INCREASED CITRULLINE
Amino Aciduria/Urea Cycle Disorder

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

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 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.

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** may be increased in both disorders which can be determined by urine organic acid analysis. In citrin deficiency, liver enzymes, lactic acid and bilirubin may be elevated. For pyruvate carboxylase deficiency blood lactate and pyruvate will be elevated.

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 developmental and to prevent hyperammonemia.

Additional Information:
(Click on the name to take you to the website. Complete URLs are listed in the Appendix)

Gene Tests/Gene Clinics

Genetics Home Reference

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

Testing

Clinical

Contact local/regional University-affiliated medical center for biochemical geneticist

(Funded in part through MCHB/HRSA/HHS grant #U22MC03957)

APPENDIX: Resources with Full URL Addresses

Additional Information:

Gene Tests/Gene Clinics
http://www.genetests.org/servlet/access?db=geneclinics&site=gt&id=8888891&key=HWrct-uSq-Lup&gry=&fcn=y&fw=b8Mv&filename=/profiles/ctlm/index.html

Genetics Home Reference
http://ghr.nlm.nih.gov/condition=citrullinemia

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

Testing http://biochemgen.ucsd.edu/UCSDW3BG/LabChoose.asp

Clinical
http://www.genetests.org/servlet/access?id=8888891&key=UoSgD2xOEgFBT&fcn=y&fw=kT1e&filename=/clinicsearch/searchclinic.html

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