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ACT Sheet

Newborn Screening ACT Sheet

[Increased Tyrosine]
Tyrosinemia

Differential Diagnosis: Tyrosinemia type I (hepatorenal); tyrosinemia type II (oculocutaneous); tyrosinemia type III; transient tyrosinemia of the neonate (TTN); liver disease; prematurity.

Condition Description: Elevated tyrosine can be caused by inherited defects in tyrosine metabolism, the pathway that converts tyrosine (from dietary protein) to other compounds integral to metabolism. Tyrosinemia type I (fumarylacetoacetate hydrolase deficiency) is accompanied by elevated succinylacetone and other toxic byproducts that damage the liver and kidneys. Tyrosinemia types II and III (tyrosine aminotransferase deficiency and 4-hydroxyphenylpyruvate dioxygenase deficiency, respectively) both have elevated plasma tyrosine, but do not have the toxic tyrosine byproducts seen in tyrosinemia type I.

You Should Take the Following Actions:

- Inform family of newborn screening result.
- Ascertain clinical status (diarrhea, vomiting, liver disease, failure to thrive).
- Consult with pediatric metabolic specialist.
- Evaluate the newborn for signs of jaundice, failure to thrive, diarrhea, vomiting.
- Initiate confirmatory/diagnostic testing and management, as recommended by the specialist.
- Provide the family with basic information about tyrosinemia and its management.

- Report final diagnostic outcome to newborn screening program.

Diagnostic Evaluation: Plasma amino acids: Tyrosine is elevated in all forms of tyrosinemia. Urine organic acids or quantitative succinylacetone: Tyrosine metabolites are elevated in all forms of tyrosinemia. Succinylacetone is elevated only in tyrosinemia type I. Because succinylacetone is included in many state NBS panels, review of the initial NBS results can help differentiate tyrosinemia type I from types II or III. Additional molecular genetic testing may be required.

Clinical Considerations: Tyrosinemia type I is the most severe form but is usually asymptomatic in the neonate. If untreated, it will cause failure to thrive, liver disease, and renal failure in the first year of life. Nitisinone (NTBC) treatment along with the dietary restriction of phenylalanine and tyrosine usually prevents these features. Tyrosinemia type II is asymptomatic in the neonate but can cause hyperkeratosis of the skin, corneal ulcers, and in some cases, developmental delay in the absence of dietary restriction. Tyrosinemia type III is extremely rare and may present similarly to tyrosinemia type II. Some newborns have transient tyrosinemia (TTN) that resolves within several weeks.

Additional Information:

- How to Communicate Newborn Screening Results
- Gene Reviews
- Medline Plus
- Condition Information for Families- HRSA Newborn Screening Clearinghouse
  - Tyrosinemia Type I
  - Tyrosinemia Type II
  - Tyrosinemia Type III

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

- Find a Genetics Clinic Directory
- Genetic Testing Registry
  - Tyrosinemia Type I
  - Tyrosinemia Type II
  - Tyrosinemia Type IIIa

State and Other Resources

State Newborn Screening Program

Metabolic (Bloodspot) Screening, Montana's Newborn Screening Programs
406-444-0984, dphhs.mt.gov/ecfsd/cshs/newbornscreeningprograms/

Short-term Follow-up Coordinator - Crystal Fortune, MT Laboratory Services Bureau
406-444-0930 or 800-821-7284 cfortune@mt.gov

Genetics/Metabolics Consultants

Shodair Children's Hospital Medical Genetics Staff will contact you with recommendations.
Metabolic Clinic: 406-444-1099; Clinics held across Montana: 406-444-1016
shodair.org/about-shodair/contact/

If emergency consultation with a metabolic specialist is necessary, contact One Call (24/7) at Children's Hospital Colorado (800-525-4871) and ask to speak to the metabolic specialist on call.

Information for Clinicians and Families

Medical Home Portal (see also the Parents & Families section)
mt.medicalhomeportal.org/newborn/tyrosinemia-type-1

Parent/Family Support

Tyrosinemia Society
www.tyrosinemia.org

National Resources (with web addresses)

Additional Information

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

Gene Reviews
www.ncbi.nlm.nih.gov/books/NBK1319/

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

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

Referral (local, state, regional and national)

Find a Genetics Clinic Directory
clinics.acmg.net

Genetic Testing Registry
www.ncbi.nlm.nih.gov/gtr/conditions/C0268490/
www.ncbi.nlm.nih.gov/gtr/conditions/C0268487/
www.ncbi.nlm.nih.gov/gtr/conditions/C0268623/