Sudden sensorineural hearing loss

Benjamin E Schreiber, Charlotte Agrup, Dorian O Haskard, Linda M Luxon

Sudden sensorineural hearing loss is usually unilateral and can be associated with tinnitus and vertigo. In most cases the cause is not identified, although various infective, vascular, and immune causes have been proposed. A careful examination is needed to exclude life threatening or treatable causes such as vascular events and malignant diseases, and patients should be referred urgently for further assessment. About half of patients completely recover, usually in about 2 weeks. Many treatments are used, including corticosteroids, antiviral drugs, and vasoactive and oxygen-based treatments. Although no treatment is proven, we recommend a short course of oral high-dose corticosteroids. There is much to learn about pathogenesis of sudden sensorineural hearing loss, and more clinical trials are needed to establish evidence-based management.

Lancet 2010; 375: 1203–11

Royal Free Hampstead NHS Trust, London, UK (B E Schreiber MRCP); **Department of Neuro-immunology, UCL Institute of Neurology, London, UK** (C Agrup PhD); **Imperial College London, Hammersmith Hospital, London, UK** (Prof D O Haskard FMedSci); **and Department of Neuro-Otology, The National Hospital for Neurology and Neurosurgery, London, UK** (Prof L M Luxon FRCP)

Correspondence to: Prof Linda M Luxon, Department of Neuro-Otology, The National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, UK **l.luxon@ucl.ac.uk**

Introduction

Hearing loss is common, affecting about a fifth of the population in the UK, and can be defined by site of disease, severity, audiometric configuration, and method of onset.[1] In adults, progressive late onset sensorineural hearing loss (so-called presbyacusis) is the most common presentation and is often associated with a genetic predisposition, exposure to excessive noise, or age-related pathological changes. Sudden sensorineural hearing loss—described by De Kleyn in 1944,[2] and defined as hearing loss of at least 30 dB in three sequential frequencies in the standard pure-tone audiogram over 3 days or less[3]—is less common than is late onset loss. National surveys[4–6] have estimated the incidence of sudden sensorineural hearing loss at between five and 30 cases per 100 000 per year. However, a study[7] from Germany has shown an incidence as high as 160 cases per 100 000 per year.

Rapidly progressive sensorineural hearing loss, which develops over weeks to months, has also been described.[8] However, these patients often initially present with a sudden sensorineural hearing loss, followed by a rapid progression or additional sudden drops in hearing. Sudden and rapidly progressive sensorineural hearing loss have many common features and possible causes, and we suggest that they should be investigated and managed in a similar way.

Patients with sudden sensorineural hearing loss often delay seeking medical attention, or might present to a range of specialties, including primary care, otolaryngology, audiovestibular medicine, and internal medicine. In primary care and non-specialist departments, patients can be inappropriately reassured, without investigation, in the mistaken view that the loss is attributable to middle-ear dysfunction secondary to upper respiratory tract infection.

Detailed investigation will show a specific cause in about 10% of patients.[9] The term idiopathic sudden sensorineural hearing loss is often used to describe the remainder of patients. An important, but poorly recognised, cause of sudden sensorineural hearing loss is immune-mediated inner-ear disorders, including both organ-specific inner-ear disease and systemic autoimmune disorders. The condition is also associated with posterior circulation events, coagulation disorders, neoplasms, demyelinating disease, and various infections. Therefore, investigation for systemic disorders should be done for all patients. Published work on this topic is confusing, and approaches to diagnosis and management vary widely.[10] This Seminar presents a practical framework for assessment and management of this disorder.

Clinical presentation

Population studies of sudden sensorineural hearing loss show a wide age distribution, with an average of 50–60 years and no sex preference. The hearing loss is unilateral in most cases, with bilateral involvement reported in less than 5%.[11] The severity of hearing loss is divided roughly equally into mild, moderate, and severe-profound. The configuration of the hearing loss varies and can affect high, low, or all frequencies. Tinnitus occurs in about 80% of patients, and vertigo, indicating an associated peripheral vestibular dysfunction, in about 30%.[12] Up to 80% of patients report a feeling of ear fullness.[13] Other common complaints are of the ear feeling numb or blocked. Sudden sensorineural hearing loss can present as an isolated problem, as the presenting symptom of systemic disease, or in the course of an established diagnosis.

