Objective: To assess the use of genetic testing by pediatric otolaryngologists in evaluating a child with prelingual sensorineural hearing impairment (SNHI).

Design: Questionnaire on the use of genetic testing in the evaluation of prelingual SNHI was made available to pediatric otolaryngologists through the American Society of Pediatric Otolaryngology (ASPO) Web site (http://www.aspo.us). Each ASPO member was invited by e-mail to complete the questionnaire.

Participants: Sixty-three ASPO members.

Results: Forty-two (69%) of 61 respondents indicated that they use genetic testing of the connexin 26 (Cx26) gene (GJB2) as an initial test in their workup of prelingual SNHI, and 30 (71%) of 42 reported that they provide genetic counseling for their patients and their families. However, 17 (45%) of 38 respondents answered questions regarding recurrence risks incorrectly or stated that they did not know the correct response. In addition, 7 (12%) of 60 respondents reported that they do not use DNA-based testing at any point in their workup.

Conclusions: Many pediatric otolaryngologists use DNA-based testing in their evaluation of prelingual SNHI. However, many pediatric otolaryngologists do not have an adequate knowledge of the implications of genetic testing. Because it will take on an increasingly large role in clinical practice, pediatric otolaryngologists must be familiar with current genetic testing, counseling, and treatment recommendations. As these results demonstrate, such knowledge is still lacking in this physician population.

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The incidence of bilateral severe to profound congenital sensorineural hearing impairment (SNHI) in the United States is estimated at 1 in 1000 live births. About half of these cases are caused by genetic factors, with the remainder due to acquired, multifactorial, or unknown causes. Of genetic deafness, about 80% of cases are transmitted in an autosomal recessive manner, 15% are autosomal dominant, and the rest are X-linked or mitochondrial in inheritance.1

Hearing impairment is among the most genetically heterogeneous conditions. Currently, 46 genes and 81 genetic loci have been identified,2 and these numbers are increasing. Despite this heterogeneity, mutations in one gene, GJB2, which encodes the protein connexin 26 (Cx26) and maps to the autosomal recessive deafness gene 1 (DFNB1) locus, account for a large portion of cases. Mutations in this gene are responsible for about one third of sporadic prelingual SNHI and more than 50% of cases with an autosomal recessive inheritance pattern.3 Mutations in GJB2 cause nonsyndromic, prelingual SNHI that is typically nonprogressive and bilateral and is without evidence of temporal bone or vestibular abnormalities. Hearing impairment related to GJB2 is typically not associated with other anomalies and carries an excellent prognosis for language development with proper habilitation.4

Clinical testing for the presence of GJB2 was introduced in the late 1990s and has quickly become an important tool in the evaluation of the child with SNHI. A recent position paper by the American College of Medical Genetics advocated the routine use of genetic testing in the evaluation of the child with a congenital hearing impairment.5 However, no similar consensus statement has come from an otolaryngology society, and questions remain as how best to integrate this testing into clinical practice.6,7 Until recently, clinicians have ordered an extensive array of tests, including urinalysis, thyroid function testing, and electrocardiograms, in an effort to identify the underlying etiology of a child’s SNHI. Unfortunately, these laboratory tests have a low yield, with only high-resolution imaging studies (com-
laryngologists have a sound understanding of genetic principles with their patient’s parents?

Discuss issues such as prenatal diagnosis and reproduction. Are pediatric otolaryngologists prepared to present meaningful counseling?

In contrast, GJB2 testing is simple, has a higher yield, and directly addresses the parent’s concerns.

A positive Cx26 gene test result has several clear benefits. It obviates the need for other diagnostic tests in search of the cause of the SNHI. It means that there is no need to screen for other medical problems, such as vision problems or learning disabilities, because Cx26-related SNHI is not associated with other abnormalities. Furthermore, Cx26-related SNHI is associated with an excellent prognosis for language development and therefore can provide encouraging information to parents. Finally, it defines the exact recurrence risk for the child’s parents: 25%.

