# American College of Medical Genetics and Genomics guideline for the clinical evaluation and etiologic diagnosis of hearing loss

Raye L. Alford, PhD, FACMG[1], Kathleen S. Arnos, PhD, FACMG[2], Michelle Fox, MS, CGC[3,4], Jerry W. Lin, MD, PhD[1], Christina G. Palmer, PhD, FACMG[5,6], Arti Pandya, MD, FACMG[7], Heidi L. Rehm, PhD, FACMG[8], Nathaniel H. Robin, MD, FACMG[9], Daryl A. Scott, MD, PhD[10,11] and Christine Yoshinaga-Itano, PhD[12]; ACMG Working Group on Update of Genetics Evaluation Guidelines for the Etiologic Diagnosis of Congenital Hearing Loss; for the Professional Practice and Guidelines Committee



Hearing loss is a common and complex condition that can occur at any age, can be inherited or acquired, and is associated with a remarkably wide array of etiologies. The diverse causes of hearing loss, combined with the highly variable and often overlapping presentations of different forms of hearing loss, challenge the ability of traditional clinical evaluations to arrive at an etiologic diagnosis for many deaf and hard-of-hearing individuals. However, identifying the etiology of a hearing loss may affect clinical management, improve prognostic accuracy, and refine genetic counseling and assessment of the likelihood of recurrence for relatives of deaf and hard-of-hearing individuals. Linguistic and cultural identities associated with being deaf or hard of hearing can complicate access to and the effectiveness of clinical care. These concerns can be minimized when genetic and other health-care services are provided in a linguistically and culturally sensitive manner. This guideline offers information about the frequency, causes, and presentations of hearing loss and suggests approaches to the clinical evaluation of deaf and hard-of-hearing individuals aimed at identifying an etiologic diagnosis and providing informative and effective patient education and genetic counseling.

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**Key Words:** genetics evaluation; deaf; Deaf; genetic counseling; genetic testing; guideline; hard of hearing; hearing loss

## DEFINITIONS

Deaf: a community with a distinct culture and language shaped by the experience of being deaf or hard of hearing, which may include deaf, hard-of-hearing, and hearing individuals

deaf: an auditory phenotype characterized by a total or near-total loss of the ability to hear

hard of hearing: an auditory phenotype characterized by a partial loss of the ability to hear

hearing loss: an auditory phenotype characterized by any degree of loss of the ability to hear; depending on cause, hearing loss can be temporary or permanent—this guideline focuses on permanent hearing loss

[1]Bobby R. Alford Department of Otolaryngology–Head and Neck Surgery, Baylor College of Medicine, Houston, Texas, USA; [2]Department of Science, Technology, and Mathematics, Gallaudet University, Washington, DC, USA; [3]Department of Pediatrics, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, California, USA; [4]Department of Genetics, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, California, USA; [5]Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, California, USA; [6]Department of Human Genetics, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, California, USA; [7]Department of Human and Molecular Genetics, Virginia Commonwealth University, Richmond, Virginia, USA; [8]Laboratory for Molecular Medicine, Harvard Medical School, Cambridge, Massachusetts, USA; [9]Department of Genetics, University of Alabama at Birmingham, Birmingham, Alabama, USA; [10]Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas, USA; [11]Department of Molecular Physiology and Biophysics, Baylor College of Medicine, Houston, Texas, USA; [12]School of Medicine, University of Colorado Denver, Aurora, Colorado, USA. Correspondence: Raye L. Alford (ralford@bcm.edu)

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## INTRODUCTION

Two to three of every 1,000 children born in the United States are deaf or have a hearing loss significant enough to affect speech and language development.[1] Early intervention has been shown to be effective in facilitating speech and language development in deaf and hard-of-hearing children.[2] As a result, newborn hearing screening, which began in 2001, is now mandated throughout the United States. Not all childhood hearing loss is present at birth, however, and hearing screening is recommended throughout childhood and adolescence to identify children with later-onset hearing loss and to permit early intervention.[3,4]

