# UPDATE ON PRESBYACUSIS

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## Introduction

Presbyacusis or age-related hearing loss (ARHL) is the 'the natural failure of hearing with advancing years, caused by degenerative changes in the internal ear'.[1] It is a common condition, increasingly prevalent with age and with the rate of decline accelerating with advancing age.[2, 3] In 1999, the World Health Organization estimated that 580 million people over the age of 60 suffered from hearing loss worldwide. By 2020, it is anticipated that this number will have increased by 75% resulting in over one billion people of 60 years or older being affected.[4]

The condition is characterised by bilateral, symmetrical changes leading from an initial high to low frequency sensorineural hearing loss (SNHL). Zwaardemaker, who originally described the condition, noted this when producing a series of notes in octaves via Galton's whistles for children and the elderly. It was noted that the highest octaves could not be heard by the elderly and it was concluded that high frequency hearing loss occurred in this group.[5]

The complexity of the underlying processes involved in presbyacusis are now being realised and it is noted that the progression and age-related onset of this condition are very variable, suggesting a multifactorial aetiology. Both extrinsic factors, such as noise exposure and intrinsic factors, such as systemic conditions and genetics are thought to play a part in the resulting SNHL.

## Pathophysiology

Ageing results in histological, electrophysiological and molecular changes in the cochlea. Histological studies have repeatedly found degenerative changes in the stria vascularis, spiral ganglion cells, inner hair cells, and outer hair cells that are associated with the severity of hearing loss.[6] Schunknecht [7] subdivided these changes into sensory ARHL (high frequency loss; loss of sensory cells), strial or metabolic (flat descending threshold pattern; atrophy of stria vascularis), neural ARHL (loss of word discrimination; loss of cochlear neurons) and cochlear conductive or mechanical ARHL (unknown pathology). However, many patients show a mixture of these pathologies.[8]

## Aetiology

Extrinsic factors thought to contribute to ARHL include noise exposure, ototoxic medication, chemical exposure and medical conditions.

Four studies have investigated the progression of ARHL in isolated communities with relatively low levels of noise exposure.[9-12] These cross sectional studies of the Mabaan tribe of Sudan,[9] an isolated hill dwelling tribe in India,[10] Orkney Islanders[11] and Kalahari Bushmen[12] found better preservation of hearing into old age. Furthermore, animal studies have demonstrated that noise exposure earlier in life leads to an increased vulnerability to ARHL,[13] with specific genes conferring increased susceptibility to this within species.[14]

Ototoxic medication such as aminoglycosides and platinum based chemotherapy agents may accelerate presbyacusis in older subjects. This may be related to increased use of these medications in this group and elevated drug levels in blood due to altered renal and hepatic function.[8] Industrial chemicals are also known to cause a higher prevalence of high frequency hearing loss, including toluene, trichloroethylene, styrene and xylene.[15, 16]

Several medical conditions, including diabetes and cardiovascular disease have been shown to have an association with ARHL. Diabetic patients are known to have a higher incidence of SNHL.[17] Early onset high frequency SNHL compared to age matched controls[18] and DNA mitochondrial mutations leading to both late onset diabetes and SNHL have been described.[19, 20] Female patients with cardiovascular disease have been shown to be at increased risk for developing ARHL, with the gender difference thought to

*Presbyacusis*

*Photo: AuDNet, Inc*

be related to hormonal differences.[21] Animal studies [22] have supported these findings with the proposed underlying mechanism related to cochlea hypoxia.[23]

Intrinsic factors, in the form of genetic factors have been the subject of much recent research interest. Using inbred mice, Erway [24] et al were able to demonstrate recessive alleles at three loci which contributed to the development of ARHL. Age-related hearing loss 1 (*Ahl1*) gene was subsequently mapped to chromosome 10 and was found to overlap with the modifier of the deaf waddler locus (*mdfw*) region in 10 strains of inbred mice including C57BL/6J, 129P1/ReJ, BALB/cByJ, A/J, BUB/BnJ, C57BR/cdJ, DBA/2J, NOD/LtJ, SKH2/J and STOCK760. The gene was demonstrated to elevate hearing thresholds in middle-aged and old mice at high frequencies.[25-27] Mice that were then genetically engineered to be identical to the C57BL/6J strain in all but *Ahl1* were found to be protected against early onset hearing loss. However, older mice still developed hearing loss. It is, therefore, proposed that more than one loci contributes to the hearing loss changes in these mice.[8] Noben-Trauth et al [28] were able to demonstrate that this gene may be allelic to Cadherin 23 and, thus, the latter may be an important gene in ARHL, as well as congenital hearing loss. Subsequent studies identified *Ahl2* and *Ahl3* on chromosome 5 and 17, respectively, in certain sub-species of mice.[29-31]

## Prevention and Treatment

Prevention of presbyacusis should address predisposing factors and would include:

- Education to raise awareness of the consequences of noise exposure
- Legislation to restrict noise exposure
- Combining ototoxic medications with protective agents, such as antioxidants and free radical scavengers in high risk groups
- Legislation to protect 'at risk' workers exposed to hazardous industrial chemicals
- Optimisation of the care of those with diabetes and cardiovascular disease.