Causes

Infectious causes

The precise cause of sudden sensorineural hearing loss has not been identified, but several pathophysiological mechanisms have been proposed. Evidence from case

Search strategy and selection criteria

We searched the Medline, Embase, and Cochrane databases for relevant studies, including basic science reports; case reports; retrospective, prospective, and cohort studies; and randomised controlled trials published between January, 1989, and October, 2009, in any language. We used the search terms “sudden deafness” and “sudden hearing loss”. We also searched the reference lists of articles identified by this search strategy and selected those that we judged relevant. We largely focused on publications in the past 5 years, but have included commonly referenced and highly regarded older publications. Several review articles are also included because they provide comprehensive overviews that are beyond the scope of this Seminar.

series[14] suggests that mumps virus can be a cause, accounting for about 7% of adult cases.[15] Varicella-zoster virus can also cause such hearing loss in patients presenting with Ramsay Hunt syndrome (herpes zoster oticus).[16] Serological data for other viruses are conflicting and incomplete. Investigators of an early study in Boston, MA, USA,[17] detected seroconversion with mumps, rubella, varicella zoster virus, cytomegalovirus, or influenza in 63% of 122 patients; whereas in a Greek series,[18] serological tests indicated recent infection with Epstein-Barr virus, herpes simplex type I and II virus, or cytomegalovirus in 27% of 262 patients with unilateral sudden sensorineural hearing loss. An Israeli report[19] of 48 patients showed positive serology for Epstein-Barr virus in three patients (6%), enterovirus in one (2%), and cytomegalovirus in none. By contrast, a German study[20] of 55 patients reported no evidence of herpes simplex virus and varicella zoster virus, but enterovirus serology was positive in 40% of patients. Thus, many viruses have been postulated as possible causes of sudden sensorineural hearing loss, but serological, epidemiological, and histopathological data are not conclusive.[21]

In a small study of 20 patients,[22] investigators recorded no rise of interferon-α/β-inducible MxA protein in peripheral leucocytes or measurable interferon-α activity in serum, both of which are markers of a systemic viral infection. Bacterial meningitis is a well recognised cause of sensorineural hearing loss,[23] affecting up to 35% of survivors;[24] lyme disease should be considered in endemic areas,[25] and lassa fever has been reported as a common cause in west Africa.[26] Sudden sensorineural hearing loss has also been described as a presenting feature of fungal meningitis,[27] otosyphilis,[28] HIV,[29] and, rarely, Creutzfeldt-Jakob disease.[30]

Vascular causes

The cochlea is supplied by an end artery, and vascular occlusion was postulated as a cause for sudden sensorineural hearing loss as early as 1949.[31] Studies have investigated several possible mechanisms including atherosclerosis, hypotension, thrombophilia, vasospasm, hyperviscosity, and paradoxical embolism. However, there is no hard histological evidence for vascular occlusion being a common cause of this disorder.[32]

Despite much published work, large longitudinal epidemiological studies are not available to establish whether sudden sensorineural hearing loss is associated with traditional cardiovascular risk factors. Hypercholesterolaemia is associated with this disorder in some case-control series[33–35] but not in others.[36] Such hearing loss can be more common and more severe in patients with diabetes mellitus than in other patients,[37] and can be a presenting symptom.[38] There does not seem to be a clear association with smoking or hypertension. A small Italian case-control study[39] in young adults with sudden sensorineural hearing loss has shown resting blood pressure to be about 10 mm Hg lower than in healthy controls, leading to the suggestion that systemic hypotension can lead to sympathetic mediated vasoconstriction causing cochlear hypoxia.

Some evidence suggests that sudden sensorineural hearing loss is associated with both acute and increased long-term risk of stroke. In a prospective series of 364 patients with acute stroke in the posterior circulation,[40] hearing loss occurred in 8%, sometimes preceding the stroke by several days. Occlusion of the anterior inferior cerebellar artery is associated with vertigo, nystagmus, facial weakness, and gait ataxia in addition to sudden sensorineural hearing loss.[41] Vertebral artery dissection is occasionally the cause, and is associated with occipital and neck pain.[42] A study from Taiwan[43] based on national health insurance claims noted that admission to hospital with the principal diagnosis of sudden sensorineural hearing loss was associated with a significant increase in the hazard of stroke during the subsequent 5 years compared with patients of similar ages admitted with appendicectomy (12·8% in patients with sudden sensorineural hearing loss *vs* 7·8% in controls, $p<0·001$). The patients with hearing loss had significantly higher rates of hypertension, hypercholesterolaemia, and diabetes mellitus, but after adjustment for other factors, the hazard of stroke during the 5-year follow-up period was 1·64-times (95% CI 1·31–2·07; $p<0·001$) greater for patients with hearing loss than for those undergoing appendicectomy.[43]

In small exploratory unreplicated studies, associations have been suggested between sudden sensorineural hearing loss and right to left shunts and mitral valve prolapse. In a small Japanese study,[44] transcranial doppler ultrasonography with saline contrast was undertaken for 23 patients with this disorder and 46 controls who were matched for age, sex, and cardiovascular risk factors. 48% of patients had right to left shunts compared with 17% of controls ($p=0·011$).[44] A Spanish study compared echocardiographic findings in 86 patients with sudden sensorineural hearing loss with 263 controls. The reporting cardiologist was masked to patient diagnosis. Mitral valve prolapse was noted in 29·1% of patients versus 2·7% in healthy controls ($p<0·001$).[45] The mechanism for this proposed association is not clear, and no link has been established between mitral valve prolapse and thromboembolic disease.[46]

