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 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

**TEST SENSITIVITY**

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

### POTENTIAL OUTCOMES & INTERPRETATION OF TEST RESULTS

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

For More Information


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

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.