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Clinical measures of auditory function: The cochlea and beyond

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Introduction

Hearing loss is one of the world's leading chronic health conditions and has become increasingly prevalent in older adults, exceeding 90% in individuals over 80 years of age.^{1–3} For many, it results in psychosocial consequences including depression and social isolation.^{4–6} Decreases in health-related quality of life have also been reported,⁷ and although it is not thought of as a life-threatening health condition, hearing loss causes communication interference that can substantially affect social integration, functional ability, and self-image. Furthermore, it may impede safety by limiting an individual's ability to hear warning signals and sirens (e.g., in agricultural settings⁸). Noise-induced hearing loss further poses a significant public health problem, as approximately 10% of US adults (22 million) between 20 and 69 years of age have permanent hearing loss due to exposure to loud noise at work or during leisure activities.⁹ Research conducted over the last 2 decades has brought attention to the ototoxic effects of medications and chemicals and their potentially synergistic effects with noise.^{10–13} In some occupational settings, such as refinery, paint industry, aviation industry, military, and fire service, it is common to encounter exposure to both noise and ototoxic chemicals,¹⁴ making early detection and intervention critical. Please refer to companion papers exploring noise-induced hearing loss by Hong and colleagues as well as ototoxicity by Campo and colleagues.

A growing number of factors associated with increased risk of hearing loss in adulthood include gender,¹⁵ genetic susceptibility,¹⁶ racial/ethnic groups,^{17,18} and other diseases such as risk factors associated with cardiovascular disease (e.g., history of hypercholesterolemia, diet, and smoking).^{19–22} Diabetes (both Types I and II) has been associated with prevalent hearing loss.^{23,24} Evaluation of hearing loss associated with the combined effects of these risk factors requires tests that can fully evaluate the auditory system, from the cochlea to the higher auditory centers; however, there is no “gold standard” audiological test protocol available for this purpose at this time. The objective of this review is to discuss the tools commonly used in the clinic and present emerging strategies to aid in the early identification of hearing loss in adults. Audiological evaluation of pediatric populations requires a unique set of considerations that are beyond the scope of this paper (for review and pediatric evaluation recommendations, see Harlor and Bower²⁵).

Hearing loss continues to be a chronic disease that significantly impacts quality of life and work productivity, especially for workers who labor in noisy environments.²⁶ The disease also places a significant financial burden on society, as it is estimated that the lifetime cost of severe to profound hearing loss exceeds \$250,000 per patient in the US²⁷ mostly due to losses in work productivity. Increased awareness and understanding of hearing loss identification and prevention will help mitigate the detrimental consequences of hearing impairment on individuals and society. This paper provides a basic appreciation of hearing loss assessment needed for this promotion and advancement in hearing health.

Anatomy and physiology

The peripheral auditory system is typically discussed in three main sections: the outer, middle, and inner ears. The outer ear serves as the initial receiver of environmental sounds and aids in localization in the vertical plane as well as differentiation between sound sources in the front and back of the listener. The middle ear, and its three ossicles (malleus, incus, and stapes), is chiefly responsible for delivering sound to the cochlea and overcoming the impedance mismatch between the external auditory canal (air-filled) and the cochlea (fluid-filled). The middle ear also houses the stapedius muscle, attached posteriorly to the stapes, which contracts in response to loud sounds, effectively decreasing sound transmission to the inner ear and providing protection from acoustic insults. Diseases affecting the outer or middle ear are known as *conductive pathologies*, and include otitis media and cholesteotoma among others.

After coursing through the middle ear, an acoustic stimulus arrives at the inner ear, or cochlea. The stimulus is mechanically transferred by the middle ear ossicles into the cochlear fluids resulting in a traveling wave that propagates along the basilar membrane, with its velocity decreasing as it approaches the place of resonance, also known as the characteristic frequency place. The cochlea's organization is *tonotopic*, meaning the mechanical properties of the cochlea in general and the basilar membrane in particular dictate that stimuli at different frequencies result in maximum traveling-wave vibration at unique locations on the basilar membrane. At the apex of the cochlea, the basilar membrane is elastic and most sensitive to low frequencies. Conversely, the stiff base responds maximally to high frequencies. In humans, the range of hearing extends nearly 10 octaves, from 20 to 20,000 Hz.