Studies have shown no association with inherited thrombophilic risk factors such as prothrombin and factor V Leiden gene mutations.[47,48] Reports of mutations in methylene-tetrahydrofolate reductase are conflicting. One study[49] reported an increased incidence of a platelet GPIaC807T polymorphism in 53·5% of patients with sudden sensorineural hearing loss compared with 38·2% of controls. Isolated case reports of sudden sensorineural hearing loss have been published in the context of hyperviscosity syndromes such as sickle-cell syndrome,[50] Waldenstrom's macroglobulinaemia,[51] and myeloma;[52] vascular pathology might be the underlying mechanism for the isolated reports in giant-cell arteritis,[53] Takayasu's arteritis,[54] Wegener's granulomatosis,[55] systemic sclerosis,[56] Sjögren's syndrome,[57] relapsing polychondritis,[58] and polyarteritis nodosa.[59] Sensorineural hearing loss is common in patients with Behçet's syndrome,[60] and can be sudden in onset.[61] Asymptomatic hearing loss can be common in patients with systemic lupus erythematosus;[62] however, sudden sensorineural hearing loss has been described in a few cases of systemic lupus erythematosus, and these patients had antiphospholipid antibodies.[63] The relation between antiphospholipid antibodies and such hearing loss is still debated.[64] Abrupt, severe, and irreversible sudden sensorineural hearing loss has been described in 13 patients with migraine. In all patients the headache preceded the hearing loss, and in 12 patients vertigo followed.[65] Susac and colleagues[66] described a rare microangiopathy affecting the brain and the retina, causing a clinical triad of subacute encephalopathy, visual loss secondary to retinal artery branch occlusions, and sensorineural hearing loss. The hearing loss is frequently sudden and usually bilateral.

Miscellaneous causes

Endolymphatic hydrops, an excess of endolymph in the scala media of the labyrinth, is a pathological finding that is commonly associated with Ménière's disease—a clinical diagnosis, which classically presents with sudden unilateral hearing loss, tinnitus, and vertigo. The sudden sensorineural hearing loss associated with Ménière's disease is often accompanied by aural fullness, is rarely severe in the first instance, often recovers within 2–3 days, and almost always recurs. Tinnitus tends to be severe and intrusive, and can precede hearing loss or vertigo. The underlying pathophysiological mechanism of endolymphatic hydrops remains obscure, although several pathways have been proposed.[67] Endolymphatic hydrops has also been reported with other otological disorders, including so-called immune-mediated inner-ear disorder and pathological changes giving rise to sensorineural hearing loss such as syphilitic labyrinthitis.

Sudden sensorineural hearing loss is sometimes associated with systemic immune-mediated diseases. Moreover, patients with this disorder can have evidence of T-cell and antibody recognition of inner-ear antigens.[68] However, the role of tissue-specific immune-responses is poorly defined. In Cogan's syndrome, IgG immunoglobulins have been detected against a supporting cell protein within the sensory epithelia of the inner ear (DEP-1/CD148) and connexin 26 (a gap junction protein), and these antibodies led to sensorineural hearing loss in mice.[69]

Several genetic diseases have been linked with sudden sensorineural hearing loss, including mutations of *GJB2* (*DNFB1*; encoding connexin 26), the presence of a widened vestibular aqueduct in Pendred syndrome, branchio-oto-renal syndrome, renal tubular acidosis, and Fabry's disease.[70–72] Mutations in the mitochondrial 12S ribosomal RNA gene are associated with rapidly progressive sudden sensorineural hearing loss secondary to an increased susceptibility to aminoglycoside ototoxicity.[73]

The most common neoplastic disease associated with sudden sensorineural hearing loss is acoustic neuroma (vestibular schwannoma), which usually presents with unilateral tinnitus and progressive sensorineural hearing loss, although it can present with sudden loss in a few cases.[74] The sudden sensorineural hearing loss associated with acoustic neuroma can recover spontaneously.[75] Sudden sensorineural hearing loss has also been reported with various cerebello-pontine angle lesions, including meningioma.[76,77] Sudden sensorineural hearing loss can rarely be seen as a paraneoplastic occurrence, sometimes in association with paraneoplastic sensory neuronopathy,[78] or as a complication of meningeal carcinomatosis.[79] It has also been reported as a presenting symptom of chronic myeloid leukaemia.[80]

Sudden sensorineural hearing loss commonly occurs with head injury and rarely after whiplash,[81] cliff jumping,[82] and diving decompression sickness.[83] Blast injuries, diving, flights in unpressurised aircraft, and even raised intracranial pressure during sneezing can lead to perilymphatic fistula with sudden sensorineural hearing loss and commonly vertigo.[84]

