



**NEWBORN SCREENING
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Tyrosinemia

Information for Physicians and Other Health Care Professionals

Definition The tyrosinemias are a group of inherited disorders of amino acid metabolism, each caused by an enzymatic defect affecting tyrosine catabolism, which leads to elevated levels of tyrosine.

Newborn screening in Illinois includes testing for the following type of tyrosinemia:

Tyrosinemia type I (hepatorenal tyrosinemia or fumarylacetoacetate hydrolase (FAH) deficiency)

Note: Some cases of tyrosinemia may not be detected by newborn screening when specimens are collected in the first few days of life, as tyrosine levels may not be sufficiently elevated for detection by tandem mass spectrometry.

Clinical Symptoms There is variability in age of onset, depending on the type of tyrosinemia. In some forms of the disease, children may be clinically diagnosed in the neonatal period.

Type I, the most severe form of tyrosinemia, results in the accumulation of tyrosine and its metabolites in the liver causing severe liver disease. Kidney function and peripheral nerves also are affected. Patients with Type I may have acute liver crisis, episodes of peripheral neuropathy and chronic liver disease. Effects on the kidneys can range from mild tubular dysfunction to renal failure. Early symptoms can include fever, diarrhea, vomiting, enlarged liver, jaundice, rickets, lethargy and irritability.

Newborn Screening and Definitive Diagnosis In Illinois, newborn screening for tyrosinemia type I is performed using tandem mass spectrometry. False positive and false negative results may be possible with this screening. Not all cases of tyrosinemia will be detected by newborn screening. Infants with a presumptive positive screening test require prompt follow-up. **When receiving a presumptive positive result, the clinician should *immediately* check on the clinical status of the baby and refer the infant to a metabolic disease specialist.**

Treatment Early diagnosis and prompt treatment is essential for an improved prognosis. Individuals with tyrosinemia need to be on a special diet and medications throughout life. Treatment of tyrosinemia type I includes a diet restricted in tyrosine and phenylalanine. Treatment with Nitisinone has been successful and has improved the outcome in tyrosinemia type I. If liver disease is already advanced before initiation of treatment, liver transplantation may be necessary.

Incidence Tyrosinemia is a rare condition, with an incidence of less than 1 in 100,000 births. However, tyrosinemia type I has an incidence of approximately 1 in 12,500 births in populations of French Canadian ethnicity.

Inheritance Pattern Tyrosinemia is inherited in an autosomal recessive pattern. As an autosomal recessive disorder, the parents of a child with this condition are unaffected, healthy carriers of the condition, and have one normal gene and one abnormal gene. With each pregnancy, carrier parents have a 25 percent chance of having a child with two copies of the abnormal gene, resulting in tyrosinemia. Carrier parents have a 50 percent chance of having a child who is an unaffected carrier, and a 25 percent chance of having an unaffected, non-carrier child. These risks would hold true for each pregnancy. All siblings of infants diagnosed with tyrosinemia should be tested; and genetic counseling services should be offered to the family.

Physiology Tyrosinemia type I is an inherited disorder that results from deficiency of an enzyme needed to metabolize tyrosine. This deficiency causes an increase in plasma tyrosine and related metabolites, resulting in the disease manifestations.

Key Points for Parents Avoid overly alarming the child's parents if the diagnosis has not yet been confirmed. If the child needs additional testing or diagnostic evaluation, make certain that the parents understand the importance of following the pediatrician's and/or specialist's recommendations for additional testing and referrals.

Follow-up After Confirmation of Diagnosis These guidelines should be followed after a diagnosis of tyrosinemia has been confirmed:

1. Parents should understand that treatment is lifelong and that compliance with dietary management is imperative to the child's health, growth and development.
2. Infants and children with tyrosinemia should have regular follow-up appointments with a metabolic disease specialist.
3. Long-term management, monitoring and compliance with treatment recommendations are essential to the child's well-being. A multi-disciplinary approach including the following specialities is recommended: pediatrics, genetics and nutrition. Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented.
4. Genetic counseling services are recommended. A list of genetic counselors and geneticists whose services are available through the Illinois Department of Public Health should be given to the parents if they have not already seen a geneticist.
5. Provide a list of available support services in the community, such as the local health department, Early Intervention service providers and the University of Illinois at Chicago Division of Specialized Care for Children (DSCC).
6. Additional information about newborn screening can be found at:
 - Baby's First Test: <http://www.babysfirsttest.org/>
Health Resource and Service Administration (HRSA), Grant no. U36MC16509, Quality Assessment of the Newborn Screening System.
 - National Center for Biotechnology Information: <http://www.ncbi.nlm.nih.gov/gtr/>
National Center for Biotechnology Information, U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda MD, 20894 USA.