Connexin 26 gene testing provides information that is useful to the parents as well as to their child’s health care providers. However, for the maximum benefit, this testing must be performed in the proper manner. First, testing must be accompanied by adequate pretest and posttest genetic counseling, so that the limitations and benefits of the test and the meaning of the result can be discussed completely. Second, testing must be performed early in the evaluation process because a positive test result can prevent the ordering of other unnecessary tests. Genetic testing, however, presents a challenge for the otolaryngologist because it has characteristics that differentiate it from routine testing that is part of the physician’s clinical practice.

For example:

• Genetic testing is specific but not sensitive. A negative GJB2 test result does not mean that the SNHI is not genetic. While this may be obvious, it is a concept that parents often fail to understand in the absence of adequate genetic counseling.

• Genetic testing provides information not only about the patient but also about the family members. Is there an obligation to notify relatives who are at risk for carrying a genetic mutation and, therefore, at risk for having a child with SNHI? The answer is not simple.

• Most physicians are unfamiliar with the language of genetics. For example, the terms polymorphism, mutation, and variance of uncertain significance all refer to alterations in the DNA sequence, but each has a different meaning.

• Genetic testing also brings with it the specter of reproduction. Are pediatric otolaryngologists prepared to discuss issues such as prenatal diagnosis and reproductive options with their patient’s parents?

Previously, our group demonstrated that pediatric otolaryngologists have a sound understanding of genetic principles and the genetic basis of SNHI. However, the same study suggested that pediatric otolaryngologists had a limited understanding of how to carry out this testing. In the present study, we were interested in how pediatric otolaryngologists use genetic testing in their workup for prelingual SNHI. We believed that this research was necessary for understanding whether pediatric otolaryngologists are familiar with the principles of genetics in a manner that would allow them to both understand test results and communicate those results effectively to patients and their families. In addition, because the issues surrounding genetic testing are complex, we sought to assess whether it is reasonable for pediatric otolaryngologists to conduct proper pretest and posttest genetic counseling within the context of their practice.

The questionnaire was developed in a stepwise process. Pertinent topics were identified, and questions were developed on the basis of the clinical experience of the authors and through discussions with attending pediatric otolaryngologists, geneticists, and genetic counselors. These questions were reviewed by the otolaryngologists for clarity and were then edited on the basis of that feedback. In the final questionnaire, the main areas of inquiry were demographic information, knowledge of genetics, and practice policies and experience regarding the evaluation of pediatric SNHI. (The questionnaire is available from the corresponding author on request.)

All 230 members of the American Society of Pediatric Otolaryngology (ASPO) were invited to complete the questionnaire, which was made available from May 6 through September 30, 2005, on the ASPO Web site (http://www.aspo.us). ASPO members were notified of the study by e-mail and were supplied a Web link to the questionnaire. In addition, 3 “reminder” e-mails were sent to ASPO members. The study received approval from the institutional review board of the University of Alabama at Birmingham.

A total of 63 questionnaires were completed. The responses are listed in the table. Most respondents (53/63 [84%]) completed their otolaryngology residency in the 1980s or 1990s, and 52 (83%) of 63 reported that they completed a fellowship training program in pediatric otolaryngology. Most (46/62 [74%]) said that they are currently in an academic practice, with 37 (60%) affiliated with a children’s hospital. The majority (54/63 [86%]) had ready access to a clinical genetics center.

When asked what initial set of tests they use in an infant with confirmed nonsyndromic SNHI, 42 (69%) of 61 responding physicians said that they order GJB2 (we used the term connexin 26 gene) testing, 42 (69%) order computed tomography of the temporal bones and/or magnetic resonance imaging, 30 (49%) order a genetics referral, 31 (51%) order an ophthalmologic consultation, 33 (54%) order audiometry for the child’s siblings, and 22 (36%) order an electrocardiogram.

