

What is tyrosinemia type 1?

Tyrosinemia type 1 is an inherited disease characterized by progressive liver disease, kidney disease, and rickets. In individuals with tyrosinemia type 1, the body is unable to break down the amino acid tyrosine, leading to the build-up of tyrosine and its byproducts. Tyrosinemia type 1 is also known as fumarylacetoacetate hydrolase (FAH) deficiency.^{1,2}

What are the symptoms of tyrosinemia type 1 and what treatment is available?

Tyrosinemia type 1 is typically diagnosed within the first year of life, with earlier onset being associated with more severe disease. The symptoms of tyrosinemia type 1 in untreated children include:^{1,2}

- Vomiting
- Diarrhea
- Jaundice (yellowing of skin and white of eyes)
- Cabbage-like odor
- Increased tendency to bleed (especially nose bleeds)
- Corneal crystals (causes eye irritation and light sensitivity)
- Liver disease and/or liver failure
- Kidney disease
- Growth failure
- Rickets (bone thinning)
- Neurologic crises (may affect breathing, mental state, and pain sensation)
- Increased risk of liver cancer

Once diagnosed, individuals with tyrosinemia type 1 are treated with medication and a low-protein diet. This improves many symptoms, including liver function, kidney function, growth, and rickets. Medication also can prevent neurological crises and decrease corneal crystals. This treatment has resulted in a reported survival rate of greater than 90%. Liver transplantation may be an option for some individuals.²

Tyrosinemia type 1 is included in newborn screening in most states in the United States.³

How is tyrosinemia type 1 inherited?

Tyrosinemia type 1 is an autosomal recessive disease caused by mutations in the *FAH* gene.² An individual who inherits one copy of an *FAH* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *FAH* mutations, one from each parent, is expected to be affected with tyrosinemia type 1.

If both members of a couple are carriers of a mutation in the same gene, the risk of having an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

Who is at risk for tyrosinemia Type 1?

Tyrosinemia type 1 occurs worldwide with an estimated incidence of 1 in 100,000 to 120,000.²

Carrier frequencies in select populations

Population	Estimated carrier frequency
French-Canadian	1 in 56 ⁴
Finnish	1 in 122 ²
Ashkenazi Jewish	1 in 158 ²
General	1 in 158 ²

Having a relative who is a carrier or who is affected can increase an individual's risk of being a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

National Organization for Rare Disorders (NORD): <http://www.rarediseases.org/rare-disease-information/rare-diseases/byID/446/viewAbstract>

Screening, Technology and Research in Genetics:
<http://www.newbornscreening.info/Parents/aminoaciddisorders/Tyrosinemia.html>

References

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3. National Newborn Screening Status Report. November 2, 2014. Available at: <http://genes-r-us.uthscsa.edu/sites/genes-r-us/files/nbsdorders.pdf>. Accessed January 6, 2016.
4. Bergeron P *et al.* Hereditary tyrosinemia in the province of Quebec: Prevalence at birth and geographic distribution *Clin Genet* 1974;5:157-162.