Ninety-five percent of newborns with hearing loss identified by newborn hearing screening programs are born to hearing parents, obscuring the fact that the majority of newborns have a hereditary cause for their hearing loss.[5,6] Analysis of family history data from school-aged children in the United States estimated that up to 60% of educationally significant congenital and early-onset hearing loss is caused by genetic factors.[5,6] The majority of genetic hearing loss is inherited in an autosomal recessive pattern and often presents in the absence of a positive family history for hearing loss. One gene, *GJB2*, which encodes the gap junction protein connexin 26, accounts for the largest proportion of autosomal recessive early childhood hearing loss in many populations.[7]

The prevalence of hearing loss increases with age, with 40–50% of the population experiencing hearing loss by age 75.[8] The contribution of genetic causes to cases of adult-onset hearing loss is less clear. However, it is evident that a significant proportion of adult-onset hearing loss is likely to be caused, or strongly influenced, by genetic factors.[9–14]

The goal of a genetics evaluation for deaf and hard-of-hearing individuals of any age is to identify an etiologic diagnosis and, in doing so, enable implementation of an individualized health-maintenance strategy.[15–17] Identification of a previously unrecognized syndromic form of hearing loss can be particularly important because it may allow early management of associated medical concerns. Obtaining an etiologic diagnosis also provides the basis for precise genetic counseling that includes an accurate estimation of the chances for recurrence of hearing loss within families.

## AUDIOMETRIC AND CLINICAL ASPECTS OF HEARING LOSS

Hearing loss is typically described in terms related to its clinical presentation. In general, hearing loss is categorized as either syndromic or nonsyndromic, depending on the presence or absence of associated defects in other organ systems. Hearing loss is also typically described by the following:

- The age of onset—congenital, prelingual (before the acquisition of speech), postlingual (after the acquisition of speech), adult-onset, or presbycusis (age-related late-onset hearing loss);
- The type of hearing loss—sensorineural, conductive, mixed, or auditory neuropathy;
- The laterality and symmetry of the hearing loss—unilateral or bilateral, symmetric or asymmetric;
- The stability of the hearing loss—progressive, nonprogressive, or fluctuating;
- The degree of hearing loss—slight (16–25 decibels (dB)), mild (26–40 dB), moderate (41–55 dB), moderately severe (56–70 dB), severe (71–90 dB), or profound (91 dB or greater)[18]; and
- The configuration of the hearing loss as seen on audiometric analysis—sloping, flat, rising, or midfrequency (cookie-bite) loss.

Hearing loss may also be described according to an apparent pattern of inheritance—autosomal recessive, autosomal dominant, X-linked, or matrilineal (mitochondrial). If a specific etiology is known, descriptions of hearing loss may also include the etiologic diagnosis, such as Usher syndrome type 1–related hearing loss or *GJB2*-related hearing loss.[15,16,19,20]

## GENETIC AND NONGENETIC ETIOLOGIES OF HEARING LOSS

Hearing loss is among the most etiologically heterogeneous disorders, with more than 400 genetic syndromes that include hearing loss as a feature, more than 100 genes associated with nonsyndromic genetic hearing loss, and a number of nongenetic causes.[20,21] Genes associated with syndromic and nonsyndromic genetic hearing loss encode a variety of proteins involved in the development and function of the auditory system, including transcription factors, structural proteins, gap junction proteins, and ion channels, to name just a few.

An estimated 30% of genetic hearing loss is syndromic. A few syndromes, such as Pendred (enlarged vestibular aqueduct, thyroid problems), Usher (retinitis pigmentosa), Waardenburg (pigmentary anomalies), and branchio-oto-renal (branchial arch and renal anomalies) syndromes, account for substantial percentages of hearing loss in some populations.[20,22–25] Syndromic hearing loss may be transmitted as an autosomal recessive, autosomal dominant, X-linked, or matrilineal trait. A review of individual conditions can be found in *Hereditary Hearing Loss and Its Syndromes* by Toriello and Smith[20] and the online database GeneReviews.[19]