Most responded that they order Cx26 gene testing at an early point in the evaluation process, either as the first test (35/60 [58%]) or at the first follow-up visit (12 [20%]).
# Table. Selected Results of the Questionnaire

<table>
<thead>
<tr>
<th>Survey Question</th>
<th>No. of Respondents/Total No. of Respondents (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What year did you complete your otolaryngology residency?</strong></td>
<td></td>
</tr>
<tr>
<td>1950s/1960s</td>
<td>3/63 (5)</td>
</tr>
<tr>
<td>1970s</td>
<td>7/63 (11)</td>
</tr>
<tr>
<td>1980s</td>
<td>23/63 (37)</td>
</tr>
<tr>
<td>1990s</td>
<td>30/63 (48)</td>
</tr>
<tr>
<td>Did you complete your pediatric fellowship? No. answering yes</td>
<td>52/63 (83)</td>
</tr>
<tr>
<td><strong>Describe your practice (circle all that apply)</strong></td>
<td></td>
</tr>
<tr>
<td>Academic/affiliated with medical center</td>
<td>46/62 (74)</td>
</tr>
<tr>
<td>Primarily clinical, some research</td>
<td>23/62 (37)</td>
</tr>
<tr>
<td>Pediatric only</td>
<td>28/62 (45)</td>
</tr>
<tr>
<td>Children’s hospital</td>
<td>37/62 (60)</td>
</tr>
<tr>
<td><strong>Is there a clinical genetics center in your hospital/university/community that you can refer patients to easily?</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>54/63 (86)</td>
</tr>
<tr>
<td>No</td>
<td>9/63 (14)</td>
</tr>
<tr>
<td><strong>Is SNHI the focus of your practice? No. answering yes</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>10/61 (16)</td>
</tr>
<tr>
<td><strong>Describe approximately how many pediatric patients do you see monthly for SNHI (not otitis media)?</strong></td>
<td></td>
</tr>
<tr>
<td>About 1</td>
<td>4/61 (7)</td>
</tr>
<tr>
<td>2-5</td>
<td>34/62 (56)</td>
</tr>
<tr>
<td>6-10</td>
<td>16/61 (26)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>7/61 (11)</td>
</tr>
<tr>
<td><strong>When did you begin to use DNA-based testing routinely?</strong></td>
<td></td>
</tr>
<tr>
<td>In the past year</td>
<td>5/60 (8)</td>
</tr>
<tr>
<td>2-3 y ago</td>
<td>21/60 (35)</td>
</tr>
<tr>
<td>3-5 y ago</td>
<td>18/60 (30)</td>
</tr>
<tr>
<td>&gt;5 y ago</td>
<td>9/60 (15)</td>
</tr>
<tr>
<td>Not using</td>
<td>7/60 (12)</td>
</tr>
<tr>
<td><strong>Which of the following do you currently order in your initial set of tests for patient with confirmed nonsyndromic SNHI (select all that apply)?</strong></td>
<td></td>
</tr>
<tr>
<td>Audiometry on parents</td>
<td>18/61 (30)</td>
</tr>
<tr>
<td>Audiometry on siblings</td>
<td>33/61 (54)</td>
</tr>
<tr>
<td>Thyroid function testing</td>
<td>17/61 (28)</td>
</tr>
<tr>
<td>Ophthalmology consultation</td>
<td>31/61 (51)</td>
</tr>
<tr>
<td>Congenital infection screening</td>
<td>11/61 (18)</td>
</tr>
<tr>
<td>CT scan of temporal bones and/or MRI</td>
<td>42/61 (69)</td>
</tr>
<tr>
<td>Electrocardiography</td>
<td>22/61 (36)</td>
</tr>
<tr>
<td>Genetics referral for counseling/evaluation/testing</td>
<td>30/61 (49)</td>
</tr>
<tr>
<td>DNA-based genetic testing for Cx26</td>
<td>42/61 (69)</td>
</tr>
<tr>
<td>Initially order =3 tests</td>
<td>36/61 (59)</td>
</tr>
<tr>
<td><strong>At what point do you offer Cx26 gene testing?</strong></td>
<td></td>
</tr>
<tr>
<td>As the first test at the initial visit after the hearing impairment is confirmed</td>
<td>35/60 (58)</td>
</tr>
<tr>
<td>As the first test at a follow-up visit</td>
<td>12/60 (20)</td>
</tr>
<tr>
<td>I do not use DNA-based testing</td>
<td>7/60 (12)</td>
</tr>
<tr>
<td><strong>I use Cx26 gene testing under the following circumstances</strong></td>
<td></td>
</tr>
<tr>
<td>For all deaf/hard-of-hearing patients</td>
<td>23/56 (41)</td>
</tr>
<tr>
<td>Only for patients who I think are appropriate</td>
<td>27/56 (48)</td>
</tr>
<tr>
<td><strong>When discussing Cx26 gene testing with parents, who explains the limitations and benefits of this testing?</strong></td>
<td></td>
</tr>
<tr>
<td>I do</td>
<td>30/42 (71)</td>
</tr>
<tr>
<td>Written material</td>
<td>1/42 (2)</td>
</tr>
<tr>
<td>I refer to a geneticist/genetic counselor</td>
<td>10/42 (24)</td>
</tr>
<tr>
<td><strong>Do you schedule extra time to discuss genetic test results with parents?</strong></td>
<td></td>
</tr>
<tr>
<td>Yes, for both positive and negative tests</td>
<td>12/39 (31)</td>
</tr>
<tr>
<td>I refer parents to a genetics professional for both positive and negative tests</td>
<td>7/39 (18)</td>
</tr>
<tr>
<td>I refer parents to a genetics professional for positive tests</td>
<td>11/39 (28)</td>
</tr>
<tr>
<td><strong>I do not order Cx26 gene testing because (circle all that apply)</strong></td>
<td></td>
</tr>
<tr>
<td>I do not understand it well enough</td>
<td>1/23 (4)</td>
</tr>
<tr>
<td>I prefer to have genetics experts carry out and explain testing</td>
<td>17/23 (74)</td>
</tr>
<tr>
<td><strong>Has the availability of genetic testing changed how you evaluate newborns/infants with confirmed nonsyndromic SNHI?</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>46/61 (75)</td>
</tr>
<tr>
<td>No</td>
<td>15/61 (25)</td>
</tr>
<tr>
<td><strong>One potential use for genetic testing for deafness-related genes would be for prenatal diagnosis. Do you support the use of prenatal genetic testing for hearing impairment?</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>28/57 (49)</td>
</tr>
<tr>
<td>No</td>
<td>27/57 (47)</td>
</tr>
</tbody>
</table>