At present the mainstay of treatment remains provision of hearing aids with amplification of sounds. However, problems remain with poor speech recognition and with differentiation of sound in noisy environments.

Promising future interventions include gene therapy and stem cell implantation and there have been promising results in animal models. In gene therapy, the introduction of *Math1*, a gene responsible for the development of hair cells in the cochlea, has been demonstrated to lead to the re-growth of hair cells which resulted in improvement in thresholds.[32] Stem cells implanted in the inner ear have been demonstrated to survive, migrate, differentiate and extend nerve projections in the auditory system of adult mammals.[33]

## Conclusion

ARHL is an increasingly prevalent condition which results in a deterioration in quality of life, communication problems and, subsequently, affects socio-economic status. It is caused by degenerative changes in the cochlea, as a result of multifactorial extrinsic and intrinsic contributions. Further investigation into the genetic factors in humans is important - and exciting areas for future interventions include gene and stem cell therapy.

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## Book Review

# TINNITUS: SOURCE READINGS (1841-1980)

**Robert T Sataloff, Dimiter I Dentchev, Mary J Hawshaw (Eds.)**

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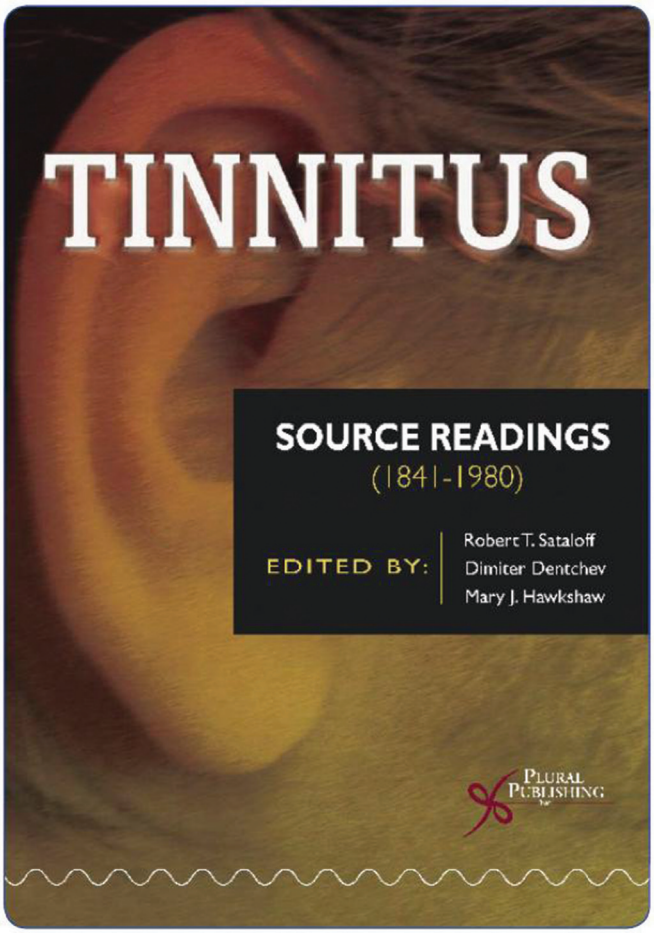


This book is a compendium of historical but current literature on the subject of **tinnitus**, pre-dating the 20th century. The authors blamed the sluggish knowledge in the management of tinnitus on deficient research interests. In contrast, they presented the rich clinical acumen of the 19th century practitioners and showed very little improvement to what is already known on the subject. In providing a summary of historical but interesting and inspiring literature, the authors hope to stimulate more research which would lead to improvements in the current management of tinnitus.

The book chapters are of unequal length but the layout is easy to follow. Chapter 1, which is the 'Overview of Tinnitus', provided a very good introductory background on the aetiology and management of this condition. The second chapter, on the 'Receptors in the Auditory Pathway', is a summary of the basic science of neurotransmission and an essential component in its understanding and future research needs. Chapters 3 to 7 outline the 140 years historical review of the case reports which dominated the publications in the 19th century. The first case report was from the *Lancet,* in 1841, and the last one, in 1897, was published in *Laryngoscope*. Extensive publications on the management of tinnitus dominated the early and mid 20th century database and ranged from the anticoagulant treatment of sudden deafness (*J Laryngol.* 1964; **78**: 583-586) to a subject which 'everybody talks about it but nobody does anything about it' (*Eye, Ear, Nose Throat Monthly*. 1965; **44:** 311).

I would have loved to see a list of the Source Articles discussed in this book for ease of reference. Notwithstanding, this is a welcome addition to the subject of tinnitus, which has more or less remained elusive to practitioners in this field for more than a century.

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