For some syndromic forms of hearing loss, such as Usher syndrome or Pendred syndrome, the nonauditory features can be subtle, especially in early childhood. For others, hearing loss is not the presenting finding or the most pressing concern. For many syndromic forms of hearing loss, there is marked variability in the phenotypic presentation and in the age of onset of syndromic features. This variability can exist both between and within families. For example, hearing loss is observed in only 20–50% of individuals with Waardenburg syndrome. As a result, this diagnosis can be easily missed if specific information about pigmentary changes or gastrointestinal disturbances is not elicited.[26] Furthermore, some hereditary forms of hearing loss, such as neurofibromatosis type 2, enlarged vestibular aqueduct syndrome, and Pendred syndrome, may present

initially as unilateral hearing loss.[19,20,27–29] Given the challenges that can exist in distinguishing between syndromic and nonsyndromic forms of hearing loss, all children and adolescents showing hearing loss without a known etiology, e.g., confirmed *GJB2* mutations or documented congenital cytomegalovirus (CMV) infection, should be evaluated for syndromic conditions by a clinical geneticist.[15,16]

An estimated 70% of genetic hearing loss is nonsyndromic. Nonsyndromic hearing loss may be transmitted as an autosomal recessive (~80%), autosomal dominant (~15%), or X-linked trait (~1%).[20] In addition, matrilineal (mitochondrial) transmission of nonsyndromic hearing loss occurs with a frequency of ~1% in Western nations but has a slightly higher incidence in Spain and East Asian countries including China, Mongolia, Korea, and Japan.[30,31]

Of particular note, the DFNB1 locus, which includes the *GJB2* gene encoding the gap junction protein connexin 26 and the *GJB6* gene encoding the gap junction protein connexin 30, accounts for an estimated 50% of all autosomal recessive nonsyndromic hearing loss and 15–40% of all deaf individuals in a variety of populations.[7,32–38] More than 150 deafness-causing variants have been identified in *GJB2,* but a few common mutations account for a large percentage of alleles in several populations.[7,34–36] *GJB2*-related hearing loss is sensorineural, usually present at birth, typically bilateral and nonprogressive, and can range from mild to profound in severity. However, progressive or later-onset hearing loss—with infants passing their newborn hearing screen—have also been described, particularly in association with nontruncating mutations.[39–42] Nonsyndromic hearing loss due to mutations at the DFNB1 locus may also be caused by (i) interaction of a *GJB2* mutation on one allele and a deletion involving *GJB6* on the other allele or (ii) biallelic deletions involving *GJB6*.[43–45] *GJB6* deletions have been observed in multiple populations, although they appear to be a relatively uncommon explanation for hearing loss in the United States.[46–48] Notably, hearing loss caused by certain dominant mutations in *GJB2*, although uncommon, may present as a syndromic hearing loss, with associated skin findings.[49–51]

Nonsyndromic mitochondrial hearing loss is characterized by audiograms that fall into the moderate-to-profound range and is associated with variants in either the *MT-RNR1* gene encoding the mitochondrial 12S ribosomal RNA or the *MT-TS1* gene encoding the mitochondrial transfer RNA Ser(UCN).[30,31,52] Of particular note, mutations in *MT-RNR1* are associated with predisposition to aminoglycoside ototoxicity.[53] Hearing loss in individuals exposed to aminoglycoside antibiotics who carry susceptibility mutations in *MT-RNR1* is bilateral, severe to profound, and typically develops within a few days to weeks after administration of any amount, including just a single dose, of an aminoglycoside antibiotic.[54] Studies offer conflicting findings with regard to the likelihood of hearing loss in individuals carrying a deafness-causing variant in *MT-RNR1* who are not exposed to aminoglycosides.[53–55]

Age-related hearing loss, or presbycusis, is a common neurosensory deficit. In the United States, presbycusis is present in 40–50% of individuals aged 75 and older. Presbycusis generally affects higher frequencies of sound disproportionately, making it difficult for those with presbycusis to understand speech.[8] Men have presbycusis more frequently than women.[56] Presbycusis is a complex condition influenced by genetic and environmental factors.[13] Much of the literature about age-related hearing loss has focused on environmental factors such as noise exposure.[9,57,58] More recently, however, several susceptibility loci for age-related hearing loss have been identified. Genes implicated in this process using linkage and genome-wide association studies include genes previously implicated in other forms of hearing loss (such as *KCNQ4* and *ACTG1*), and genes involved in oxidative stress (such as *GRM7*, *GRHL2*, mitochondrial oxidative genes, and *N*-acetyltransferase).[9,10,12–14, 20]

