

# Chapter 25

## Noise-induced Hearing Loss

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### INTRODUCTION

Exposure to excessively strong sounds may injure the peripheral auditory organ, resulting in hearing loss. Although any sound—noise, speech, music—of sufficient intensity will damage hearing, such losses are often referred to as “noise-induced hearing loss” (NIHL). Noise-induced hearing loss is the most common cause of adult sensorineural hearing loss before old age, with profound effects ranging from social isolation of individuals to serious national economic burdens. Although NIHL is not medically and surgically treatable, in most cases, it is preventable. By informing, counseling, and motivating people to protect their hearing, we as otolaryngologists, can make an enormous impact on preventing hearing impairment.

### EPIDEMIOLOGY

Occupational noise and nonoccupational noise have been estimated to cause 5–10% of the adult hearing loss burden in the United States.<sup>1</sup> Approximately, 30 million American workers are exposed to hazardous noises in their jobs; in Europe, about 35 million people are exposed to detrimental noise levels in industrial plants; and it is estimated that approximately 600 million workers are exposed to occupational noise worldwide. Occupational deafness is a leading occupational compensable disease in all countries.

Hazardous nonoccupational noise exposure is much more prevalent. The most important nonoccupational cause of NIHL is gunfire. About 65 million Americans own guns, and many of them participate in hunting or target shooting. Data from the interindustry noise study showed that men in non-noisy jobs who reported hunting and shooting sustained hearing loss that was the equivalent to 20 years' occupational exposure at 89 dBA.<sup>2</sup> With the growing

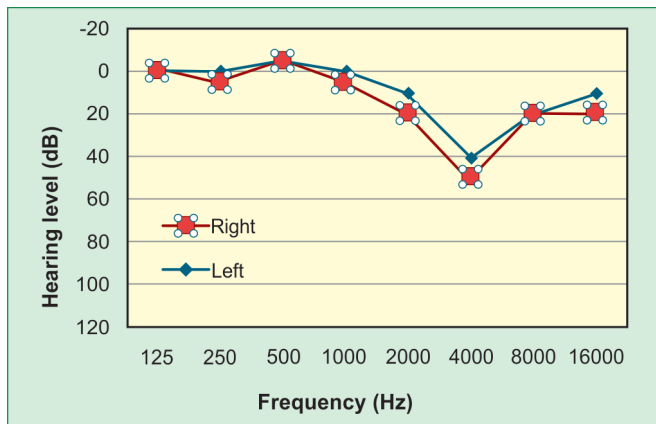
popularity of portable music players, the concern for long-term risk of cumulative recreational noise exposures also increases. Recent studies have shown that due to the time spent each day listening to personal listening devices (PLDs) at the average volume levels, approximately 5–10% of listeners are in danger of developing permanent hearing loss after five or more years of exposure.<sup>3</sup>

### PATHOGENESIS

#### Pure Tone Threshold Shift

Depending on the level of the sound exposure, either reversible or permanent damage can occur in the inner ear. The reversible loss, typically referred to as a temporary threshold shift (TTS), results from exposures to moderately intense sounds. An audiogram will show elevated thresholds, mainly at the 3- to 6-kHz frequency region. Depending on the intensity of the noise and the duration of exposure, recovery from TTS can occur over minutes, hours, or days.

If TTS does not recover, a permanent change in hearing occurs that is referred to as a permanent threshold shift (PTS). The precise relationship between the TTS and PTS stages of hearing loss due to noise exposure is unknown. Histopathological studies<sup>4</sup> showed that there was a focal loss of outer hair cells (OHCs) and a complete degeneration of the corresponding nerve-fiber endings in PTS. In contrast, TTS was correlated with a buckling of the supporting pillar bodies in the frequency region of the maximal exposure effect. Because PTS eventually develops from repeated exposures to stimuli that initially produce only TTS, it is likely that the latter condition is also associated with subtle changes to the sensitive OHC system that are undetected by light microscopy.