Many drugs have been associated with ototoxicity, but the hearing loss is usually slowly evolving. Nonetheless, there are case reports of sudden sensorineural hearing loss associated with penicillin,[85] oestrogens,[86] phosphodiesterase-5 inhibitors,[87] pegylated interferon and ribavirin,[88] aminoglycosides,[89] chemotherapeutic agents,[90] and intravenous cocaine use.[91] This disorder has been described many years after radiotherapy, but causation has not been proven.[92] Occasionally it can occur in association with general anaesthesia and both general[93] and otological surgery such as stapedectomy.[94]

Unilateral or bilateral sudden sensorineural hearing loss can present during the course of demyelination or as the initial symptom,[95] and there is often complete recovery. The lesion is proposed to be in the intramedullary auditory nerve or cochlear nucleus.[96] MRI imaging shows enhancing lesions at the root entry zone.[97] Hearing loss occurs in 20% of cases of neurosarcoidosis, and sudden sensorineural hearing loss can be the presenting symptom alone[98] or in combination with other neurological signs. Such hearing loss is seen in association with psychogenic events in about 2·5% of cases, mostly in young women.[99] Pseudohypacusis, in which hearing loss is apparent in the absence of clinical or audiological evidence, is a not infrequent cause of apparent sudden hearing loss in school-aged children and young women.[100,101] Other rarely reported associations include ulcerative colitis,[102] Crohn's disease,[103] Vogt-Koyanagi-Harada syndrome,[104] and Langerhan's cell histiocytosis.[105] Sudden sensorineural hearing loss is rarely associated with pregnancy.[106]

The rare combination of hearing loss and inflammatory eye disease is termed Cogan's syndrome. About half of

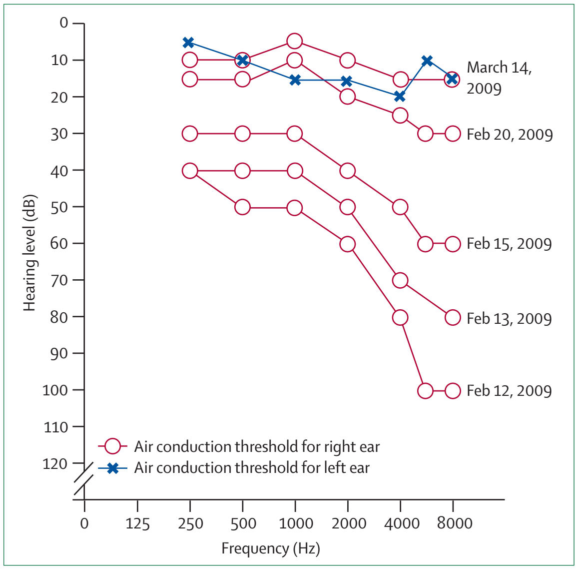

Figure 1: **Pure tone audiogram showing serial results of audiometric thresholds in a case of a unilateral, sudden, sensorineural hearing loss of undiagnosed cause, with spontaneous recovery in a 48-year-old white man**

patients present with sudden sensorineural hearing loss, which is usually bilateral, but asymmetric, and often progressive over 1–3 months.[107] It is often accompanied by acute vertiginous episodes and balance loss, indicating accompanying vestibular pathology.[108] The most feared complication, reported in about 10% of cases, is a medium-large vessel vasculitis. Aortitis can lead to aneurysmal dilatation, aortic regurgitation, and rarely aortic rupture.

Clinical assessment

A thorough history and detailed medical examination is mandatory, with special attention directed toward the otolaryngological and neurological aspects. Clinical examination will be guided by the patient's history, but should include otoscopy to exclude cerumen impaction, middle-ear effusion, infection, mass or a perforated tympanic membrane, and the Rinne and Weber test to screen for a conductive or sensorineural hearing loss. Any patient with sudden hearing loss should have an urgent assessment with a minimum of pure tone audiometry (with air and bone conduction thresholds) to avoid the pitfall of misdiagnosis of a middle-ear pathological change. When a sudden hearing loss is confirmed as sensorineural, an urgent referral to an otolaryngologist or audiovestibular physician should be made.

Patients with confirmed sudden sensorineural hearing loss should undergo a neuro-otological examination to establish the presence or absence of concomitant peripheral or central vestibular dysfunction. This assessment should include examination of gait, eye movements for nystagmus (spontaneous, positional, and optokinetic nystagmus), convergence, smooth pursuit, saccades, and cranial nerves.[109] The detailed neurological examination should focus on evidence of inner-ear dysfunction, cerebellopontine angle lesions, posterior circulation abnormalities, or demyelination. Cardiovascular examination should exclude atrial fibrillation, aortic and mitral murmurs, and carotid bruits. Aortic valve murmurs will prompt consideration of Cogan's syndrome, whereas atrial fibrillation, mitral valve murmurs, or bruits will raise the suspicion of thrombo-embolic disease. An electrocardiogram is indicated to exclude atrial fibrillation.

