Aetiological causes of reversible sensorineural hearing loss
A Ahmed, S Quraishi

Citation

Abstract
The vast majority of sensorineural hearing loss cases are irreversible. However there is a significant proportion of cases in which the hearing loss recovers. A knowledge of the aetiological causes of reversible sensorineural deafness cases can allow early diagnosis and correct treatment to be implemented. The purpose of this article is to review the documented literature on the aetiological causes of reversible sensorineural hearing loss.

INTRODUCTION
Reversible sensorineural hearing loss occurs in a significant proportion of cases. Although the precise pathophysiology in many of these causative factors remains unclear it is nevertheless important to be aware of numerous aetiologies to enable a prompt diagnosis and correct treatment to be implemented. This article reviews the documented aetiological causes of sensorineural hearing loss.

AETIOLOGIES
(I) OTOTOXICITY
There are numerous drugs which are known to cause damage to the inner ear which can result in reversible or irreversible hearing loss, tinnitus and dysequilibrium. Drugs which have been associated with reversible sensorineural hearing loss (SNHL) include:

a) Salicylate-induced ototoxicity was first reported in 1877 by Muller. Aspirin is probably the most common cause of drug-induced ototoxicity although the majority of it is reversible. Tinnitus tends to precede the deafness which is bilateral and affects all the frequencies. Both the tinnitus and SNHL develop within a few days of treatment and tend to reverse within a few days of withdrawing aspirin. Although the required dose of aspirin to produce these symptoms is variable, most individuals exhibit some degree of symptoms at serum levels of 35mg/dl.

The exact mechanism of action by the salicylates is not clearly understood. A change in the membrane permeability of the outer hair cells appears to play a significant role.

A change in the cochlear blood supply as a result of the salicylate-induced imbalance of vasodilatory prostaglandins and vasoconstricting leukotrienes may also have an integral role.

b) Quinine like aspirin can cause reversible SNHL associated with tinnitus and can occur in both healthy and malaria patients. The effects are rapid and resolve completely following withdrawal of the drug. It appears to alter the membrane function of the outer hair cells especially in the region of the lateral cisternae.

Five months of treatment of rheumatoid arthritis with hydroxychloroquine which resulted in reversible SNHL has been reported in a patient. The mechanism of this ototoxicity is not known.

c) In 1965 Maher and Schreiner first described the reversible SNHL and vertigo following intravenous administration of the loop diuretic ethacrynic acid. Loop diuretics e.g ethacrynic acid and frusemide may cause SNHL when administered parenterally in high doses, or if given rapidly even in low doses. Patients with existing hearing deficits, severe hypoalbinemia, heart failure or severe renal failure are particularly susceptible to the ototoxic effects of these drugs. Experimental studies suggest that loop diuretics damage the stria vascularis and/or the outer hair cells of the cochlea. It has been demonstrated that loop diuretics inhibit Na-K ATPase and adenyl cyclase in the stria. Concurrent administration of loop diuretics with aminoglycosides can exacerbate or cause aminoglycoside ototoxicity.
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d) The macrolide antibiotic erythromycin is associated on rare occasions with SNHL which is reversible on discontinuation of the antibiotic. Patients at increased risk of developing erythromycin-induced deafness include the elderly, pre-existing hepatic or renal failure, and patients undergoing liver or renal transplantation. The precise mechanism of action is unknown.

e) Reversible bilateral SNHL has been reported following the administration of oral metronidazole. Withdrawal of the antibiotic and oral steroid therapy resulted in return of normal hearing thresholds. The exact mechanism of action is unknown.

f) The chemotherapeutic agent cisplatin is known to cause permanent or transient SNHL. The deafness can also be associated with tinnitus. Clinical studies have shown that this type of hearing loss is directly related to the total dose of cisplatin administered and to the peak serum concentrations.

The precise mechanism of action is unknown but there is associated hair cell damage, inhibition of Na\(^{+}\)\text{+K\text{ATPase}} in the outer hair cells of the cochlea and atrophy of the stria vascularis.

g) With the increasing use of interferon, several new adverse effects including audiovestibular symptoms have been recognised. Sudden SNHL associated frequently with tinnitus has been reported to have developed several days after the commencement of interferon (both alpha and beta interferon). Complete resolution of the hearing loss in all the cases occurred within a month after discontinuation of interferon. The exact mechanism of action is unknown.

h) OKT3 (muromonab-CD3) is a murine monoclonal antibody used as an immunosuppressant following cadaveric renal transplants. Sudden SNHL (high frequency) within 48-72 hours of commencing OKT3 has been reported followed by complete resolution within 2 weeks after discontinuation of the drug. Transient tinnitus was also a frequent associated symptom. The mechanism of how OKT3 produces ototoxicity remains unclear.

