

# 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:** <u>Plasma amino acids:</u> Tyrosine is elevated in all forms of tyrosinemia. <u>Urine organic acids or</u> <u>quantitative succinylacetone:</u> 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 <u>molecular genetic testing</u> 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 III

 Tyrosinemia Type III

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

 Find a Genetics Clinic Directory

 Genetic Testing Registry

 Tyrosinemia Type II

 Tyrosinemia Type III

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 specime. Clinicians are encouraged to document the reasons for the use of a particular procedure 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. @ American College of Medical Genetics and Genomics, 2022 Content Updated: March 2022 (Funded in part through MCHB/HRSA/HHS grant #U22MC03957; <u>National Coordinating Center for the Regional Genetics</u> Networks)



#### Local Resources (Insert Local Website Links) State Resource Site (Insert Website Information)

Name	
URL	
Comments	

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Comments	

# Appendix (Resources with Full URL Addresses)

#### Additional Information

How to Communicate Newborn Screening Results

 https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/Resources/achdnccommunication-guide-newborn.pdf

Gene Reviews

• https://www.ncbi.nlm.nih.gov/books/NBK1319/

Medline Plus

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

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

Find a Genetics Clinic Directory

#### <u>https://clinics.acmg.net</u>

Genetic Testing Registry

- https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268490/
- https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268487/
- https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268623/

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