Abbreviations: CT, computed tomography; Cx26, connexin 26; MRI, magnetic resonance imaging; SNHI, sensorineural hearing impairment.

*For some questions, the number of respondents listed is fewer than the total number of respondents because not all of the responses are listed.
When asked under what circumstances *GJB2* testing is ordered, 27 (48%) of 56 respondents said only patients for whom they believe it is appropriate and 23 (41%) answered “for all deaf/hard-of-hearing patients.” Seven (12%) of 60 answered that they do not use DNA-based testing. All 7 of these respondents had finished their fellowship training relatively recently; 5 were practicing in an academic setting, and the remaining 2 were in a community practice.

Thirty (71%) of 42 respondents stated that they explain the benefits and limitations of Cx26 gene testing, while 10 (24%) refer the parents to a genetics professional. Similar numbers (24 [59%] and 27 [66%] of 41 respondents, respectively) were recorded in answer to the questions “Who explains a positive test result?” and “Who explains a negative test result?” When asked if they schedule extra time to explain test results, 12 (31%) of 39 respondents, respectively) were recorded in answer to the question “Who explains a positive test result?” and “Who explains a negative test result?” When asked if they schedule extra time to explain test results, 12 (31%) of 39 respondents said that they do for both positive and negative results, while 6 (15%) responded that they do only for positive results. Many refer the parents to a genetics professional to explain the results.