i) Carbamazepine has been shown to be capable of delaying conduction of the auditory system both centrally and peripherally. Temporary bilateral SNHL has been reported following an overdose of carbamazepine (36g) in a patient. Two weeks later there was complete resolution of the deafness and the associated tinnitus and dizziness.

j) Treatment of partial seizures with sodium valproate has resulted in SNHL which resolved following discontinuation of the drug. The mechanism of this rare adverse effect of sodium valproate is unclear.

k) The anti-epileptic drug vigabatrin has recently been reported to cause reversible SNHL. Discontinuation of the drug led to complete recovery of the hearing loss. Vigabatrin is a GABA-based drug and animal studies have shown that GABA is an important inhibitory neurotransmitter for cochlear inner and outer hair cells.

l) Chronic use of amphetamines has been reported to cause SNHL which has reversed within 4 to 10 days of cessation of amphetamine use. Prolonged and heavy use of amphetamines can lead to neuronal damage and neurotransmitter depletion but the precise mechanism of the ototoxic effect is unknown.

m) Animal model studies have demonstrated SNHL induced by lithium and also interleukin-2 which has reversed following discontinuation of the drugs.

n) Chronic carbon monoxide (CO) exposure usually results in permanent, symmetrical and high frequency hearing loss and was first documented in 1948. Reversible SNHL following chronic CO exposure has been reported with improvement occurring over a period ranging from several weeks to 21 months.

Acute CO exposure is less common and typically produces a U shaped audiogram which is usually bilateral and may be asymmetrical with recovery usually taking several months.

Carbon monoxide poisoning is often associated with headaches, nausea, lethargy, pulmonary oedema and arrhythmias. The symptoms are presumed to be due to tissue hypoxia due to the formation of carboxyhaemoglobin. Animal model studies suggest that free radicals may have an integral role and there may be an excitotoxic component as MK-801 which blocks the glutamate NMDA receptor has been shown to protect against CO ototoxicity.
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II) ANAESTHESIA
A) GENERAL ANAESTHESIA
Sudden reversible and irreversible SNHL has been reported following general anaesthesia involving both otolaryngological and non-otolaryngological procedures. The reversible hearing loss is unilateral or bilateral and the degree of recovery is variable.\textsuperscript{49,60,74,81,85}

It is thought that the anaesthetic agent has a causative role in the deafness. The most common anaesthetic agent in these cases is nitrous oxide. Two theories have been suggested—‘implosive’ and ‘explosive’ routes. In the first route, rapid penetration of the highly soluble nitrous oxide results in an acute increase in middle ear pressure and subsequent rupture of the round window membrane.\textsuperscript{51} In the second, the nitrous oxide-induced increases in the venous and CSF pressure are transmitted to the perilymphatic space via the cochlear duct causing displacement or rupture of the membrane.\textsuperscript{53} The other anaesthetic agents e.g isoflurane and fentanyl may act indirectly on the auditory pathway by altering the general haemodynamics e.g hypotension.\textsuperscript{53}

B) SPINAL ANAESTHESIA AND LUMBAR PUNCTURE
The first reported case of hearing impairment after spinal anaesthesia was reported in 1914.\textsuperscript{32} Since then, it has been well documented that reversible SNHL can occur after spinal anaesthesia and following procedures involving lumbar puncture.\textsuperscript{55,56,57,58,59,60,61} The hearing loss is either unilateral or bilateral, low frequency and usually reverses spontaneously although there are a few documented cases where the SNHL has not reversed.\textsuperscript{48}

The precise mechanism of this transient hearing loss has not yet been completely established. It has been suggested that following dural puncture the decrease in the CSF volume and pressure that occurs leads to a decrease of perilymph as there is a direct communication between the CSF and perilymph via the cochlear aqueduct. The reduction in perilymphatic pressure would then induce a transient endolymphatic expansion for equilibration.\textsuperscript{55,62,63} This endolymphatic hydrops is associated with the hearing loss and restoration of the CSF and inner ear volumes would then lead to a return of normal hearing thresholds.

