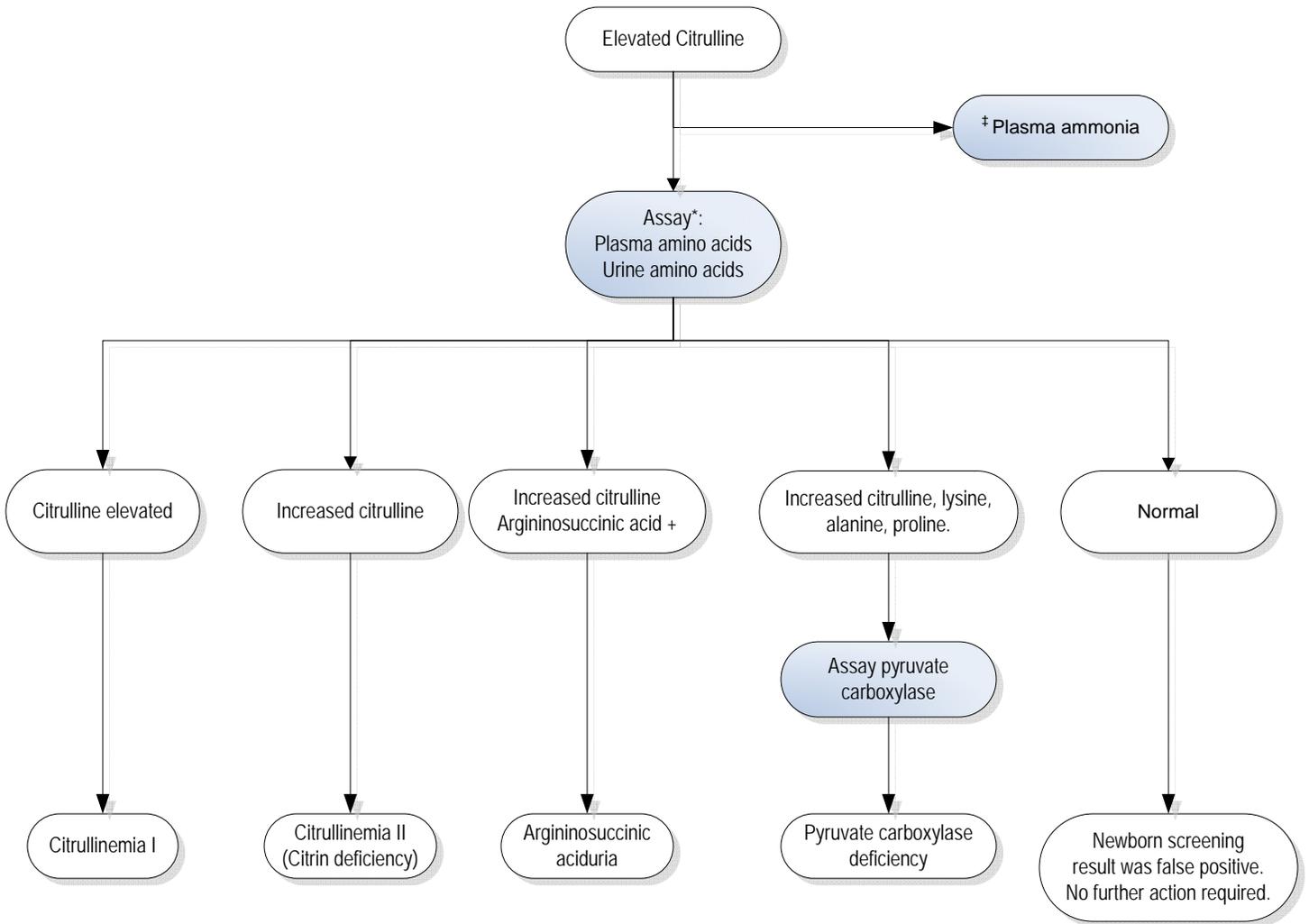
[Testing](#)

[Clinical Services](#)

Disclaimer: This guideline is designed primarily as an educational resource for clinicians to help them provide quality medical care. It 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. Adherence to this guideline does not necessarily ensure a successful medical outcome. 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 guideline. Clinicians also are advised to take notice of the date this guideline was adopted, and to consider other medical and scientific information that become available after that date.



Citrulline Elevated



Actions are shown in shaded boxes; results are in the unshaded boxes.

Abbreviations/Key

‡ = When the positive predictive values of screening are sufficiently high and the risk to the infant is high, some initiate diagnostic studies that are locally available at the same time as confirmation of the screening result is done.

* = Urine organic acids (orotic) may be informative.

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