A case scenario was included in the questionnaire:

In evaluating an otherwise well 9-month-old deaf girl, you ordered genetic testing for Cx26-related deafness. You now learn that her genetic test results are positive—she has 2 *GJB2* mutations, 35delG and 167delT. The child's parents now ask you to test their 2 normal-hearing children, aged 13 and 7 years, to determine whether they are carriers and are therefore at risk for having a deaf child themselves. Would you order the testing?

Of the 37 who answered, 25 (68%) responded yes, while 12 (32%) responded no.

When asked what the recurrence risk would be for the parents of a child who tested positive for Cx26 gene mutations, only slightly more than half (21/38 [55%]) correctly answered that this recurrence risk is 25%. When asked the recurrence risk if testing was negative, the vast majority (27/38 [71%]) responded that they did not know, and 5 (13%) responded with the incorrect figure of less than 1%. Only 6 (16%) chose 15%, which is the correct approximate figure.

When asked why they do not order testing themselves, most (17/23 [74%]) answered that they prefer to have the genetics expert carry out and explain the testing. Single answers (of which there were 23, each representing 4% of respondents) included that they did not have the time to obtain consent, that they did not understand the testing well enough to properly obtain informed consent from families, and that they did not understand the testing well enough to explain the results to families.

When asked whether genetic testing had changed how they evaluate newborns/infants with SNHI, most (46/61 [75%]) responded yes. Furthermore, most recognized how effective it had been in helping them establish the diagnosis of Cx26-related SNHI; 50/56 (89%) of respondents agreed that genetic testing permits accurate recurrence risk counseling (50/57 [88%]) and relieved parental anxiety (44/56 [79%]), while more than half agreed that testing reduced the overall cost of the evaluation (30/56 [54%]) and was useful in habilitation (28/55 [51%]). The respondents were essentially evenly split on questions regarding the use of prenatal genetic testing for hearing impairment. Almost half (27/57 [47%]) agreed that it should not be used for this purpose.

The purpose of this study was to learn how pediatric otolaryngologists are currently using genetic testing in the evaluation of the child with hearing impairment. While most agree that this testing is a useful tool and report that they are using it, there is no universally accepted method for how it should be carried out. In a 2002 consensus statement written by a panel of experts that included 1 of us, an otolaryngologist (R.J.H.S.), the American College of Medical Genetics advocated the early use of genetic testing. They commented that with an “appropriate genetic evaluation . . . it is possible to avoid unnecessary, costly clinical tests such as electroretinograms, temporal bone imaging, or electrocardiograms.”5(p168) The American Academy for Otolaryngology–Head and Neck Surgery has yet to issue guidelines.

In the past, the workup for congenital, nonsyndromic SNHI has included a long list of tests that are expensive and have limited clinical value in the absence of clinical indication.4,13 In contrast, genetic testing for *GJB2* has a high likelihood of yielding positive results, thereby providing important, clinically useful information for the child's family and health care providers. Furthermore, establishing the diagnosis of Cx26-related SNHI spares these children further diagnostic tests. However, to achieve this goal, testing must be done early in the evaluation process.36 Most pediatric otolaryngologists who responded to our question recognized this fact: 69% indicated that they order such testing in the initial evaluation. However, many (36/61 [59%]) report that they still use a broad approach by initially ordering 3 or more of the following: computed tomography, electrocardiogram, ophthalmology consultation, thyroid function tests, audiometry on family members, and congenital infection screening. A limitation of the questionnaire was that respondents were not asked to justify their clinical practices. Some respondents may not have understood what we consider standard of care, while others may simply not agree with our premise. Unfortunately, we did not provide an opportunity for respondents to describe the clinical reasoning for their differing approaches to the workup of patients with congenital, nonsyndromic SNHI.