The contrast medium, metrizamide which is used in lumbar myelography is associated with transient deafness. The mechanism of action is probably due to a hydrostatic imbalance between the perilymph and CSF resulting from a decreased CSF osmolality.\textsuperscript{61}

III) INFECTIVE
A) BACTERIAL
Bacterial meningitis can leave up to 10% of patients particularly children with permanent SNHL.\textsuperscript{64,65} Transient SNHL has also been reported following bacterial meningitis.\textsuperscript{66,67,68,69} Both types of hearing loss tend to develop in the early part of the illness.\textsuperscript{66,67} In the majority of the reports the deafness tends to reverse after weeks or months\textsuperscript{66,67,69} but in a large multicentre trial involving children the improvement in most of the affected cases occurred within 48 hours.\textsuperscript{66}

The cochlea appears to be an auditory lesion site due to the loss of otoacoustic emissions.\textsuperscript{60} Animal studies also support the integral role played by the cochlea.\textsuperscript{71,72} The mechanism is unclear but it may result from the effect of bacterial toxins or inflammatory mediators on the hair cells of the organ of Corti.\textsuperscript{71,73}

Syphilis (congenital or acquired) can produce otological manifestations including SNHL, tinnitus and imbalance.\textsuperscript{74,75,76,77,78,79} The SNHL may be sudden, fluctuant, progressive, unilateral or bilateral. Treponema pallidum has an ability to persist in several sites including the temporal bone.\textsuperscript{77} Treatment with antibiotics and steroids shows a variation in response.\textsuperscript{79}

Lyme disease is caused by infection with the spirochaete Borrelia burgdorferi and like syphilis may result in neurological manifestations e.g facial nerve palsy and SNHL. The SNHL which is sudden in onset, can affect low or high frequencies and may respond to treatment with antibiotics. Both partial\textsuperscript{80} and complete recovery\textsuperscript{81} (usually after a few months) of the hearing loss following treatment has been reported. Indeed a case has been reported in which the hearing loss completely reversed more than two years following treatment.\textsuperscript{82} SNHL has been reported to occur in 15% of cases of late Lyme disease without recovery of hearing.\textsuperscript{83} The precise pathogenesis of hearing loss in Lyme disease is presently not known.\textsuperscript{82}

Animal studies involving instillation of pseudomonas aeruginosa exotoxin A and pneumococcal toxins into middle ear have demonstrated the onset of SNHL which has reversed in a few weeks.\textsuperscript{84,85}

B) FUNGAL
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Reports in the literature have shown an association between hearing loss and cryptococcal meningitis. A case of a patient with cryptococcal meningoencephalitis in whom the SNHL hearing loss reversed following antifungal treatment has been reported.87

C) MYCOPLASMAS

Infection with Mycoplasma pneumoniae has been reported in a case which resulted in unilateral SNHL (associated with tinnitus and vertigo) which reversed completely following treatment with doxycycline.88

Mycoplasma, bacteria and viruses have all been implicated in the aetiology of bullous myringitis. Prospective studies of bullous myringitis by Hoffman89 and Hariri90 have demonstrated a significant incidence of SNHL (65% and 66% respectively) with complete resolution of the hearing loss in 57% and 60% in the 2 series respectively. The mechanism of the hearing loss remains unclear.

D) VIRAL

Infection with varicella zoster virus typically results in SNHL and facial palsy. There is great variation in the degree of hearing loss and the amount of recovery of the loss. Acute SNHL which is usually unilateral is a well reported reversible complication of mumps.91

The exact mechanism has not yet been definitively proven but host immune mediated response in the cochlea appears significant.92

IV) AUTOIMMUNE

Autoimmune SNHL was first described as a clinical entity in 1979 by McCabe.93 Clinical presentation and prompt diagnostic confirmation can lead to successful management of the deafness by medical therapy. However recognition of the disease is not straightforward in particular due to lack of simple and reliable diagnostic tests and the paucity of temporal bone tissue from untreated patients.94

The precise mechanisms involved in the hearing loss are unclear. Animal model studies have led to several immunological mechanisms being postulated. These include humoral mechanisms involving specific autoantigens in the inner ear (Type II); circulating immune complexes involving bacterial and viral antibodies (Type III); cell mediated immunity involving cytotoxic T cells (Type IV); and autoantibodies directed against type II collagen.94 There are no randomised trials of therapy for autoimmune SNHL and the treatment approach is based upon anecdotal experience, case series and inference from treatment of related conditions. Steroid and cyclophosphamide immunosuppression has been the main form of treatment.88,95

Reversible SNHL has been reported in the following specific autoimmune disorders:

A) COGAN’S SYNDROME

This syndrome is characterised by ocular inflammation classically interstitial keratitis and audio-vestibular symptoms including SNHL, vertigo and tinnitus. Hearing fluctuation coincides with exacerbations and remissions of the disease. Temporal bone histopathological findings include endolymphatic hydrops, lymphocyte infiltration and organ of Corti degeneration.96,97 Steroid and cyclophosphamide therapy are the mainstay of treatment.

