

# **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** 

Networks)

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

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

#### **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

Medical Home Portal (see also the Parents & Families section) ri.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/