The coiled cochlea is delineated by three *scalae*: the vestibuli, media, and tympani. The basilar membrane separates the scala media from the scala tympani. Three rows of outer hair cells (OHCs) sit atop the basilar membrane, with their tuft-like stereocilia protruding into the tectorial membrane above. The delicate organ of Corti is found in the scala media with cellular constituents bathed in a high-K⁺, low-Na⁺ fluid known as the endolymph. The high-K⁺ concentration in the scala media provides a unique driving force for K⁺ and Ca²⁺ cations to enter hair cells upon excitation. Low-level stimuli are detectable because they are amplified in the cochlea via a process collectively called “cochlear amplification” in which it is well understood that OHCs are involved in some capacity; however, the precise mechanism responsible for this process remains debatable.²⁸ Traveling waves on the basilar membrane push hair bundles toward the tallest stereocilia (the kinocilium) and hair cells are depolarized (excited). Inner hair cells are connected to afferent nerve fibers and upon stimulation, glutamate is released and signals are transmitted to the brain. Hearing loss that occurs in the cochlea or beyond (i.e., in the eighth nerve or higher-level neural centers) is considered *sensorineural hearing loss*.

Standard clinical assessment of hearing

Evaluation of the full auditory system, from the cochlea to the higher auditory pathways, requires a combination of physiological and psychoacoustic measures. A variety of tests of auditory function targeting the peripheral and central segments of the auditory system have

been applied to accomplish this; however, this can be costly and time intensive. Psychoacoustic tests tend to provide a global measure of auditory system function as well as target the integration of auditory information across the two ears, such as behavioral hearing thresholds and tests of speech perception with or without background distracters. Physiological tests aid in determination of the general site of lesion in the auditory periphery (e.g., lower brainstem) and offer objective measures of auditory function. In this domain, measures of otoacoustic emissions (OAEs) and auditory brainstem responses (ABRs) are highlighted and detailed below.

The basic clinical assessment provides a global evaluation of hearing, with more advanced and localized testing pursued when warranted. Standard tests used for this purpose typically include behavioral audiometry, speech testing, and immittance testing.

Behavioral audiometry

Currently, the “gold standard” test of hearing is behavioral audiometry in the standard frequency range (up to 8 kHz). Pure tone signals are delivered via insert earphones or supra-aural headphones at inter-octave frequencies from 0.25 to 8 kHz and the patient responds by raising his or her hand or pressing a button when a sound is heard. Delivery of auditory stimuli in this way (through the outer, middle, and inner ear) using earphones results in air conduction thresholds as the entire auditory pathway is utilized. In each ear, hearing thresholds (i.e., the lowest intensity at which the presence of the signal can be identified at least 50% of the time) are obtained for each frequency. The most commonly employed and recommended procedure for obtaining threshold is the modified Hughson–Westlake procedure.²⁹

Bone conduction testing is often warranted to bypass the outer and the middle ear (i.e., the conductive auditory pathway) to find threshold when sound is delivered directly to the cochlea. This is done using a bone conduction vibrator (placed on the forehead or mastoid process). Bone conduction testing is often unnecessary if air conduction thresholds are normal.

Threshold values are measured in decibel hearing level (dB HL) and recorded on a graph known as the audiogram (Fig. 1), where 0 dB HL represents the mean threshold for persons

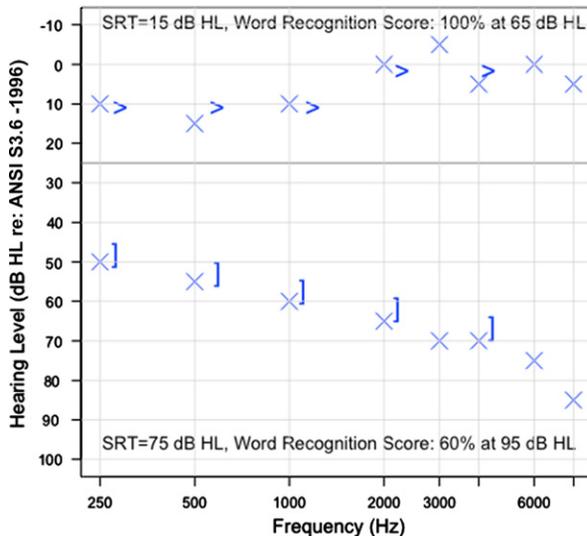


Fig. 1. Audiogram depicting behavioral hearing thresholds for the left ears of an individual with normal hearing (blue “X” and “>”) and an individual with asymmetric severe hearing loss (blue “X” and “]”). Masking for bone conduction was not necessary when testing the normal hearing person, but it was necessary for the hearing-impaired individual due to the marked threshold asymmetry between ears. The horizontal line at 25 dB HL indicates the boundary of clinically normal hearing. Responses above this line are considered within normal limits. Speech reception threshold and word recognition scores (with presentation levels) are also shown. (Color version of the figure is available online.)

