



Autosomal Recessive Nonsyndromic Deafness: Molecular Diagnosis and Carrier Testing

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The National Institute on Deafness and Other Communicative Disorders (NIDCD) estimates that about 2 or 3 out of every 1,000 children in the United States are born deaf or hard-of-hearing. More lose their hearing later during childhood. Many of these children may need to learn speech and language differently, so it is important to detect deafness or hearing loss as early as possible.

Regardless of its etiology, uncorrected hearing loss has consistent sequelae. Auditory deprivation through the age of two years is associated with poor reading performance, poor communication skills, and poor speech production. Educational intervention is insufficient to completely remedy these deficiencies. In contrast, early auditory intervention, whether through amplification, otologic surgery, or cochlear implantation, is effective. Thus, early identification and timely intervention are essential for optimal cognitive development in children with prelingual deafness.

Congenital hearing loss can be identified through universal screening of newborns, which has been advocated by the National Institutes of Health and the Center for Disease Control and Prevention and is available in many states. Although legislation mandating newborn hearing screening has passed in the majority of states, requirements and implementation success varies. As a minimum, all children with a risk for hereditary hearing loss should receive screening audiometry. Parental concerns about possible hearing loss or observed delays in speech development require auditory screening in any child.

Over one-half of prelingual deafness is genetic, most often autosomal recessive and nonsyndromic. Approximately 50% of autosomal recessive nonsyndromic deafness are caused by mutations at the DFNB1 locus in the *GJB2* gene which codes for the protein connexin 26. The carrier rate in the general US population for a recessive deafness-causing *GJB2* mutation is about one in 33. The other 50% of cases are attributed to mutations in numerous other genes, many of which have been found to cause deafness in only one or two families. DNA-based testing of *GJB2* (connexin 26) should be considered in the evaluation of any individual with congenital nonsyndromic sensorineural hearing loss.

In May 2002, the American College of Medical Genetics (ACMG) issued guidelines on the genetic evaluation for the etiologic diagnosis of congenital hearing loss (see reference below). The statement advocates mutation screening of *GJB2* (connexin 26) by sequence analysis as part of the evaluation of individuals with congenital nonsyndromic sensorineural hearing loss. Accordingly, PAML is now offering *GJB2* (connexin 26) molecular genetic testing consistent with the ACMG recommendations. The identification of the genetic causes of deafness allows carrier screening of at risk individuals and earlier detection and intervention in relatives.

Any questions can be directed to Bassem A. Bejjani, M.D. (Co-director) or Marcy L. Hoffmann, Ph.D. (Technical Director) in the Molecular Diagnostic Laboratory at 509-474-6880.

Reference

Genetic Evaluation of Congenital Hearing Loss Expert Panel. Genetic Evaluation Guidelines for the Etiologic Diagnosis of Congenital Hearing Loss. *Genetics in Medicine* 2002;4:162-171.

Quick Facts

- ▶ Two or 3 out of every 1,000 children in the United States are born deaf or hard-of-hearing.
- ▶ Early identification and timely intervention are essential for optimal cognitive development in children with prelingual deafness.
- ▶ About 25% of all cases of deafness are due to mutations at the DFNB1 locus in the *GJB2* gene, which codes for the protein connexin 26.
- ▶ According to the American College of Medical Genetics, mutation screening of *GJB2* (connexin 26) by sequence analysis should be part of the evaluation of individuals with congenital nonsyndromic sensorineural hearing loss.

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Test Information

DESCRIPTION **CONNEXIN 26 (GJB2) SEQUENCE ANALYSIS**

METHOD PCR and Sequence Analysis

ORDER CODE CONN26

CPT CODE 83891, 83898, 83904×4, 83912

SPECIMEN 5 mL EDTA, ACD or sodium citrate whole blood (lavender, yellow or blue top tube).
Submit original and unopened tube only. Store and transport at room temperature or refrigerated. Include patient's family history and clinical indication for testing.

This test must be ordered on a paper requisition that accompanies the specimen. It is not orderable on the PAML computer system.

COMMENTS *Minimum amount:* 3 mL

Unacceptable conditions: plasma, serum, heparinized whole blood, frozen whole blood, severely hemolyzed specimens, specimens in leaking containers or over 5 days old, specimens not received in the original collection tubes, or aliquoted specimens.

Stability: 72 hours at room temperature, 5 days refrigerated, unacceptable frozen.

SCHEDULE Weekly

TURNAROUND 2-3 weeks

RANGES "See separate report."

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