B) WEGENER’S GRANULOMATOSIS

The 3 main components of this disease are focal necrotising glomerulonephritis, necrotising granulomatous lesions in the upper and/or lower respiratory tracts and systemic vasculitis. In contrast to Cogan’s syndrome the most common otologic deficit is conductive loss (otitis media with effusion).94,95

However SNHL usually in combination with conductive deafness has been reported.98,99,100,101 The SNHL has improved following treatment with steroids and cyclophosphamide.99,101

C) POLYARTERITIS NODOSA

This vasculitic disease affects small and medium-sized arteries. Although uncommon SNHL which is sudden and bilateral has been reported.102,103,104 Temporal bone histopathological findings include arteritis of the internal auditory artery.105 Treatment with steroids and cyclophosphamide102,103 or azathioprine104 has resulted in improvement of the hearing loss.

D) KAWASAKI DISEASE

Kawasaki disease is an acute self-limited vasculitis that affects primarily medium sized arteries of infants and children. Prospective studies have demonstrated transient SNHL over a period ranging from 1 week to 4 months.106,107

The mechanism of the hearing loss remains unclear.

V) METABOLIC

HAEMODIALYSIS

SNHL is frequently reported in patients with chronic renal failure.108 The aetiology of this hearing impairment remains unclear, however factors such as uraemic toxins, electrolyte...
imbalance and hypotension have been suggested to play a role. However opinion remains divided on the effect haemodialysis has on the hearing impairment. Studies involving long term haemodialysed patients who had been receiving dialysis ranging from 5 years to 10 years have shown no significant alteration in the hearing. These are supported by studies assessing hearing after a single haemodialysis session and hearing assessed by distortion product otoacoustic emissions both in children and adults. In contrast other studies have reported that following a single session of haemodialysis, the hearing impairment has either deteriorated or improved.

VI) HAEMATOLOGICAL HYPERVERSICOSITY SYNDROME

The features of hyperviscosity syndrome include headache, visual disturbances, vertigo, tinnitus and SNHL. These clinical features are due to the elevated blood viscosity and resulting slowly circulating oxygen-deficient blood. It is postulated that the elevated viscosity causes partial occlusion of the cochlear vessels resulting in ischaemia of the cochlea and subsequent hearing loss.

Haematological disorders that have exhibited reversible SNHL which is attributable to hyperviscosity syndrome include:

Leukaemia: recent studies have implicated both acute and chronic leukaemia in the development of sudden SNHL which can be the presenting clinical feature. Temporal bone histopathological studies of affected patients include leukocyte infiltration and inner ear haemorrhage. Lowering of the leukocyte count by leukapheresis or steroid and chemotherapy treatment can lead to reversal of the hearing loss.

Essential thrombocytosis: a case of sudden SNHL in a patient with thrombocytosis which reversed following plateletpheresis is reported in the literature.

Waldenstrom's macroglobulinaemia is an uncommon disorder in which there is excess production of monoclonal macroglobulin IgM. A case has been reported in a patient with Waldenstrom's macroglobulinaemia in whom the SNHL improved along with the other hyperviscosity-related symptoms following treatment with fludarabine.

VII) NEOPLASMS

A) VESTIBULAR SCHWANNOMAS

Hearing loss associated with vestibular schwannomas (VS) has been reported to resolve spontaneously or to improve following corticosteroid treatment.

Reports of hearing improvement after surgical removal of VS in particular small tumours exist but not extensively. Although the exact mechanism for the deafness is unclear, one theory that has been put forward is that it is due to a vascular compression phenomenon which is relieved following removal of the tumour and the reduction of tumour mass in the case of corticosteroids. Others postulate a mechanical conduction block of the cochlear nerve action potential theory.

B) CEREBELLO-PONTINE ANGLE TUMOURS

Recovery of severe SNHL following total surgical removal of cerebellopontine angle tumours –meningioma and jugular foramen neurinoma has been reported. It is thought relief of tumour compression maintaining the arachnoidal sheaths of the cochlear nerve would make the recovery of its function possible.

C) CAROTID BODY TUMOUR

Removal of a carotid body tumour in a patient with dysphagia, tinnitus and ipsilateral SNHL led to recovery of the hearing loss.

VIII) VESTIBULAR MENIERE'S DISEASE

Meniere's disease is characterised by recurrent attacks of deafness, tinnitus and vertigo. The SNHL improves between attacks even to normal levels. The pattern of hearing loss is typically low frequency but eventually affects all frequencies and is progressive.