**Fig. 25.1:** Example audiogram showing noise-induced notch.

Obviously, more intense sounds lead to larger threshold shifts. However, simply measuring the physical intensity of the stimulus as a sound pressure level cannot assess the potentially damaging effect of noise. The human ear does not respond equally to all frequencies—high frequencies are much more damaging than low frequencies at the same physical intensity level. Consequently, most sound level meters are equipped with a filter that is designed to de-emphasize the physical contribution from frequencies at which the human ear is less sensitive to. This filter is referred to as the A filter. The hazardous noise will be measured based on the A scale (dBA), which gives greater weight to those frequencies most hazardous to human hearing (1–5 kHz) and less weight to higher and lower frequencies.

Typically, hearing loss from noise begins in a notch pattern (noise notch) in the 3–6 kHz, with maximum loss at 4 kHz (Fig. 25.1). As the length of time of exposure to loud noise increases, hearing loss becomes greater and begins to affect adjacent higher and lower frequencies. According to Taylor's<sup>5</sup> landmark cross-sectional study of the progression of NIHL, with consistent exposure to noise level >100 dBA, there were approximate 10–20 dB shifts at the higher frequencies (3–6 kHz) during the 1–2 years of exposure, growing to be a 20 dB or greater loss after a 3-year exposure; there was a 40 dB or greater threshold shift after 8-year exposure. However, hearing loss levels are rarely beyond about 70–90 dB, even after more than 30 years of continuous noise exposure. For 1 kHz, growth of threshold shift is somewhat more gradual, but >50% of NIHL is accrued in the first 10 years. Most data show that NIHL does not progress after cessation of the offending exposure. Contrast to the accelerating process in age-related hearing loss (ARHL) (i.e. the rate of change of hearing

loss increases with time), NIHL is a decelerating process (i.e. the rate of change decreases with time). This contrast can be helpful in determining the relative contribution of these two sources of hearing loss in individual cases.

There are several explanations for the familiar 4-kHz notch: the protective effect of the acoustic reflex (contraction of the stapedius muscle in response to loud sound) for frequencies <2 kHz<sup>6</sup>; the fact that intermittency of noise exposure is most protective for low frequencies; and OHC at the base of the cochlea are especially susceptible to oxidative stress.<sup>7</sup> On the other hand, a notch is not proof of NIHL and can be seen after head injury, after barotrauma, or even in the absence of any explanatory history.

## Inner Ear Damage

Noise overexposure may result in significant damage to the cochlear portion of the inner ear. This damage may result from mechanical trauma and/or metabolic processes that perpetuate cell death. Mechanical trauma typically occurs from blast exposures (often called acoustic trauma), and results in tearing, sharing, or rupturing of cells/tissues in the cochlea, particularly in the organ of Corti. The most common form of NIHL is due to metabolic processes that result in cell death. Although most cochlear cells are vulnerable, hair cells and neurons are often considered the most susceptible to noise injury. Hair cells and neurons are particularly important for hearing sensitivity; therefore, understanding the underlying metabolic cascades that result in the death of these cells may lead to future otoprotective strategies. It is known that noise overexposure induces multiple types of cell death among hair cells, suggesting that several metabolic cascades are activated by the same noise exposure.<sup>8</sup> Interestingly, most of these metabolic cascades ultimately result in DNA damage, which is a signature characteristic of the cell death process. Furthermore, DNA damage has been shown to precipitate specifically in hair cells and spiral ganglion neurons as a result of noise exposure. Such DNA damage may accumulate within minutes after exposure. This is important because hair cells and spiral ganglion neurons are poor at repairing damaged DNA, which may explain why these cells are among the most vulnerable to noise-induced cell death.<sup>9,10</sup>

