Branchio-oto-renal (BOR) syndrome is an autosomal dominant condition characterized by hearing loss, and branchial, otic and renal anomalies. Branchial arch defects include cysts and fistulae. Otologic findings include sensorineural, conductive or mixed hearing loss with malformations of the outer, middle and inner ear. Renal malformations range from mild renal hypoplasia to bilateral renal agenesis, with some individuals progressing to end-stage renal disease later in life. Penetrance of BOR syndrome is high, although there is variable expressivity, which can lead to variable clinical manifestations.

For More Information
The Canadian Association of the Deaf http://www.cad.ca/
To locate a genetics centre 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

Genetics
BOR syndrome is present when an individual has one copy of the defective EYA1 gene. Affected individuals have a 50% chance of transmitting the disorder to each child. There is a 50% chance that the affected individual’s offspring will not be affected with BOR syndrome.

BOR syndrome is genetically heterogeneous; however, mutations in the EYA1 gene on chromosome 8 (8q13.3) have been implicated in about 40% of BOR syndrome cases. Of BOR syndrome patients with EYA1 mutations, approximately 75–80% have point mutations in the EYA1 gene while the remainder may have rearrangements of the gene causing large deletions or insertions.

Who Should be Tested?
- Individuals clinically suspected of being affected with BOR syndrome
- Relatives of probands with identified EYA1 mutations
- Pregnancies at risk due to a family history of BOR syndrome

Test Methods
- Complete sequencing of the coding region and flanking exon/intron boundaries of the EYA1 gene to identify point mutations.
- Quantitative testing of the EYA1 gene to detect larger deletions or duplications, using MLPA (Multiplex Ligation-dependent Probe Amplification)

Test Sensitivity
Approximately 40% of clinically diagnosed BOR patients have point mutations or large deletions/duplications in the EYA1 gene. A negative result does not rule out the possibility that the individual has an EYA1 mutation not detected by the current assays, or a mutation in another gene associated with BOR syndrome. Individuals with BOS (Branchiootic syndrome), which shares features with BOR, but lacks renal involvement will also be detected.

Potential Outcomes & Interpretation of Test Results

<table>
<thead>
<tr>
<th>EYA1 Gene Mutations</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>None detected</td>
<td>This result does not support a diagnosis of BOR syndrome</td>
</tr>
<tr>
<td>Mutation detected</td>
<td>This result supports a diagnosis of BOR syndrome</td>
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</tbody>
</table>

1. Current molecular testing may not detect all possible mutations for this disease. A negative test does not rule out the possibility of BOR syndrome.
2. The clinical course or severity of symptoms cannot be predicted by molecular analysis.
3. Test results should be interpreted in the context of clinical findings, family history and other laboratory data.
4. 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.