with normal hearing.³⁰ On the audiogram, universal symbols are used to define the left ear (X) and right ear (O) air conduction thresholds. Other symbols (<, >, and ~) refer to bone conduction testing. In cases of unilateral or asymmetric hearing loss, “masking” of the non-test ear may be necessary to define an accurate threshold for the poorer ear (the test ear; see Fig. 1 for example). When masking noise is used in the non-test ear, the resultant threshold is known as a masked threshold. Specific symbols ([and]) are used to demark masked bone conduction thresholds.

Hearing loss can be classified by type (i.e., sensorineural, conductive, or mixed), configuration (e.g., flat, sloping), and severity (e.g., mild, moderate, severe, or profound). Individuals with sensorineural hearing loss (i.e., cochlear or neural degeneration) demonstrate similar air and bone conduction thresholds. According to the American Speech–Language–Hearing Association, a difference greater than 10 dB is considered a significant air–bone gap and requires the use of masking to find the true threshold of the test ear and eliminate a response from the non-test ear.³¹ In the case of conductive pathologies (e.g., otitis media), the audiogram will show an air–bone gap where the bone conduction thresholds are significantly better (> 15 dB) than the air conduction thresholds. Cases where both an air–bone gap and elevated bone conduction thresholds are observed suggest a loss of mixed etiology. Older adults with age-related hearing loss commonly demonstrate sloping or steeply sloping audiograms, where low-frequency thresholds are normal and thresholds at higher frequencies (e.g., 4–8 kHz) are elevated.³¹ Flat audiograms are also quite common, especially among females. Notched configurations (especially at 4 kHz) are often seen in patients with a history of significant noise exposure.³² Figure 1 shows an audiogram for an individual with clinically normal hearing (all thresholds < 25 dB HL) and one with a severe sensorineural hearing loss. For clarity, only the left ear is illustrated for each individual. Masking for bone conduction was only necessary when testing the person with hearing loss.

Identifying the severity of hearing loss is fundamental to determine appropriate intervention strategies. Hearing losses between 26 and 40 dB HL are considered mild, 41 and 55 dB HL moderate, 56 and 70 dB HL moderately severe, 71 and 90 dB HL severe, and > 91 dB HL profound.³³ Severity of loss may be interpreted based on thresholds at individual frequencies or the pure tone average (i.e., the average hearing threshold at 0.5, 1, and 2 kHz). Once the type, degree, and severity of loss are established, a fitting intervention can be selected, which may include hearing aids, aural rehabilitation, cochlear implants, medical intervention, or other approaches.

Speech audiometry

Speech testing supplements pure tone audiometry and may facilitate differential diagnosis of site of lesion. The most commonly employed speech tests, typically via air conduction, are speech reception threshold (SRT) and word recognition scores (WRS). The SRT is akin to the behavioral hearing threshold and is the intensity at which the listener can repeat 50% of presented stimuli, which are typically two-syllable words known as “spondees” (e.g., baseball, steamboat). Word recognition score (percent correct) is ascertained by presenting monosyllabic words at a level 20–40 dB above the SRT and represents the ability of the individual to understand speech materials under a controlled test condition (in quiet). In Figure 1, the individual with normal hearing demonstrated a lower SRT (15 dB HL) compared to the case of hearing loss (75 dB HL) consistent with the difference in hearing thresholds. Furthermore, an excellent word recognition score (100%) was obtained in the individual with normal hearing, whereas a poor word recognition score of 60% was observed in the one with hearing loss.

A chief complaint of adults with hearing loss is the inability to comprehend a target speaker in noisy environments (e.g., crowded restaurants), but this ability cannot be reliably predicted from the pure tone audiogram or other standard speech tests in quiet conditions described thus far. Therefore, another method is needed to assess this ability and a range of instruments targeting understanding speech in noisy conditions are available for this purpose. In particular,

the QuickSIN is a standard clinical speech-in-noise test that has gained popularity in the last decade and comprises sentences recorded in four-talker babble.³⁴ It represents a realistic simulation of a social gathering, in which the listener must “tune in” the target talker and “tune out” one or more of the background talkers. Each of the 12 QuickSIN lists has six sentences, one sentence at each signal-to-noise ratio (SNR) of 25, 20, 15, 10, 5, and 0 dB. A single QuickSIN list takes approximately one minute to administer and score.³⁵ The average score from two or more lists is often reported.