### *Metabolic Cascades that Perpetuate Cell Death after Noise Overexposure*

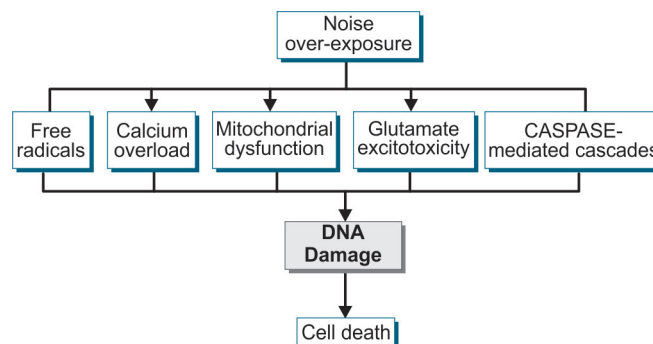
Noise generates toxic free radicals in the cochlea. Free radicals damage important biomolecules such as DNA,

proteins, and lipids. Although, proteins and lipids can be resynthesized, damage to DNA is particularly significant to terminally differentiated cells such as hair cell and neurons. This is due to the fact that hair cells and neurons cannot re-enter the cell cycle to resynthesize new DNA. DNA damage induced specifically by free radicals has been shown to accumulate in the cochlea after noise overexposure. For instance, the free radical induced 8-hydroxy-2'-deoxyguanosine DNA adduct accumulates >8 hours after noise exposure.<sup>11</sup> This is particularly important because DNA damage is one of the most potent triggers of cell death. In addition to free radicals, noise overexposure may stimulate mitochondria to released cell death mediators, such as endonuclease-G and the apoptosome-inducing factor, both of which translocate to the nucleus to damage DNA and perpetuate cell death.<sup>12,13</sup> Additionally, noise exposure may induce both the extrinsic and intrinsic caspase-mediated cell death pathways that use the DNA fragmentation factor enzyme to damage DNA.<sup>14,15</sup> Furthermore, noise exposure increases intracellular concentrations of calcium to levels that may force calcium-mediated nucleases to fragment DNA.<sup>14,16</sup> Noise overexposure disrupts cochlear ionic homeostasis and such alterations may promote DNA damage within spiral ganglion neurons. For instance, noise overexposure induces excess glutamate in the synaptic cleft between inner hair cell and spiral ganglion neurons. This results in cellular influx of excessive sodium and chloride coupled with excessive efflux of potassium ions.<sup>14</sup> In addition to osmotic stress, this situation promotes DNA damage. For instance, excess influx of sodium and chloride induces DNA strand breaks by restricting strand break repair enzymes from the nucleus which then promotes cell death.<sup>17</sup> Additionally, the maintenance of intracellular potassium levels is necessary to suppress the DNA fragmentation factor enzyme, an enzyme that will damage DNA when potassium levels are low.<sup>18</sup> Therefore, noise-induced cellular efflux of potassium may promote DNA fragmentation. Indeed, cochlear DNA fragmentation is a common biomarker of noise injury.<sup>19</sup>

## Biomedical Approaches to Limit Noise-induced Cell Death

A fundamental principle of metabolic noise injury is that noise overexposure induces multiple independent and complementary biochemical cascades that all eventually result in DNA damage that leads to cell death. These cell death cascades are driven by subcellular events such as

**Flowchart 25.1:** Noise-induced cell death in the inner ear. Noise overexposure triggers multiple biochemical cascades that are dependent on free radical production, calcium overload, dysfunctional mitochondria, excess production of glutamate, and caspase-mediated processes. Each of these mechanisms ultimately results in DNA damage that then elicits cell death.