Pure tone audiometry (with air and bone conduction thresholds) and impedance studies will differentiate conductive from sensorineural loss and define the severity and configuration of impairment, providing a baseline for assessment of recovery and the efficacy of treatment. An otolaryngologist or audiovestibular physician might request additional audiovestibular tests to identify the site of pathological change and to elucidate the nature of vestibular symptoms, which could indicate specific diagnoses. For example, stapedial reflex threshold and auditory brainstem evoked response abnormalities might suggest auditory neuropathy;[110] visuo-vestibular dysfunction might raise the possibility of multiple sclerosis, whereas a sudden profound vestibular loss in the ear opposite to sudden sensorineural hearing loss might suggest the possibility of Cogan's syndrome.

Blood tests appropriate to most cases include full blood count, erythrocyte sedimentation rate, C-reactive protein, antinuclear antibodies, anticardiolipin antibodies, lupus anticoagulant, antineutrophil cytoplasmic antibodies, clotting factors, and syphilis serology. Patients with positive anticardiolipin antibodies or lupus anticoagulant and negative syphilis serology should undergo repeat testing 6–12 weeks later.

Investigators of a prospective series of MRI of the brain and inner ears in patients with sudden sensorineural hearing loss referred to a university hospital in Helsinki, Finland,[111] and attending an emergency room in São Paulo, Brazil,[112] detected acoustic neuroma in about one in 20 patients. By contrast, acoustic neuroma is rarely noted in asymptomatic patients.[113] The British Association of Otolaryngologists-Head and Neck Surgeons recommends that any patient complaining of unilateral or asymmetrical auditory symptoms (either hearing loss or tinnitus), whether of progressive or sudden onset, in whom there is no other obvious cause, should be screened for acoustic neuromas with MRI, even if the auditory brainstem response is normal.[114] Other abnormalities that can be detected include meningiomas, demyelination, and evidence of thrombotic and haemorrhagic vascular events.[77,111]

Prognosis

The prognosis in cases of isolated sudden sensorineural hearing loss is generally good, and improvement within a matter of days is common (figure 1). Patients in whom there is no change within 2 weeks are unlikely to show much recovery.[115] Despite some evidence in case series linking prognosis to severity of hearing

In a multicentre randomised controlled trial,[136] methotrexate was no more effective than was placebo in maintaining the hearing improvement of patients with idiopathic, progressive, bilateral hearing loss who responded initially to prednisolone. Case reports have shown variable benefit of the use of other immunosuppressants (cyclophosphamide, azathioprine, mycophenolate mofetil) in patients with progressive idiopathic sensorineural hearing loss,[137] but no studies have been done in sudden sensorineural hearing loss.

Patients with Cogan's syndrome have been treated with intravenous and oral corticosteroids, usually with more substantial improvement in the ocular than in the audiovestibular symptoms. Various immunosuppressants have been tried empirically, and methotrexate was reported to improve hearing in four patients and stabilised hearing in two others.[138] Infliximab might also have a role.[139] In our clinical experience, patients with Cogan's syndrome can need continuous immunosuppressants to retain audiovestibular function.

In cases in which a vascular cause is not excluded, empiric low-dose oral aspirin could be of benefit. To our knowledge, no data are available for the use of warfarin to treat patients with sudden sensorineural hearing loss, and little evidence for use of heparin[140] and intravenous thrombolytics.[141] Optimum management of patients with sudden sensorineural hearing loss and antiphospholipid antibodies or lupus anticoagulant is controversial. No evidence base is available to guide treatment of patients with persistent high titre IgG anticardiolipin antibodies, but anticoagulation can be considered. A UK study[142] suggested long-term treatment with warfarin to maintain an international normalised ratio between 3 and 4, but this recommendation is debated.

Several other treatments have been investigated because of speculation about pathogenesis. Treatment with antiviral agents (eg, aciclovir, valaciclovir) has not shown benefit in randomised controlled trials.[123] No high-quality randomised controlled trials have shown evidence of benefit of vasoactive treatments, such as plasma expansion with hydroxyethyl starch or dextran, plasmapheresis, and vasodilators (eg, pentoxyfilline or prostacyclin analogues).[143] A meta-analysis[144] of randomised controlled trials based mainly on trials undertaken in China suggested that prostaglandin E_1 provides some benefit. A Cochrane database systematic review[145] of vasoactive therapies in sudden sensorineural hearing loss reported no evidence of effectiveness. Stellate ganglion blocks have also been examined to achieve vasodilatation via sympathetic blockade.[146]

A systematic review[147] showed no evidence of benefit with hyperbaric oxygen therapy. Oral magnesium was associated with benefit in a small randomised controlled trial[148] comparing treatment with steroid and magnesium with steroid and placebo. Treatment with carbogen, a gaseous mixture of 5% carbon dioxide and 95% oxygen, has been investigated in two small randomised controlled trials with variable benefit.[149,150]

Small series have been reported with other therapies including ginkgo biloba and vitamin E without good evidence of benefit. Traditional Chinese approaches have included acupuncture,[151] Chinese medicine,[152] and even ocular needling.[153] Exploratory tympanotomy was thought to be of benefit in uncontrolled retrospective series.[154,155] It is indicated for the management of sudden sensorineural hearing loss occurring in the context of head trauma, barotrauma, and chronic otitis media with cholesteatoma, and in patients with congenital inner-ear abnormalities.