Certain environmental (nongenetic) factors play a major etiologic role in hearing loss.[59] In the United States, congenital CMV infection is the most common nongenetic cause of hearing loss among children. Of the 20,000-40,000 infants born with congenital CMV infection each year, 90% have no detectable clinical abnormalities at birth, yet 10–15% of these asymptomatic infants will develop sensorineural hearing loss which can present in early childhood, can be unilateral or bilateral, and is often progressive.[60–62] As a result, congenital CMV infection may go undetected even in children who undergo newborn hearing screening and receive a thorough physical examination in the neonatal period.[16,20,62]

Congenital rubella, which was a common cause of hearing loss in the mid-1960s, occurs less frequently in Western populations today as a result of successful immunization programs.[63,64] According to the World Health Organization, no cases of endemic rubella infection are known to have occurred in the Americas between 2009 and 2012.[65] Similarly, the occurrence of postmeningitic hearing loss in children has been substantially reduced in developed countries as a result of vaccination against *Haemophilus influenzae*.[66] However, other environmental causes for hearing loss—including prematurity and exposure to noise or ototoxic drugs such as aminoglycosides and cyclophosphamides (which may have a genetically determined predisposition in some cases)—persist in the United States today.[20, 67–69]

## THE IMPORTANCE OF GENETIC EVALUATION AND GENETIC COUNSELING FOR DEAF AND HARD-OF-HEARING INDIVIDUALS

When a genetic etiology is possible, a clinical genetics evaluation, including genetic counseling, offers a number of potential benefits for children and adults with hearing loss and their families. Benefits can include providing etiologic information, identifying (or allaying concerns about) comorbidities that may need referral for specialty care, planning for future medical and educational needs, facilitating estimations of the likelihood of recurrence, allowing families to better plan for the birth of a deaf or hard-of-hearing child, relieving the guilt that some parents may feel about having a child with hearing loss, enhancing

psychological well-being, dispelling misinformation, and facilitating referral for unrelated hereditary conditions such as familial cancer.[48,70–79] Furthermore, if mitochondrial DNA mutations associated with genetic susceptibility to aminoglycoside ototoxicity are discovered, it may be possible for relatives to avoid precipitating medications.[53–55]

As with any genetics evaluation, clear communication between the genetics professionals and their patients is important for the provision of effective genetics services. Deaf and hard-of-hearing individuals use a variety of communication methods, including spoken and signed language, lip reading, and written notes. Special training may be needed to optimize communication between individuals with hearing loss and genetics professionals. Such training may include (i) training sign language interpreters in medical and genetics terminology and (ii) training genetics professionals to work effectively with sign language interpreters and use a variety of communication aids, including videophones, video relay services, instant messaging, and visual aids.[80]

In addition, deafness is considered by some to be a nonmedical trait. Many deaf individuals consider themselves to be part of a linguistic and cultural minority group, viewing their deafness as a neutral or positive trait.[81,82] By contrast, the medical perspective—which views deafness as a pathology—is pervasive among most hearing individuals and some deaf individuals. This difference in perspective may affect the willingness of some individuals to obtain genetic services and genetic counseling.[83,84] However, when given accurate information about the nature of genetic counseling and how to obtain a referral, Deaf adults are often interested in receiving genetic services in order to learn more about themselves and why they are deaf or hard of hearing. In addition, many Deaf and hard-of-hearing individuals report an enhanced sense of self-understanding and self-identity, as well as an enhanced cultural and group identity, as a result of genetic testing.[72,85] Providing genetic services in a linguistically and culturally sensitive manner has been shown to improve outcomes such as genetics knowledge and understanding.[86,87] Furthermore, using neutral or balanced terminology, such as "chance" instead of "risk," "deaf" or "hearing" instead of "affected" or "unaffected," and exercising caution in the use of terms such as "handicapped," "pathology," and "impairment" can enhance the provision of genetic services to deaf and hard-of-hearing individuals and their families.[86,88,89]