the proliferation of free radicals, dysfunctional mitochondria and loss of cellular energy, elevation of calcium to dangerous micromolar levels, excessive accumulation of glutamate, and the stimulation of extrinsic and intrinsic caspase-mediated cell death pathways. In order to provide protection from noise injury, hearing researchers have blocked one or more of these biochemical cascades with antioxidants, calcium inhibitors, energy enhancers, growth factors, caspase inhibitors, and an impressive variety of other bioactive compounds.<sup>20</sup> These efforts are necessary and have provided valuable information about the underlying pathophysiology. However, to date there are no widely accepted biomedical therapies for NIHL. This suggests a need for new ways of thinking about the underlying pathophysiology. For instance, noise-induced cell death cascades are driven by events that are all upstream to DNA damage, which suggest that damaged DNA is a common node in the cell death process. If DNA damage is common to the various biochemical cascades (Flowchart 25.1), then approaches aimed at improving DNA repair might be more efficacious than blocking individual upstream cascades. This notion of improving cochlear DNA repair capacity in order to achieve otoprotection is particularly attractive since clinically significant improvement in DNA repair capacity is amenable to therapeutic manipulations. For instance, small molecular weight molecules called carboxy alkyl esters (CAEs) have been shown in randomized control clinical trials to improve systemic DNA repair capacity that prevents cell death from toxic chemotherapy exposures.<sup>21</sup> Furthermore, animal studies have shown that treatments with CAEs mobilize DNA repair enzymes in the cochlea, reduce noise-induced

DNA damage levels in the cochlea, prevent hair cell death, and preserve hair cell and neural functions after noise damage.<sup>22–24</sup> However, human studies have not been conducted.

Improvements in DNA repair may also be important for the regeneration of cochlear cells after injury. For instance, current efforts to stimulate hair cells to re-enter the cell cycle often results in the upregulation of DNA damage signaling and then cell death. This is due to the fact that nondividing cells accumulate DNA damage in regions of their genome that are not used (called gene deserts), under normal conditions, such accumulation of damage poses little or no threat to the cell. However, when these cells are stimulated to re-enter the cell cycle, the replication machinery becomes overwhelmed by the level of DNA damage that has accumulated and DNA damage and cell death signaling ensues. This mechanism would be particularly potent for cells with high intrinsic metabolic demands such as hair cells. Indeed, genetic manipulations of cell cycle mediators have been shown to stimulate hair cells to re-enter the cell cycle that results in DNA damage and cell death signaling.<sup>25</sup> It is known in the DNA repair field that repairing damaged DNA first will improve the capacity of cells to re-enter the cell cycle in order to regenerate lost tissue. Therefore, improving DNA repair through CAEs treatment might be a novel strategy that complements current efforts to regenerate hair cells.

## Susceptibility

It has been noticed that some ears are more easily damaged by noise than others. Significant efforts have been given to predict, measure, or explain these differences in susceptibility, and a number of pertinent factors have been identified. However, the majority of data is still inconclusive.

The effect of aging on noise-induced hearing impairment has been controversial. The majority of data considers age to simply produce additive effects,<sup>26</sup> counting net hearing loss as the decibel sum of threshold shifts from aging and noise exposure. In terms of gender, men often display more hearing loss in noisy occupations than do women, but this may be due to different nonoccupational exposures (especially shooting) between the genders. What is more certain is that the acoustic reflex is protective against NIHL, at least for frequencies <2 kHz, where the acoustic reflex effectively attenuates sound. Borg et al. found that PTS and TTS both increase dramatically for lower frequencies when the reflex is inactivated in both experimental animals and in humans with Bell palsy.<sup>26</sup>

Animal experiments suggest that certain genes may play a significant role in susceptibility to noise damage. For example, several studies<sup>27,28</sup> have shown that the inbred mouse, mutant C57BL/6J (C57) strain, often used as a model of early ARHL, is more susceptible to noise damage as well. When C57 mice are backcrossed with a mouse strain exhibiting normal aging, they display neither ARHL nor susceptibility to noise exposure aftereffects. This suggests that the ARHL gene, *Ahl*, may potentiate noise damage. Moreover, wild-type inbred MOLF/Ei (MOLF) mice and the 129S6/SvEvTac mice with normal cochlear function are exceptionally resistant to acoustic overstimulation. In combination, findings in inbred mouse models of NIHL provide the basis for applying suitable molecular techniques that permit the mapping of NIHLs gene to specific chromosomal loci. Identification of such NIHL gene would have great implications for developing a diagnostic indicator of the susceptibility of a particular human ear to the adverse effects of sound overexposure.