Immittance audiometry

Tympanometry in combination with acoustic reflex testing comprises the acoustic immittance battery, which aids in identifying the type of hearing loss. Tympanometry includes measures of ear canal volume, static compliance, and middle ear pressure.^{36,37} The tympanogram graphically represents the middle ear compliance (in ml or millimhos) as a function of changes in pressure (in daPa). The peak of the tympanogram represents maximum compliance, the point at which the outer and middle ear pressures are the same in a normal functioning system. A classification scheme has been adopted to interpret tympanometric findings.^{36,38} Type A tympanograms are considered normal (i.e., compliance is maximal when the middle ear and ear canal pressure are the same as the atmospheric pressure), whereas Type B tympanograms are flat and indicative of middle ear pathology such as otitis media with effusion or other infection of the middle ear space. Type C tympanograms show negative peak pressure, which is common with allergies or congestion. The Type C tympanogram is graphically similar to the Type A, with a horizontal shift in the negative direction. Abnormal tympanometric findings are indicative of conductive pathologies, which are often treatable via pharmacological or surgical intervention.

Acoustic reflex testing

Acoustic reflex testing measures the reaction of the stapedius muscle in response to intense sound and has been described in detail.³⁹ The response is bilateral, thus if the right ear is stimulated, both the middle ear muscles contract. Contraction of the stapedius stiffens the stapes and the alteration can be detected as increased acoustic impedance at the tympanic membrane. Immittance devices permit stimulation of the ipsilateral (probe) or contralateral (opposite) ear, allowing for isolation of the site of lesion within the reflex pathway. The ipsilateral pathway targets the ipsilateral eighth nerve, brainstem connections, and ipsilateral seventh nerve, which innervates the stapedius. The contralateral arc includes the contralateral eighth nerve, crossed brainstem connections, and the ipsilateral seventh nerve and middle ear. In normal systems, reflexes are present when a pure tone stimulus is 85–100 dB SPL at 0.5, 1, or 2 kHz.⁴⁰ Conductive pathologies will elevate the acoustic reflex threshold, and at times, the reflex may be absent. Retrocochlear pathologies are also associated with elevated or absent reflexes, but tympanometric and behavioral audiometric findings can further assist in identifying the site of lesion.

Advanced clinical assessment of hearing

Otoacoustic emissions (OAEs)

Pure tone and speech audiometry are subjective measures of auditory function that require a stimulus to be heard by the patient and, in turn, actively respond to that stimulus. In some patient populations these measurement tools are not practical (e.g., in neonates or the mentally handicapped), highlighting the importance of objective measures of auditory function such as OAEs.

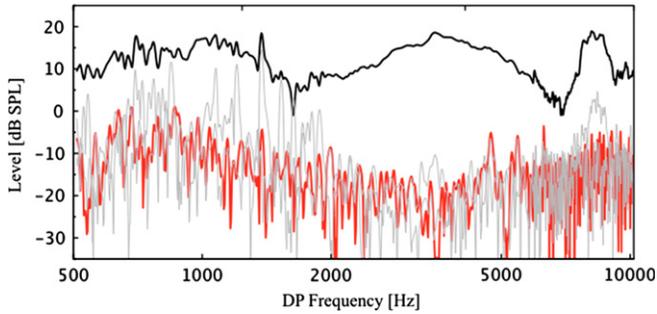


Fig. 2. Example of DPOAE level (dB SPL) as a function of DP frequency (Hz) from an individual with normal hearing (black) and one with severe hearing loss (red). Thin traces represent noise floors. Responses were elicited with $L_1 = L_2 = 75$ dB SPL and f_2/f_1 ratio of 1.22. Note the significantly more robust amplitude of the DPOAE in the normal hearing individual compared to the patient with hearing loss. (Color version of the figure is available online.)