## GENETIC TESTING FOR THE ETIOLOGIC DIAGNOSIS OF HEREDITARY HEARING LOSS

Historically, molecular diagnostic tests for hearing loss have used genotyping or DNA sequencing to identify specific hearing loss variants or to screen individual genes, or small collections of genes, for changes associated with hearing loss. This approach has proven to be effective in cases in which there is a single gene, or limited number of genes, responsible for a subtype of hearing loss. Examples include *SLC26A4* gene sequencing in individuals suspected of having Pendred syndrome, *PAX3* gene sequencing in individuals with features of Waardenburg syndrome type I, *MITF* and *SOX10* gene sequencing in individuals with features of Waardenburg syndrome type II, or sequencing of *MYO7A* or *USH2A*, the most common genes involved in Usher syndrome types I and II, respectively.[90,91] Such screening can also be cost effective in individuals with genetically heterogeneous hearing loss phenotypes when a single gene is responsible for a significant percentage of cases. For example, *GJB2* gene sequencing can identify the underlying etiology for many individuals whose clinical presentation is consistent with autosomal recessive nonsyndromic hearing loss.

Today, tests based on next-generation sequencing (NGS) technologies are rapidly replacing many single gene–sequencing tests for hearing loss (**Figure 1**). These tests use disease-targeted exon capture, whole-exome sequencing (WES), or whole-genome sequencing (WGS) strategies. The main advantage of these tests is their ability to address the problem of genetic heterogeneity, wherein many different genes result in phenotypes that cannot be easily distinguished clinically.[92–96] Several NGS tests are now clinically available and can be found by querying the GeneTests and Genetic Testing Registry websites.[97,98]

NGS tests that use disease-targeted exon-capture approaches restrict sequencing to specific genes, such as genes known to be associated with hearing loss. Such tests can provide excellent coverage of the genes selected for study but are limited by our present knowledge of which genes are involved in hearing loss. Furthermore, some tests may sequence only a subset of the genes known to be associated with hearing loss. WES is also based on exon capture but does not rely on a list of genes involved in a particular disease process. Instead, WES seeks to evaluate all exons in the genome for variations. This approach can identify variants in known hearing loss–related genes and genes that have yet to be associated with hearing loss. WGS is not limited to screening exons and therefore has the potential to identify changes outside of exons that may be related to hearing loss.

The ability of WES and WGS approaches to detect a larger subset of all hearing loss–related changes needs to be balanced with the difficulties in interpretation that come from identifying an ever-increasing number of variants, the challenge of causally linking variants in new genes to hearing loss, and the likelihood of identifying genetic susceptibilities unrelated to hearing loss (i.e., incidental findings).[99] In 2013, the ACMG published recommendations for reporting incidental findings from genomic sequencing.[100]

Furthermore, not all regions of the genome are efficiently captured and analyzed by current exon-capture or WGS approaches, and large deletions and duplications, in addition to copy-number and structural variations, may not be efficiently detected.[99] These limitations of NGS technologies may necessitate use of alternative or complementary genetic testing strategies in some cases.

NGS technologies are expected to continue to improve over time, but it will always be important to pay close attention to the performance characteristics of tests, including coverage, analytic sensitivity, the genes that are and are not analyzed, and the types of mutations that are and are not detected. In some cases, it may be helpful to have tests performed in laboratories that

