SickKids | Genome Diagnostics

Dopamine Beta-Hydroxylase Deficiency

Dopamine Beta-Hydroxylase deficiency (DBHD) is a rare form of primary autonomic failure. Dopamine beta-hydroxylase is a copper-containing enzyme important in the synthesis of catecholamines, namely the conversion of dopamine to norepinephrine. Biochemical findings in individuals with DBHD include complete absence of plasma norepinephrine and epinephrine in conjunction with elevated plasma dopamine levels. DBHD is mainly characterized by impaired exercise tolerance, severe orthostatic hypotension and persistent ptosis. These findings generally worsen in late adolescence and early adulthood.

Genetics

DBHD is a rare autosomal recessive condition caused by mutations in the *DBH* gene, located on chromosome 9 (9q34). DBHD occurs when an individual receives two copies of a defective *DBH* gene, one from each parent. Any person with one copy of the defective *DBH* gene is a carrier. Carriers do not have DBHD and will not develop the disease. However, if their partner is also a carrier, there is a one in four chance (25%) that their baby will be born with DBHD. There is a three in four chance (75%) that their baby will not have DBHD.

Test Sensitivity

50-100% of all *DBH* mutations can be detected by molecular analysis.

Test Methods

- Complete sequencing of the 12 exon coding region and flanking exon/intron boundaries of the *DBH* gene to identify point mutations.

Who Should Be Tested?

- Individuals clinically and/or biochemically suspected of being affected with dopamine beta hydroxylase deficiency
- Individuals with a family history of dopamine beta-hydroxylase deficiency, to determine carrier status

Potential Outcomes & Interpretation of Test Results

Reason for referral	*DBH* Gene Mutations Allele 1 / allele 2	Explanation
Diagnosis	None detected / none detected	This result does not support a diagnosis of DBHD
Diagnosis	Mutation detected / none detected	This result is unable to confirm a diagnosis of DBHD
Diagnosis	Mutation detected / mutation detected	This result confirms a diagnosis of DBHD
Carrier testing	None detected / none detected	This individual is unlikely to be a carrier of DBHD
Carrier testing	Mutation detected / none detected	This individual is a carrier of DBHD and may transmit a mutation to offspring

For More Information

Online Mendelian Inheritance in Man http://www.ncbi.nlm.nih.gov/omim/ Item # 223360

GeneReviews online clinical information resource http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=dbh#dbh

To locate a genetics center near you, please visit the Canadian Association of Genetic Counsellors website at www.cagc-accg.ca or the National Society of Genetic Counsellors website at www.nsgc.org

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1. Test results should be interpreted in the context of clinical findings, family history and other laboratory data.

2. Biochemical testing for plasma norepinephrine and dopamine is advised in addition to molecular analysis.

3. This test was developed and its performance characteristics validated by the Genome Diagnostics Laboratory at the Hospital for Sick Children. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes.