

# Branchiootorenal Syndrome

Also known as: Branchiootoureteral (BOU) syndrome, Branchiooto syndrome, Melnick-Fraser syndrome

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## Clinical Characteristics

Branchiootorenal (BOR) syndrome is characterized by branchial fistulae and cysts, ear abnormalities resulting in hearing loss, and renal malformations. End-stage renal disease later in life is a possibility for some individuals. A few findings have been reported in a minority of cases, including cleft palate, euthyroid goiter, retrognathia, facial nerve paralysis, and incomplete development of the lacrimal ducts. Some patients develop tears while chewing.

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## Branchiootorenal Syndrome and Hearing Loss

Over 90% of individuals with BOR syndrome have a form of hearing loss. Around one-half have mixed hearing loss, about one-third have conductive hearing loss, and about one-fourth have sensorineural hearing loss. There is a full range of severity as well: about 30% have mild hearing loss, 20% have moderate, 30% have severe, and 20% have profound hearing loss. Most individuals have non-progressive hearing loss, but about 30% have progressive loss associated with the presence of dilated vestibular aqueducts.

Physical abnormalities of the ear can be present in the outer, middle, and/or inner ear. Pinnae abnormalities include preauricular pits (in 82% of patients), lop-ear deformity (36%), and preauricular tags (13%). Almost one-third of individuals have atresia or stenosis of the external auditory canal. Middle ear abnormalities include malformation, malposition, dislocation or fixation of ossicles, and malformation or reduction in size of the middle ear space. Inner ear abnormalities include cochlear hypoplasia, hypoplasia of the lateral semicircular canals, and enlargement of the cochlear and vestibular aqueducts.

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## Natural History

BOR syndrome is diagnosed in both males and females, and in all ethnicities. The prevalence of the syndrome is unknown, but is estimated to be around 1 in 40,000. It has also been estimated that around 2% of profoundly deaf children have BOR syndrome.

The clinical expression of the condition can vary from right side to left side in an affected individual, and among individuals in the same family. The manifestation and severity of the characteristics is also variable. All findings are generally present at birth, though both hearing loss and renal function may progressively decline. About 50% of individuals have branchial cleft cysts, which may be filled with or discharge fluid, and can become infected. The prevalence of renal malformations is unknown. Malformations

may be unilateral or bilateral, and include renal agenesis, hypoplasia, dysplasia, uretero-pelvic junction obstruction, calyceal cyst, calyectasis, pelviectasis, hydronephrosis, and vesicoureteral reflux.

The prognosis for those with BOR syndrome is good, overall. Intelligence is usually normal, and life expectancy is normal with proper care and management.

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## Genetics

Two genes have been found to be associated with BOR syndrome: *EYA1* on chromosome 8 and *SIX1* on chromosome 14. The *EYA1* gene is the “major” gene associated; *SIX1* mutations have been identified in a small percentage of cases and genetic testing of the gene is available on a research basis only. The normal function of these genes is unknown. BOR syndrome is **autosomal dominant**. This means that an affected individual has a 50% chance with each pregnancy of having an affected child, and a 50% chance of having an unaffected child. About 90% of patients inherit the condition from a parent, though some cases are *de novo* (spontaneous) and no history of the disorder is seen in the family.

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## Management

The diagnosis of BOR syndrome is made clinically. Genetic testing of the *EYA1* gene will find mutations in about 40% of patients. Test results may be used for confirmation of diagnosis, or for prenatal diagnosis in future pregnancies if the mutation in the family has been identified.

An initial evaluation following diagnosis should include a cervical exam for masses (and follow-up with computed topography for positive findings), renal function tests, urinalysis, and an audiologic examination. This exam should include computed topography of the temporal bones, and an assessment of auditory acuity through ABR, emission testing, and pure tone audiometry. Referral to the appropriate specialists should be made early. Any cysts or fistulae should be surgically removed. Renal abnormalities require treatment with a specialist as needed. Hearing loss may be treated with aids or other appropriate habilitation. A canaloplasty can be considered for correction of canal atresia, but middle ear abnormalities may not allow such a procedure.

A semiannual or annual appointment with an urologist or nephrologist for those with renal abnormalities is recommended, as is a semiannual otologic exam by physical, and annual audiometry to track the stability of the hearing loss.

A scheduled appointment with a geneticist is recommended. If parents of an affected child have not been diagnosed with BOR syndrome, they should each undergo clinical examination to fully confirm a negative family history.

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## **Resources for Families**

Statewide Genetics Program

Phone: 608-267-7148

Fax: 608-267-3824

Email: [meyeram@dhfs.state.wi.us](mailto:meyeram@dhfs.state.wi.us)

Wisconsin First Step Hotline

Phone: 1-800-642-7837 voice/TTY

Website: [www.mch-hotlines.org](http://www.mch-hotlines.org)

Wisconsin Office for Deaf and Hard of Hearing

Phone: 1-608-266-3118 voice/TTY

Website: [www.dhfs.state.wi.us/sensory](http://www.dhfs.state.wi.us/sensory)

Regional Children and Youth with Special Health Care Needs Centers

Centers in Green Bay, Wausau, Milwaukee, Madison, and Chippewa Falls

Website: [http://dfhs.wisconsin.gov/DPH\\_BFCH/cshcn/index.HTM](http://dfhs.wisconsin.gov/DPH_BFCH/cshcn/index.HTM)

WI Chapter of Families for Hands & Voices

Phone: (920) 437-7370

Website: [www.handsandvoices.org](http://www.handsandvoices.org)

Parent-to-Parent of Wisconsin

Phone: 1-888-266-0028

Email: [rmathea@shsmh.org](mailto:rmathea@shsmh.org)

National Organization for Rare Disorders (NORD)

[www.rarediseases.org](http://www.rarediseases.org)