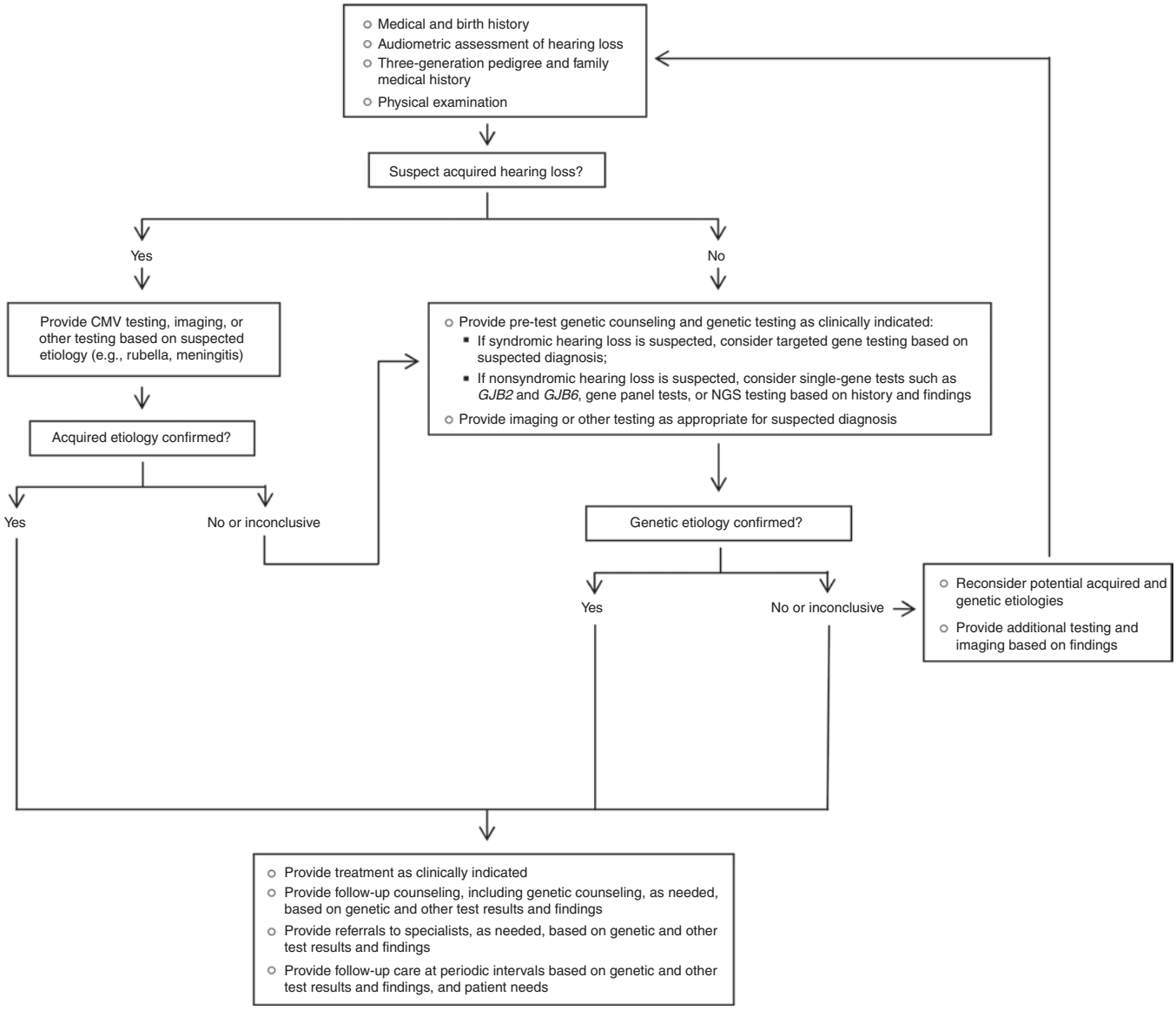


**Figure 1 Graphic overview of approaches to the clinical evaluation and etiologic diagnosis of hearing loss.** CMV, cytomegalovirus; NGS, next-generation sequencing.

focus on genetic causes of hearing loss because these laboratories may be more likely to report test performance with respect to hearing-related genes and to have developed approaches to specifically analyze relevant regions of the genome that may be refractory to more general NGS approaches.[92–96,99]

## OTHER TESTING IMPORTANT TO THE ETIOLOGIC DIAGNOSIS OF HEARING LOSS

Because CMV remains a common cause of pediatric hearing loss, testing for congenital CMV infection by rapid culture or polymerase chain reaction of saliva or urine samples from newborns is recommended as an initial test once a newborn hearing loss is confirmed (**Figure 1**). However, testing for CMV is most diagnostic when done before ~6 weeks of age.[101–105] A negative result most likely excludes CMV as the cause of the hearing loss, but a positive result may not necessarily indicate that the hearing loss is due to CMV infection, especially if obtained in older children who may have been exposed to CMV after birth.

