

# BRANCHIO-OTO-RENAL SYNDROME

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.

## 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

## POTENTIAL OUTCOMES & INTERPRETATION OF TEST RESULTS

<b><i>EYA1</i> Gene Mutations</b>	<b>Explanation</b>
None detected	This result does not support a diagnosis of BOR syndrome
Mutation detected	This result supports a diagnosis 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.

## For More Information

Online Mendelian Inheritance in Man <http://www.ncbi.nlm.nih.gov/omim/> Item # 113650

GeneReviews online clinical information resource <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=deafness-overview>

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](http://www.cagc-accg.ca) or the National Society of Genetic Counsellors website at [www.nsgc.org](http://www.nsgc.org)



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.*