Patients with persistent symptoms should be referred to the appropriate specialists for continuing management of their auditory symptoms. This management can include counselling, information about lifestyle changes, and techniques (such as amplification) for overcoming the communication handicap that hearing loss imposes.[156] Patients should be considered for audiological rehabilitation, and those with persistent tinnitus might benefit from tinnitus retraining therapy.[157]

Conclusions

Most patients with sudden sensorineural hearing loss cannot be given a cause for their diagnosis. Patients with sudden hearing loss presenting to general practice should be assessed with a minimum of pure tone audiometry (with air and bone conduction thresholds), and those with sensorineural hearing loss should be urgently referred to a specialist. A careful assessment is necessary to exclude life threatening or treatable causes such as vascular events and malignant disease. About half of patients show complete recovery, usually in about 2 weeks. We recommend that patients with sudden sensorineural hearing loss with no clear underlying cause after investigation are treated with a short course of oral prednisolone started within 2 weeks after onset. Much needs to be learnt about pathogenesis, and more clinical trials are necessary to establish evidence-based treatment. The strategy outlined in this Seminar provides a pragmatic approach to the management of this complex and poorly understood group of patients.

Contributors

BES did the literature search and LML provided figure 1. All authors contributed to the writing and revisions.

Conflicts of interest

We declare that we have no conflicts of interest.

Acknowledgments

DOH is funded by the British Heart Foundation. LML is supported by the National Institute for Health Research, UCLH/UCL Comprehensive Biomedical Research Centre.

References

1 Davis AC. The prevalence of hearing impairment and reported hearing disability among adults in Great Britain. *Int J Epidemiol* 1989; **18:** 911–17.
2 De Kleyn A. Sudden complete or partial loss of function of the octavus-system in apparently normal persons. *Acta Otolaryngol (Stockh)* 1944; **32:** 407–29.
3 National Institute of Health. Sudden deafness. Bethesda: National Institutes of Health, 2000. NIH publication 00-4757. http://www.nidcd.nih.gov/health/hearing/sudden.asp (accessed May 19, 2009).

4 Wu CS, Lin HC, Chao PZ. Sudden sensorineural hearing loss: evidence from Taiwan. *Audiol Neurootol* 2006; **11:** 151–56.

5 Nosrati-Zarenoe R, Arlinger S, Hultcrantz E. Idiopathic sudden sensorineural hearing loss: results drawn from the Swedish national database. *Acta Otolaryngol* 2007; **127:** 1168–75.

6 Teranishi M, Katayama N, Uchida Y, Tominaga M, Nakashima T. Thirty-year trends in sudden deafness from four nationwide epidemiological surveys in Japan. *Acta Oto-Laryngologica* 2007; **127:** 1259–65.

7 Klemm E, Deutscher A, Mösges R. A present investigation of the epidemiology in idiopathic sudden sensorineural hearing loss. [in German] *Laryngorhinootologie* 2009; **88:** 524–27.

8 McCabe BF: Autoimmune sensorineural hearing loss. *Ann Otol Rhinol Laryngol* 1979; **88:** 585–89.

9 Penido NO, Cruz OL, Zanoni A, Inoue DP. Classification and hearing evolution of patients with sudden sensorineural hearing loss. *Braz J Med Biol Res* 2009; **42:** 712–16.

10 Loughran S. Management of sudden sensorineural hearing loss: a consultant survey. *J Laryngol Otol* 2000; **114:** 837–39.

11 Oh JH, Park K, Lee SJ, Shin YR, Choung YH. Bilateral versus unilateral sudden sensorineural hearing loss. *Otolaryngol Head Neck Surg* 2007; **136:** 87–91.

12 Nosrati-Zarenoe R, Arlinger S, Hultcrantz E. Idiopathic sudden sensorineural hearing loss: results drawn from the Swedish national database. *Acta Otolaryngol* 2007; **127:** 1168–75.

13 Sakata T, Kato T. Feeling of ear fullness in acute sensorineural hearing loss. *Acta Otolaryngol* 2006; **126:** 828–33.

14 van Dishoeck H, Bierman T. Sudden perceptive deafness and viral infection (report of the first one hundred patients). *Ann Otol Rhinol Laryngol* 1957; **66:** 963–80.

15 Fukuda S, Chida E, Kuroda T, Kashiwamura M, Inuyama Y. An anti-mumps IgM antibody level in the serum of idiopathic sudden sensorineural hearing loss. *Auris Nasus Larynx* 2001; **28:** S3–5.

