

### What is primary hyperoxaluria?

Primary hyperoxaluria is an inherited disease characterized by recurrent kidney stones and eventual kidney failure. Individuals with primary hyperoxaluria have defects in one of two enzymes produced by the liver: those with type 1 have defects in alanine-glyoxylate-aminotransferase, and those with type 2 have defects in glyoxylate reductase/hydroxypyruvate reductase.<sup>1</sup> The two enzymes prevent the build-up of oxalate, a waste product normally produced by cells. Symptoms are due to the accumulation of oxalate, which combines with calcium to form crystals that build up in the body, primarily in the kidneys.<sup>1</sup>

### What are the symptoms of primary hyperoxaluria and what treatment is available?

Primary hyperoxaluria varies in severity and age at onset, even within families.<sup>3</sup> Onset of symptoms typically occurs during childhood, although some individuals may not be diagnosed until later in life.<sup>4</sup> Approximately 20% of individuals develop severe disease by six months of age, but the majority of individuals develop symptoms in late childhood or early adolescence. It is estimated that 25% of individuals are not diagnosed until adulthood. Typically, the earlier the symptoms begin, the more severe the course of disease.

Symptoms of primary hyperoxaluria may include:<sup>2,4</sup>

- Recurrent nephrolithiasis (kidney stones)
- Nephrocalcinosis (build of calcium in the kidneys)--rare in primary hyperoxaluria type 2
- End-stage renal disease (kidney failure)

End-stage renal disease can occur as early as infancy and is present in half of children at the time of diagnosis. The typical age for end-stage renal disease is 25 to 40 years old.<sup>2,3</sup> Once end-stage renal disease occurs, additional symptoms may arise, including:<sup>2,4</sup>

- Bone pain and fracture
- Vision problems
- Peripheral neuropathy (pain and/or tingling in hands and feet)
- Heart problems

There is no cure for primary hyperoxaluria. Treatment includes drinking large amounts of water and may also include nutrition supplements and medications that can slow or prevent the formation of kidney stones. Some individuals may benefit from treatment with pyridoxine (vitamin B<sub>6</sub>).<sup>2</sup> Avoiding certain foods high in oxalate, such as chocolate, rhubarb, and spinach, and high amounts of vitamins C and D may also be recommended. Dialysis is necessary for individuals with end-stage renal disease. Kidney and/or liver transplant may also be considered.<sup>2,3,4</sup>

### How is primary hyperoxaluria inherited?

Primary hyperoxaluria is an autosomal recessive disease caused by mutations in one of two different genes, *AGXT* (type 1) or *GRHPR* (type 2).<sup>1</sup> An individual who inherits one mutation in either of these genes is a carrier and is not expected to have related health problems. An individual who inherits two mutations in the same gene, one from each parent, is expected to be affected with primary hyperoxaluria. For example, a child with two *AGXT* mutations is expected to be affected, and a child with one *AGXT* mutation and one *GRHPR* mutation is a carrier.

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 primary hyperoxaluria?

Primary hyperoxaluria can occur in individuals of all races and ethnicities. Type 1 appears to be most common in individuals from Tunisia, Kuwait, and Iran, as well as in Israeli Arabs and Druze. The estimated incidence of type 1 in Europe is 1 in 120,000,<sup>2</sup> with a calculated carrier frequency of 1 in 173. The worldwide carrier frequency of type 1 is approximately 1 in 289.<sup>2</sup> Primary hyperoxaluria type 2 is less common than type 1 and the incidence is unknown.<sup>4</sup>

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?

Oxalosis and Hyperoxaluria Foundation: <http://www.ohf.org>

Rare Kidney Stone Consortium: <http://www.rarekidneystones.org>

### References

1. Primary hyperoxaluria. *Genetics Home Reference* Available at:<http://ghr.nlm.nih.gov/condition/primary-hyperoxaluria> Accessed on March 7, 2012
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4. Rumsby, G Primary hyperoxaluria type 2. *GeneReviews* Available at:<http://www.ncbi.nlm.nih.gov/books/NBK2692/> Accessed on: March 7, 2012.