Recent algorithms for the evaluation of hearing loss suggest that other nongenetic tests, such as computed tomography, magnetic resonance imaging, renal ultrasonography, electrocardiography, and ophthalmologic consultation, have an important role because their results can guide genetic testing or interpretation of DNA sequence variants.[106] For example, temporal bone imaging is commonly recommended to look for an enlarged vestibular aqueduct, which would prompt genetic testing for Pendred syndrome.[27,107,108] However, many nongenetic tests have low diagnostic yield in patients with hearing loss.[109] Furthermore, recent advances in genetic testing technologies that permit the analysis of many genes simultaneously at rapidly decreasing cost may soon prompt reassessment of the clinical utility of certain nongenetic tests as part of the initial

workup for the etiologic diagnosis of hearing loss. Such reassessments will need to consider the clinical utility of various nongenetic tests versus the risks associated with those tests, such as the clinical utility of computed tomography and magnetic resonance imaging versus the risks associated with radiation exposure and sedation.[17,109] As evidence for the clinical utility of NGS tests for the etiologic diagnosis of hearing loss is accumulated and evaluated, physicians should continue to rely on their best clinical judgment and consider the use of nongenetic tests for the evaluation of hearing loss on a case-by-case basis. For example, unless cochlear implantation is being considered, auditory neuropathy is detected, progressive hearing loss is identified, or other specific clinical concerns exist, it could be argued that temporal bone imaging might, in some cases, be better used as a complement or follow-up to genetic testing rather than as a part of the initial diagnostic evaluation.[109,110] In addition, in the absence of specific clinical concerns or family history, tests such as electrocardiographic studies, thyroid function testing, urinalysis, and renal ultrasonography might also be postponed until results of genetic testing are obtained, and then ordered as clinically indicated.[109,111,112]

## GUIDELINE

1. All newborns and infants with confirmed hearing loss should undergo a comprehensive evaluation in which patient-focused medical and birth histories and a three-generation pedigree and family medical history are obtained, and a physical examination that focuses on dysmorphic physical findings is performed. Evaluation of children and young adults with hearing loss should follow a similar approach. Evaluation of deaf or hard-of-hearing adults should be customized based on the age of onset and other characteristics of the hearing loss (**Figure 1**).
   - The medical and birth histories may be helpful in differentiating between acquired versus inherited causes of hearing loss. Elements of medical and birth histories focused on hearing loss include the following:
     - Prenatal history, including maternal infections (e.g., CMV, rubella) and illnesses (e.g., syphilis), or medication or drug exposures (e.g., thalidomide, retinoic acid)[113,114];
     - Neonatal history, including premature birth, low birth weight, birth hypoxia, hyperbilirubinemia, sepsis, and exposure to ototoxic medications;
     - Postnatal history, including viral illnesses, bacterial meningitis, head trauma, noise exposure, and exposure to ototoxic medications; and
     - Audiometric assessment of the hearing loss, including sensorineural versus conductive or mixed hearing loss; age of onset; progressive, nonprogressive, or fluctuating nature of the hearing loss; laterality, symmetry, severity, and configuration of the hearing loss; and the presence or absence of vestibular dysfunction or auditory neuropathy.
   - The pedigree and family medical history should focus on identifying the following:
     - First- and second-degree relatives with hearing loss or with features commonly associated with hearing loss (such as pigmentary, branchial, or renal anomalies) or sudden cardiac death;
     - A pattern of inheritance;
     - Ethnicity and country of origin;
     - A common origin from ethnically or geographically isolated areas; and
     - Consanguinity.
   - The physical examination should focus on dysmorphic and other physical findings such as the following:
     - Unusual facial appearance, with attention to asymmetry;
     - Pigmentary anomalies;
     - Neck, skin, facial, or ear anomalies;
     - Neurological abnormalities;
     - Balance disturbances;
     - Skeletal abnormalities; and
     - Other unusual physical findings.
2. For individuals with findings that suggest a syndromic genetic etiology for their hearing loss,
   - Pretest genetic counseling should be provided, and, with patient's informed consent, genetic testing, if available, should be ordered to confirm the diagnosis—this testing may include single-gene tests, hearing loss sequencing panels, WES, WGS, chromosome analysis, or microarray-based copy-number analysis, depending on clinical findings;
   - Appropriate studies should be undertaken to determine whether other organs are involved; and
   - Appropriate near-term and long-term screening and management should be arranged, including referrals to specialists, as indicated by the associated manifestations of the particular syndrome.
3. For individuals lacking physical findings suggestive of a known syndrome and having medical and birth histories that do not suggest an environmental cause of hearing loss, a tiered diagnostic approach should be implemented.
   - Pretest genetic counseling should be provided, and, with patient's informed consent, genetic testing should be ordered.
     - Single-gene testing may be warranted in cases in which the medical or family history, or presentation of the hearing loss, suggests a specific etiology. For example, testing for mitochondrial DNA mutations associated with aminoglycoside ototoxicity may be considered for individuals with a history of use of aminoglycoside antibiotics.
     - In the absence of any specific clinical indications and for singleton cases and cases with apparent autosomal recessive inheritance, the next step should be testing for DFNB1-related hearing loss (due to mutations in *GJB2* and adjacent deletions in *GJB6*).