OAEs are low-intensity “echo” sounds that emanate from OHCs due to the nonlinear nature of the healthy cochlea.⁴¹ The emissions are classified by their evoking stimulus (clicks or pure tones) or the lack thereof (spontaneous OAEs). The evoked OAEs are of greater clinical importance and can be further differentiated by the nature of the evoking stimulus from transient evoked OAEs (TEOAEs) evoked by clicks or tone pips (i.e., stimuli that are very brief in duration) as opposed to distortion product OAEs (DPOAEs) elicited using two pure tones (f_1 and f_2 , $f_1 < f_2$). Upon stimulation with two tones, distortion generated in the cochlea can be recorded in the ear canal at frequencies mathematically related to the stimulus frequencies.⁴² Of these, the most extensively studied and clinically used is the DPOAE at the frequency $2f_1 - f_2$.⁴³ Commonly the level of DPOAEs as a function of frequency is used as an indicator of cochlear health (Fig. 2). Compared to normal hearing, DPOAE levels are reduced with mild to moderate hearing losses and are rarely present when hearing thresholds exceed 60 dB HL.⁴⁴ DPOAEs offer a noninvasive, objective measure of cochlear function known to be sensitive to minor changes in cochlear physiology.^{45,46}

Auditory brainstem response (ABR) testing

Changes in brainstem electrical activity (i.e., electrical potentials) are measurable using surface electrodes and recorded in the auditory brainstem response (ABR) test. The ABR (Fig. 3) is a waveform with seven peaks occurring within 15 ms of stimulus onset. Clicks or tone-bursts are commonly used to evoke a response. The ABR peaks represent neural activity from the eighth nerve fibers and brainstem nuclei including the cochlear nucleus, superior olivary complex, and inferior colliculus. Waves I, III, and V (Fig. 3) are the most robust and therefore provide the greatest clinical utility. The latency of these waves will increase and the amplitude will decrease, with reductions in stimulus intensity. The ABR can be obtained using rapid stimulus presentation (20–33 clicks/s), making it a time-efficient means to estimate hearing threshold or aid in the diagnosis of various retrocochlear pathologies.

The ABR is a useful clinical tool, especially for aiding in the identification of the site of lesions in individuals with sensorineural hearing loss. However, because synchrony of neural firing is key for a normal response, neuropathy may severely degrade the waveform morphology, making it difficult to approximate the degree of hearing loss. Nonetheless, the ABR offers an objective assay of central auditory function and is an important tool for the identification of primary neuronal degeneration (i.e., neuronal damage in the absence of peripheral dysfunction). A test battery that combines OAE and ABR measures helps further isolate the site of lesion and may elucidate the specific patterns of age- or occupational-related auditory damage. Hazardous occupational exposures including noise and chemicals have been

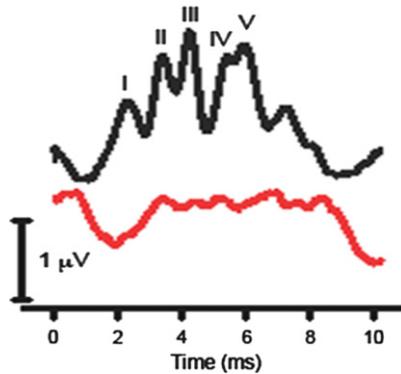


Fig. 3. Example supra-threshold ABR responses [amplitude (μV) as a function of time (ms)] from an individual with normal hearing (black trace) and a patient with severe sensorineural hearing loss (red trace). Waves I, III, and V are indicated on the trace of the normal hearing subject, but poor waveform morphology makes labeling difficult for the lower trace. (Color version of the figure is available online.)

shown to negatively impact the central auditory pathway,⁴⁷ suggesting that the ABR can be helpful in occupational settings for monitoring or diagnostic purposes.

Summary and conclusions

This is an exciting time for hearing healthcare and audiology, as emerging strategies for early identification of hearing loss are surfacing. For example, although the healthy human ear is able to detect sounds up to 20 kHz, typical clinical protocols limit evaluation to 8 kHz. Evidence is accumulating to suggest measurement of auditory function at extended high frequencies (> 8 kHz) is useful for the early detection of chemical-, noise-, and age-related hearing loss.^{1,48} Recent work has shown that age-related discrepancies are apparent in behavioral hearing thresholds above 8 kHz in individuals who are as young as 10–21 years and 22–35 years of age.¹ This higher frequency auditory assessment, both in the behavioral and physiological realms, can advance hearing healthcare by aiding in earlier detection of hearing loss that progresses from base to apex (i.e., from high to low frequencies). High-frequency OAE measurements have already demonstrated utility in detecting age-related hearing loss as well as early-stage ototoxic exposures.^{1,48,49} These risk factors often influence the basal end of the cochlea first. In the future, high-frequency assessment will undoubtedly play a vital role in hearing loss identification and targeted therapeutics.