Most (54/63 [86%]) of the responding pediatric otolaryngologists reported that they have access to a genetics center for referrals. However, 71% (30 of 42) answered that they explain the limitations and benefits of Cx26 gene testing to the families, and 59% (24 of 41) and 66% (27 of 41), respectively, explain the meanings of the positive and negative test results. A significant number reported that they schedule extra time when they discuss both positive and negative test results with families (12/39 [31%]), or that they refer the families to a genetics professional to discuss these results (7/39 [18%]), but
many only do so for positive results (11/39 [28%]). As shown in previous work,
7 it is as important for the par-
ents of children with negative test results to have a discus-
sion regarding the testing as it is for families for whom the results are positive. It is particularly important—
and often more difficult—to communicate that a nega-
tive Cx26 gene test result does not rule out a genetic cause
for the child's SNHI. Family members frequently mis-
terpret Cx26 gene test result as proof that their child did not have the gene that causes deafness.

Many otolaryngologists refer their patients to genet-
ics professionals for counseling. This is understandable
because it is unlikely that, in a typically busy practice,
an otolaryngologist is able to spend sufficient time with families to adequately address these issues during an of-
fice visit. Several otolaryngologists cited discomfort with
various aspects of genetic testing as the reason they did
not order it. Included in their reasons were insufficient understanding of the testing and test results and insuffi-
cient time to properly carry out informed consent. In
such cases it is best to refer patients to a genetics pro-
fessional, but that is not always possible. Some respond-
ents (9/63 [14%]) reported that they do not have easy
access to a genetics center. This highlights the fact that
it is not mandatory that pretest and posttest counseling
be carried out by a genetics professional. In some in-
stances, it is not even possible. Therefore, otolaryngolo-
gists must be prepared to discuss and answer parents' ques-
tions. It is unacceptable to not use genetic testing
because that would deny patients and their families in-
formation that is important for the child's health care.

Opinions were essentially evenly divided regarding the
use of genetic testing for prenatal diagnosis. Proponents
argue that the sooner a diagnosis is made, the sooner ha-
bilitation may begin. Those opposed cite confounding per-
sonal, moral, and ethical reasons related to prenatal test-
ing in general and state that this testing may increase
abortions.17 For professionals who are not well versed in
addressing these issues with families, such topics are dif-
cult to address and highlight an important role that ge-
netics professionals can play in the care of these families.

The answers given for the scenario about Cx26 gene
testing for the siblings of a child with 2 GJB2 mutations
revealed a telling finding. The majority of physicians
(25/37 [68%]) responded that they would order testing
of the unaffected siblings when asked to do so by the par-
ents. This decision is not consistent with the American
Society of Human Genetics guidelines on genetic test-
ing for minors.18 Testing the unaffected children would
in essence be carrier testing, because they are unaf-
fected, and would have no direct medical benefit. The
information on their genetic status would only be rel-

In this study, we have shown that pediatric otolaryn-
gologists understand basic genetic principles such as men-
delian inheritance and know the genetic basis of SNHI.
However, these physicians are less comfortable with car-
ying out genetic testing. This finding is significant
because the role of genetics will only increase in the com-
ing years. Genetic testing has become an integral part of
the evaluation of the child with SNHI, but to date this
testing has focused on relatively few genes for a limited
number of clinical situations. In the future, the number
of clinically relevant genetic tests will increase, and these
tests will be important not only for diagnosis but also for
making treatment and management decisions. It will be
increasingly important for pediatric otolaryngologists to
have a basic understanding of genetic testing, including
when it is appropriate. Pediatric otolaryngologists should
be able to understand test results, communicate them to
the patient and family, discuss their implications, and rec-
ognize when it is appropriate to consult a genetics pro-
fessional. While these things can be learned through clini-
cal experience, an emphasis needs to be placed on such
education during residency training. Genetics content
should be added to the otolaryngology residency curric-
ulum to prepare future otolaryngologists for ge-
nomic medicine—the routine use of genetic test results
in medical management.

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the study and take responsibility for the integrity of the
data and the accuracy of the data analysis. Study concept
and design: Prucka, Smith, and Robin. Acquisition of data:
Duncan, Wiatrak, and Robin. Analysis and interpreta-
tion of data: Duncan and Robin. Drafting of the manu-
script: Duncan and Robin. Critical revision of the manu-
script for important intellectual content: Prucka, Wiatrak,
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REFERENCES


