

What is dihydropyrimidine dehydrogenase deficiency?

Dihydropyrimidine dehydrogenase deficiency is an inherited disease of variable severity that is typically characterized by the presence of childhood-onset neurological problems. Individuals with dihydropyrimidine dehydrogenase deficiency have defects in making the enzyme dihydropyrimidine dehydrogenase that is needed to break down uracil and thymine (two of the basic building blocks of RNA and DNA). Symptoms associated with dihydropyrimidine dehydrogenase deficiency are a result of the toxic build-up of uracil and thymine in the body. Dihydropyrimidine dehydrogenase deficiency is also known as dihydropyrimidinuria and familial pyrimidemia.¹

What are the symptoms of dihydropyrimidine dehydrogenase deficiency and what treatment is available?

The severity of dihydropyrimidine dehydrogenase deficiency varies widely in symptoms and age at onset. Some individuals show no symptoms while others have varying levels of neurological issues. The severe form, which is rare, usually presents in infancy. Symptoms of dihydropyrimidine dehydrogenase deficiency may include:^{1,2}

- Seizures
- Developmental delays
- Intellectual disability
- Hypertonia (increased muscle tone)
- Microcephaly (small head size)
- Delayed growth
- Autistic features

There is no cure for dihydropyrimidine dehydrogenase deficiency. Treatment includes supportive care for symptoms. All individuals with dihydropyrimidine dehydrogenase deficiency, whether symptomatic or not, are unable to break down certain drugs used to treat cancer. If administered, complications (including infections and potentially life-threatening bleeding problems) may arise.¹ If affected individuals are diagnosed with cancer, therapeutic decisions may be tailored to modify or avoid treatment with certain chemotherapy drugs.³

How is dihydropyrimidine dehydrogenase deficiency inherited?

Dihydropyrimidine dehydrogenase deficiency is an autosomal recessive disease caused by mutations in the *DPYD* gene.¹ An individual who inherits one *DPYD* gene mutation is a carrier. Carriers usually do not have related health problems, but they do have an increased risk of complications when treated with certain chemotherapy drugs.¹ An individual who inherits two *DPYD* gene mutations, one from each parent, is expected to be affected with dihydropyrimidine dehydrogenase deficiency, although clinical severity is highly variable.

If both members of a couple are carriers, 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 dihydropyrimidine dehydrogenase deficiency?

Dihydropyrimidine dehydrogenase deficiency can occur in individuals of all races and ethnicities. It has been reported more frequently in individuals of Northern European ancestry, but the overall incidence is unknown.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 Information Centre for Metabolic Diseases: <http://www.climb.org.uk/>

Office of Rare Diseases Research: <http://rarediseases.info.nih.gov/GARD/Disease.aspx?PageID=4&DiseaseID=19>

References

1. Dihydropyrimidine dehydrogenase deficiency. *Genetics Home Reference*. Available at: <http://ghr.nlm.nih.gov/condition/dihydropyrimidine-dehydrogenase-deficiency>. Accessed: March 29, 2012.
2. Van Kuilenburg A *et al.* Genotype and phenotype in patients with dihydropyrimidine dehydrogenase deficiency. *Hum Genet.* 1999;104:1-9.
3. Deenen M *et al.* Relationship between Single Nucleotide Polymorphisms and Haplotypes in *DPYD* and Toxicity and Efficacy of Capecitabine in Advanced Colorectal Cancer. *Clin Cancer Res* 2011; 17: 3455-3468.