Distension of the endolymphatic space is the main feature and another frequent histopathological finding is membranous labyrinth rupture. The exact mechanism involved remains unclear. One theory involves rupture of the membranes leading to mixing of the endolymph and perilymph leading to electrochemical imbalance. Another theory postulates alteration in the blood supply leading to alteration in the constituents of the endolymph.

Symptomatic relief of symptoms which is primarily aimed at vertigo includes dietary advice, medical e.g vestibular sedatives, and surgical interventions e.g saccus decompression.
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IX) NEUROLOGICAL

A) MULTIPLE SCLEROSIS

Sudden SNHL is a rare manifestation of multiple sclerosis (MS) and it tends to occur within the first years of the disease although later onset is also described. It is due to the demyelination of the auditory pathway and usually occurs when other areas of the brainstem are affected. Recovery of the hearing loss has been reported in the literature. A case of a child with total biotinidase deficiency who developed bilateral SNHL is reported. Treatment with biotin led to improvement of the hearing thresholds.

B) SARCOIDOSIS

This multisystem granulomatous disease can involve the VIIIth cranial nerve leading to SNHL and vertigo. It is presumed that the symptoms are due to direct infiltration or compression of the cranial nerve. Reversal of the SNHL has been reported following steroid treatment but this is very rare.

X) TRAUMATIC

A) BLAST INJURY

SNHL following blast injuries is most severe immediately after the explosion and usually recovers within 24 hours. This temporary threshold shift is often accompanied by vertigo and tinnitus which are also usually transient. The mechanism of the hearing loss involves damage to the outer hair cells.

B) PERILYMPH FISTULA

Leakage of perilymph into the middle ear following rupture of inner ear membranes can occur following head injury, diving barotraumas and stapedial surgery. Dizziness may be accompanied by tinnitus and SNHL which may fluctuate. Spontaneous resolution may occur following a period of bed rest with elevation of the head. Surgical attempt at closure of the leak may result in improvement of the dizziness and prevent further deterioration in the deafness.

XI) MISCELLANEOUS

A) HYPOTENSION

A retrospective study demonstrated that a group of patients with sudden SNHL which improved had lower mean arterial pressures and in whom the deafness recovered more easily following treatment. This has led to the suggestion that at least in some cases cochlear damage may be caused by a perfusion deficit as a result of the combined effect hypotension and impaired vasomotor regulation.

B) BIOTINIDASE DEFICIENCY

A case of a child with total biotinidase deficiency who developed bilateral SNHL is reported. Treatment with biotin led to improvement of the hearing thresholds.

C) MENSTRUAL CYCLE

Bilateral transient SNHL associated with the onset of menstruation has been reported in a patient. Treatment with diuretics perimenstrually led to improvement in the transient loss. The precise mechanism of action in this case remains unclear.

D) PSYCHOGENIC

A case of a patient with acute SNHL who demonstrated further deterioration in the hearing levels following a panic anxiety attack has been reported. Treatment with corticosteroids and psychiatric counselling resulted in a return to normal thresholds except in the high-frequency range immediately after the treatment.

E) INTRA-OPERATIVE DEAFNESS DURING POSTERIOR FOSSA SURGERY

Two patients undergoing microvascular decompression for trigeminal neuralgia developed intra-operative hearing loss diagnosed by complete loss of brainstem evoked potentials during the surgery. The resulting prominent vascular compression around the cochlear nerve in both patients was immediately decompressed resulting in restoration of the hearing loss.

CONCLUSIONS

It must be emphasised that the above is not a complete list of all the aetiological causes of reversible SNHL but it is nevertheless hopefully a comprehensive report of the documented causes.

An accurate history taking with a background knowledge of the possible causes of SNHL can lead to appropriate investigations being undertaken. Although the vast majority of SNHL cases are irreversible, there are however as highlighted above certain aetiologies which can be reversed if recognised early and appropriate management implemented. A prompt and correct diagnosis and treatment may prevent further deterioration of the hearing loss and even result in recovery.

CORRESPONDENCE TO

Mr Aftab Ahmed Department of ENT Doncaster Royal Infirmary Armthorpe Road Doncaster. South Yorkshire DN2
5LT England. Email: ahmed.aftab@virgin.net

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Author Information

Aftab Ahmed, FRCS (ORL-HNS)
Specialist Registrar, Department of Otolaryngology, Doncaster Royal Infirmary

Shahed Quraishi, FRCS (ORL-HNS)
Consultant, Department of Otolaryngology, Doncaster Royal Infirmary