## Interactions

It has been established that NIHL can be influenced by other agents and by some physical characteristic of the individual. It is reasonable to assume that noise in combination with ototoxic agents will produce stronger reactions than each stimulus applied singly. A number of laboratories have established in animal models that kanamycin, neomycin, or amikacin in combination with different types of noise produces a marked potentiating interaction. However, majority of studies suggest that no substantial risk of hearing loss occurs from combining a noise exposure and an aminoglycoside drug when neither is present in sufficient amounts to cause hearing loss on its own.<sup>29</sup> Several laboratory research in animal models suggested that the antineoplastic agent cisplatin significantly increased the amount of hearing and hair cell losses from exposure to noise.<sup>30,31</sup>

The ototoxicity of environmental agents like carbon monoxide, xylene, styrene, and toluene, and their interaction with noise, has been reported in the literature. In a series of laboratory studies in the rat model, Fechter and colleagues<sup>32</sup> found that simultaneous exposure to noise and environmental pollutants of carbon monoxide or hydrogen cyanide resulted in more permanent hearing loss at the high frequencies than the sum of the losses produced by each agent administered alone. In human studies, it has been found that workers exposed to toluene or xylene in addition to noise developed more hearing loss

than those exposed to noise alone.<sup>33,34</sup> Specifically, styrene exposure even below currently recommended levels, plus noise exposure, was associated with more hearing loss than noise exposure alone.<sup>35</sup>

Evidence has accumulated in recent years for the adverse effects of smoking on hearing within the working population. A recent cross-sectional study regarding the effect of smoking in workers in a large food-producing factory concluded that smoking can accelerate NIHL.<sup>36</sup> A possible explanation for the underlying pathogenic mechanism may be the well-known vascular changes and the consequent cochlear hypoxia related to smoking.

## EVALUATION AND DIAGNOSIS

### Damage Risk Criteria

How long and how loud can we be exposed to sound without risking hearing impairment? Epidemiologic studies measuring the hearing of noise-exposed workers have helped to estimate the risk of hearing damage with various exposures. Levels <80 dBA have negligible risk to human hearing over a working lifetime. Above 85 dBA, the risk grows rapidly for higher frequencies and more slowly for lower frequencies. Occupational Health and Safety Administration (OSHA) has established guidelines for permissible noise exposure levels for a working day, assuming constant steady-state noise and a 20-year work life (Table 25.1).<sup>37</sup>

### Diagnosis

Diagnosis of NIHL should not be made on the basis of audiometric contour alone, but must include a careful history of occupational and nonoccupational noise exposure. If it is available, noise exposure measurements from the workplace will be very helpful. Currently, routine audiometric testing of behavioral thresholds to pure tone is the main tool to detect the NIHL. A series of audiograms prior to employment and at intervals throughout a worker's career is ideal to reflect the hearing change over time. While majority of NIHL is symmetric, asymmetric noise exposure, such as rifles and shotguns, will cause asymmetric sensorineural hearing loss. In this case, the ear pointed

toward the source of noise would have worse hearing than the ear directed away from the source by 15–30 dB due to the absence of the protective head-shadow effect. It means that a right-handed shooter will have a worse hearing on his left ear. However, in any case when pure tone average asymmetry is >15 dB, further evaluation with an imaging study is warranted to rule out a retrocochlear lesion such as an acoustic neuroma, before attributing the loss to noise exposure.

The American College of Occupational and Environmental Medicine has recently (2012) updated its criteria for diagnosis of occupation noise-induced hearing loss, and its main principles are as follows<sup>38</sup>:

- A neurosensory loss
- Almost always bilateral
- High-frequency losses rarely exceed 75 dB, and low frequency losses rarely exceed 40 dB
- Hearing loss does not progress after noise exposure is discontinued
- As hearing loss progresses, the rate of hearing loss decreases
- Loss is always greater at the frequencies 3–6 kHz.