  - If initial genetic testing is negative, genetic testing using gene panel tests, NGS technologies such as large sequencing panels targeted toward hearing loss–related genes, WES, or WGS may be considered. Because several tests are clinically available, the clinician must be aware of the genes included in the test (panel) chosen and the performance characteristics of the platform chosen, including coverage, analytic sensitivity, and what types of mutations will be detected. It should be noted that the cost of these new genetic sequencing technologies is decreasing so rapidly that a tiered approach to testing may soon no longer be cost effective. In particular, for large sequencing panels targeted toward hearing loss–related genes, it may, in some cases, already be more cost effective to use NGS technologies as the initial test in the evaluation of hearing loss. However, issues related to genomic testing, such as the likelihood of incidental findings, will have to be addressed.
  - If genetic testing reveals mutation(s) in a hearing loss–related gene, mutation-specific genetic counseling should be provided, followed by appropriate medical evaluations and referrals.
  - If genetic testing fails to identify an etiology for a patient's hearing loss, the possibility of a genetic or acquired etiology remains. This point must be emphasized because it can be misunderstood by clinicians and by patients and their families. For interested patients and families, further genetic testing may be pursued on a research basis.
- Temporal bone imaging by computed tomography or magnetic resonance imaging should be considered as a complement to genetic testing, particularly if the diagnosis remains unclear, if cochlear implantation is being considered, if auditory neuropathy is noted, in cases of progressive hearing loss, or if other clinical concerns exist. The anticipated clinical utility of imaging studies should be balanced against the risks associated with radiation exposure and sedation.
- CMV testing should be done at the same time as genetic testing for infants with congenital hearing loss. For later-onset or progressive hearing loss, CMV testing can be obtained, but the likelihood that a positive test is due to postnatal exposure increases with age.

4. Referral to a multidisciplinary care center, when available, is recommended.
   - A team approach that includes otolaryngologists, clinical geneticists, genetic counselors, audiologists, speech and language specialists, early hearing intervention and family support specialists (which may include other individuals who are deaf or hard of hearing or other parents of deaf or hard-of-hearing children), and other appropriate specialists offers optimal opportunity to provide ongoing management and support of deaf and hard-of-hearing individuals and their families as their needs change over time.
   - For cases in which the genetic evaluation failed to identify an underlying cause, periodic follow-up care every 3 years with a geneticist may be appropriate for several reasons. First, subtle features of syndromic forms of hearing loss may not be apparent at birth or early in childhood but may appear as deaf or hard-of-hearing individuals grow into adulthood. These may prompt additional medical tests or referrals for specialty care. Second, follow-up visits offer the opportunity to inform individuals about new genetic tests that may have become available or changes in the interpretation of previous test results as medical knowledge advances. Finally, follow-up visits may also help identify clinical concerns unrelated to hearing loss, for which referral for specialty care may be appropriate (**Figure 1**).
5. Regardless of whether genetic test results are positive, negative, or inconclusive, results should be communicated through the process of genetic counseling.

## DISCLOSURE

C.G.P. has received grant support to develop educational materials on cancer for the Deaf community. H.L.R. is employed by a fee-for-service laboratory that offers diagnostic testing for hearing loss. The other authors declare no conflict of interest.

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