16 Wackym PA. Molecular temporal bone pathology: II. Ramsay Hunt syndrome (herpes zoster oticus). *Laryngoscope* 1997; **107:** 1165–75.

17 Wilson WR, Veltri RW, Laird N, Sprinkle PM. Viral and epidemiologic studies of idiopathic sudden hearing loss. *Otolaryngol Head Neck Surg* 1983; **91:** 653–58.

18 Xenellis J, Nikolopoulos TP, Stavroulaki P, et al. Simultaneous and sequential bilateral sudden sensorineural hearing loss: are they different from unilateral sudden sensorineural hearing loss? *J Otorhinolaryngol Relat Spec* 2007; **69:** 306–10.

19 Gross M, Wolf DG, Elidan J, Eliashar R. Enterovirus, cytomegalovirus, and Epstein-Barr virus infection screening in idiopathic sudden sensorineural hearing loss. *Audiol Neurootol* 2007; **12:** 179–82.

20 Mentel R, Kaftan H, Wegner U, Reissmann A, Gürtler L. Are enterovirus infections a co-factor in sudden hearing loss? *J Med Virol* 2004; **72:** 625–29.

21 Merchant SN, Durand ML, Adams JC. Sudden deafness: is it viral? *J Otorhinolaryngol Relat Spec* 2008; **70:** 52–60

22 Pitkaranta A, Julkunen I. Sudden deafness: lack of evidence for systemic viral infection. *Otolaryngol Head Neck Surg* 1998; **118:** 397–99.

23 Ruben R. Bacterial meningitic deafness: historical development of epidemiology and cellular pathology. *Acta Otolaryngol* 2008; **128:** 388–92.

24 Kutz JW, Simon LM, Chennupati SK, Giannoni CM, Manolidis S. Clinical predictors for hearing loss in children with bacterial meningitis. *Arch Otolaryngol Head Neck Surg* 2006; **132:** 941–45.

25 Peltomaa M, Pyykkö I, Sappälä I, Viitanen L, Viljanen M. Lyme borreliosis, an etiological factor in sensorineural hearing loss? *Eur Arch Otorhinolaryngol* 2000; **257:** 317–22.

26 Cummins D, McCormick JB, Bennett D, et al. Acute sensorineural deafness in Lassa fever. *JAMA* 1990; **264:** 2093–96.

27 Maslan MJ, Graham MD, Flood LM. Cryptococcal meningitis: presentation as sudden deafness. *Am J Otol* 1985; **6:** 435–37.

28 García-Berrocal JR, Górriz C, Ramírez-Camacho R, et al. Otosyphilis mimics immune disorders of the inner ear. *Acta Otolaryngol* 2006; **126:** 679–84.

29 Timon CI, Walsh MA. Sudden sensorineural hearing loss as a presentation of HIV infection. *J Laryngol Otol* 1989; **103:** 1071–72.

30 Bigelow DC, Eisen MD, Yen DM, Saull SC, Solomon D, Schmidt DE. Otolaryngological manifestations of Creutzfeldt-Jakob disease. *Arch Otolaryngol Head Neck Surg* 1998; **124:** 707–10.

31 Rasmussen H. Sudden deafness. *Acta Otolaryngol* 1949; **37:** 65–70.

32 Merchant SN, Adams JC, Nadol JB Jr. Pathology and pathophysiology of idiopathic sudden sensorineural hearing loss. *Otol Neurotol* 2005; **26:** 151–60.

33 Aimoni C, Bianchini C, Borin M, et al. Diabetes, cardiovascular risk factors and idiopathic sudden sensorineural hearing loss: a case-control study. *Audiol Neurootol* 2009; **15:** 111–15.

34 Marcucci R, Alessandrello Liotta A, Cellai AP, et al. Cardiovascular and thrombophilic risk factors for idiopathic sudden sensorineural hearing loss. *J Thromb Haemost* 2005; **3:** 929–34.

35 Capaccio P, Ottaviani F, Cuccarini V, et al. Methylenetetrahydrofolate reductase gene mutations as risk factors for sudden hearing loss. *Am J Otolaryngol* 2005; **26:** 383–87.

36 Rudack C, Langer C, Stoll W, Rust S, Walter M. Vascular risk factors in sudden hearing loss. *Thromb Haemost* 2006; **95:** 454–61.

37 Fukui M, Kitagawa Y, Nakamura N, et al. Idiopathic sudden hearing loss in patients with type 2 diabetes. *Diabetes Res Clin Pract* 2004; **63:** 205–11.

38 Assimakopoulos D, Danielides V, Kontogianis N, Skevas A, Tsatsoulis A. Sudden hearing loss as the presenting symptom of diabetes mellitus. *Diab Res Clin Pract* 2001; **53:** 201–03.

39 Pirodda A, Ferri GG, Modugno GC, Borghi C. Systemic hypotension and the development of acute sensorineural hearing loss in young healthy subjects. *Arch Otolaryngol Head Neck Surg* 2001; **127:** 1049–52.