## MANAGEMENT

### Hearing Conservation

Whereas NIHL is not medically or surgically treatable, it is almost entirely preventable. Its prevention requires education, engineering, and administrative controls, as well as the proper use of hearing protection. According to OSHA's initial regulation,<sup>38</sup> the maximum permissible exposure (without hearing protection) is 90 dBA time-weighted average (TWA). But in 1981, OSHA promulgated the Hearing Conservation Amendment (HCA), which effectively lowered the criterion level to 85 dB by requiring employers to implement a hearing conservation program (HCP) when exposures reached 85 dB TWA. Impulse noise exposure is limited to a 140 dB peak level.

An HCP has the following main components:

- Assess the level and cumulative dose of noise exposure
- Engineering or administrative controls to reduce exposure
- Use of personal hearing protection devices (HPDs) if sound cannot be brought within safe levels
- Monitoring hearing: periodic audiometry with follow-up and referral
- Education, motivation, and counseling.

**Table 25.1:** Duration (in hours) of allowable exposures based on Occupational Health and Safety Administration criteria.

Noise level (dBA)	90	95	100	105	110	115
Duration (hours/day)	8	4	2	1	0.5	0.25

The personal noise dosimeter is typically used to measure noise exposure in the workplace. Exposures that exceed permissible limits can be reduced by noise control or by reducing the time that employees spend in the noise. In situations in which neither engineering nor administrative controls can reduce exposures < 85 dBA TWA, a program for annual audiometry must be instituted. Occupational Health and Safety Administration defines a standard threshold shift as a 10 dB or greater increase in threshold for the 2-, 3-, and 4-Hz average in either ear. Workers who demonstrate standard threshold shift (STS) or who have exposures > 90 dBA TWA must use HPDs.

Commonly used HPDs in the form of inserted earplugs or earmuffs vary considerably in effectiveness and produce an attenuation that is highly frequency dependent. For example, when sealed correctly into the ear canal, earplugs reduce the noise reaching the middle ear by 15–30 dB and work best for the mid-to-higher frequency region (i.e. 2–5 kHz). Earmuffs are more effective protectors, especially for frequencies between 500 Hz and 1 kHz, where noise is attenuated by 30–40 dB. In areas with extremely high noise levels, earplugs do not afford sufficient protection, and individuals should be advised to wear both earplugs and earmuff. Hearing protectors should be worn all the time because, if they are removed for even a few minutes, their effective cumulative attenuation capability is severely reduced. For example, removing hearing protection for only 15 minutes of an 8-hour work shift can cut protection efficacy in half.

In a specific setting with intermittent noise exposure only (such as recreational shooting), an electronic level-dependent HPD has proved to be very useful. Such device has an external microphone, an internal speaker, and circuitry that allows sounds below about 85 dB to pass into the ear while louder sounds are blocked. A special designed earplug such as ER 10 or ER 20 is suitable for musicians. They attenuate sounds equally in all frequencies to keep music clear and natural.

## Clinical Management

With the established diagnosis of NIHL, the main role of the otolaryngologist in management is counseling to prevent further hearing loss. The patient should be educated about the hazards of noise and appropriate use of HPDs. A simple way to estimate the noise level in a working place is: if it is noisy enough that a worker must speak very loudly or shout to converse at ordinary conversational distances, then it can be concluded that levels are probably > 80 dBA.

A physician can also teach a patient how to recognize the danger sign of potential NIHL, like the development of the sensation of painful or muffled sound and tinnitus. The influence of otolaryngology in the areas of education and motivation can be a major force in preventing NIHL. Hearing aids are helpful when hearing loss becomes handicapping and the patient should be scheduled for periodic monitoring audiometry. Other common symptoms associated with NIHL like tinnitus should also be evaluated and properly addressed.

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