Current identification and treatment of hearing loss continues to be suboptimal. Many individuals with hearing impairment fail to seek treatment altogether, leaving the disease undiagnosed and unmanaged. People who have strong support networks may be more likely to seek treatment, as the treated demographic tends to be older, have supportive significant others, and the perception that their hearing is poor.⁵⁰ Social stigma and personal reservations continue to deter potential hearing aid wearers, and thus, in the past three decades, hearing aid adoption rates have hovered around 20%.⁵¹ In an attempt to increase diagnosis and management, physicians have been urged to screen for hearing loss at annual wellness visits, but fewer than one in five individuals report receiving a screening at such a visit.⁵¹ These healthcare providers have the unique opportunity to discuss hearing concerns and provide screenings or referral recommendations for the undiagnosed.

Physicians (especially those in primary care, otology, and otolaryngology) and audiologists play an important role in identifying and treating hearing impairment. The primary care physician is often the first point of contact for persons who express hearing concerns and it is

critical that a referral to an audiologist is made for further evaluation when needed. The annual physical examination visit is an opportune time to screen individuals, particularly those with multiple risk factors or family history of hearing loss, and question them about any difficulty in hearing or change in their hearing abilities. Self-report measures can be used for this purpose and are easily administered and analyzed. The Hearing Handicap Inventory for Adults (HHIA) or the Hearing Handicap Inventory for Adults Elderly (HHIE for individuals over the age of 65 years) is one such tool and considers social and emotional effects of hearing loss using a 25-item questionnaire.⁵² A tool for the elderly is also available,⁵³ and an abbreviated screening version can be administered in only a couple of minutes to assess functional impairment.⁵⁴ The HHIA includes questions such as “Do you have difficulty hearing when someone speaks in a whisper?” and “Do you feel that any difficulty with your hearing limits or hampers you personal or social life?”

Although self-report metrics are reasonably valuable for identifying hearing loss and psychosocial consequences, they do not reveal the complete physiological deficit. Therefore, they should not be used as adequate substitutes for the standardized audiometric test in the primary care settings or occupational health clinics where the audiometric tests are available. Individuals with hearing loss exhibit marked variability in their social and emotional responses to the disease, particularly when severity is mild.⁵⁵ Self-report assessments are valuable in identifying individuals who could benefit from a full audiological evaluation and suitable intervention strategies. As primary care physicians act as gatekeepers for audiological referrals and hearing healthcare, it is important that they understand the benefit of brief screenings and simple questions to assess the patient’s hearing status. Most physicians are aware of treatment options such as cochlear implants and hearing aids, but few make referrals, on account of poor understanding of treatment eligibility and limited knowledge of appropriate referral sites.⁵⁶ Time permitting, questions regarding the patient’s ability to hear in quiet and in disruptive listening situations (e.g., crowded restaurants), as well as history of tinnitus and vertigo, should be asked. Taking the complete patient profile into consideration (including genetic predisposition and risk factors such as chemical exposures or cardiovascular disease) will also help the physician to recognize individuals who should be referred to an audiologist for a more thorough auditory assessment.

Treatment of hearing loss differs depending on the etiology and severity. Conductive pathologies can often be treated with surgical or medical interventions. Treatments for sensorineural hearing loss remain limited and consist largely of amplification devices, which do not correct the damage to the auditory system when hearing loss is present, but help overcome the audibility (and to some degree, processing) limitations. Hearing aids are a viable treatment strategy for many degrees (and types) of hearing loss, and over six million people in the US were hearing aid users (in 2004).⁵¹ Amplification devices do improve the quality of life, but many hearing aid wearers continue to express dissatisfaction, especially regarding speech understanding in noisy environments. Surgical improvements in cochlear implantation are continuing to surface and the treatment margin for implantation, once considered suitable only for profound hearing loss, is expanding (for review, see Cohen⁵⁷). Other advancements in pharmacologic interventions or cellular regeneration are in the works.⁵⁸ In the future, advances in differential diagnosis of hearing loss (i.e., separation of specific cochlear pathologies from neural loss), coupled with novel treatment strategies, may provide individuals with therapies to alleviate some of the stressors associated with hearing impairment.

There is a certain allure to emerging therapies for hearing loss, but early detection and prevention of hearing loss remains the best line of defense. In some settings, hearing loss prevention can be aided through the use of otoprotectants such as N-acetylcysteine (NAC) which can prevent or mitigate noise-induced hearing loss.⁵⁹ At the forefront of prevention are public health initiatives to promote hearing healthcare and screenings. Taken together, prevention, early identification, and innovative treatment strategies will ultimately help reduce the disease burden associated with hearing loss, a highly prevalent health issue.

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