40 Lee H, Baloh RW. Sudden deafness in vertebrobasilar ischemia: clinical features, vascular topographical patterns and long-term outcome. *J Neurol Sci* 2005; **228:** 99–104.

41 Lee H, Sohn SI, Jung DK, et al. Sudden deafness and anterior inferior cerebellar artery infarction. *Stroke* 2002; **33:** 2807–12.

42 Sauvaget E, Kici S, Petelle B, et al. Vertebrobasilar occlusive disorders presenting as sudden sensorineural hearing loss. *Laryngoscope* 2004; **114:** 327–32.

43 Lin HC, Chao PZ, Lee HC. Sudden sensorineural hearing loss increases the risk of stroke: a 5-year follow-up study. *Stroke* 2008; **39:** 2744–48.

44 Iguchi Y, Kimura K, Kobayashi K, Tachi T, Aihara T, Harada T. Sudden deafness and right-to-left shunts. *Cerebrovasc Dis* 2008; **26:** 409–12.

45 Vazquez R, Solanellas J, Alfageme I, et al. Mitral valve prolapse and sudden deafness. *Int J Cardiol* 2008; **124:** 370–71.

46 Jacobs W, Chamoun A, Stouffer GA. Mitral valve prolapse: a review of the literature. *Am J Med Sci* 2001; **321:** 401–10.

47 Ballesteros F, Alobid I, Tassies D, et al. Is there an overlap between sudden neurosensorial hearing loss and cardiovascular risk factors? *Audiol Neurootol* 2009; **14:** 139–45.

48 Capaccio P, Ottaviani F, Cuccarini V, et al. Sudden hearing loss and MTHFR 677C>T/1298A>C gene polymorphisms. *Genet Med* 2005; **7:** 206–08.

49 Rudack C, Langer C, Junker R. Platelet GPIaC807T polymorphism is associated with negative outcome of sudden hearing loss. *Hearing Res* 2004; **191:** 41–48.

50 O'Keeffe LJ, Maw AR. Sudden total deafness in sickle cell disease. *J Laryngol Otol* 1991; **105:** 653–55.

51 Ruben RJ, Distenfeld A, Berg P, Carr R. Sudden sequential deafness as the presenting symptom of macroglobulinemia. *JAMA* 1969; **209**: 1364–65.

52 Ahmad M. Myeloma cast nephropathy presenting as acute onset bilateral reversible hearing loss. *Int Urol Nephrol* 2007; **39:** 963–65.

53 Wolfovitz E, Levy Y, Brook JG. Sudden deafness in a patient with temporal arteritis. *J Rheumatol* 1987; **14:** 384–85.

54 Maruyoshi H, Toyama K, Kojima S, et al. Sensorineural hearing loss combined with Takayasu's arteritis. *Intern Med* 2005; **44:** 124–28.

55 Kempf HG. Ear involvement in Wegener's granulomatosis. *Clin Otolaryngol Allied Sci* 1989; **14:** 451–56.

56 Deroee AF, Huang TC, Morita N, Hojjati M. Sudden hearing loss as the presenting symptom of systemic sclerosis. *Otol Neurotol* 2009; **30:** 277–79.

57 García Berrocal JR, Arellano B, Vargas JA, Trinidad A, Ramírez Camacho R, Vergara J. Immune-mediated inner ear disease: report of clinical cases. *Acta Otorrinolaringol Esp* 1997; **48:** 565–70.

58 Kumakiri K, Sakamoto T, Karahashi T, Mineta H, Takebayashi S. A case of relapsing polychondritis preceded by inner ear involvement. *Auris Nasus Larynx* 2005; **32:** 71–76.

59 Rowe-Jones JM, Macallan DC, Sorooshian M. Polyarteritis nodosa presenting as bilateral sudden onset cochleo-vestibular failure in a young woman. *J Laryngol Otol* 1990; **104:** 562–64.
60 Pollak L, Luxon LM, Haskard DO. Labyrinthine involvement in Behçet's syndrome. *J Laryngol Otol* 2001; **115:** 522–29.
61 Narváez J, Valverde-García J, Alegre-Sancho JJ, Juanola X, Clavaguera MT, Roig-Escofet D. Sudden cochlear hearing loss in a patient with Behçet's disease. *Rev Rhum Engl Ed* 1998; **65:** 63–64.
62 Roverano S, Cassano G, Paira S, et al. Asymptomatic sensorineural hearing loss in patients with systemic lupus erythematosus. *J Clin Rheumatol* 2006; **12:** 217–20.
63 Green L, Miller EB. Sudden sensorineural hearing loss as a first manifestation of systemic lupus erythematosus: association with anticardiolipin antibodies. *Clin Rheumatol* 2001; **20:** 220–22.
64 Asherson RA, Cervera R. Microvascular and microangiopathic antiphospholipid-associated syndromes ("MAPS"): semantic or antisemantic? *Autoimmun Rev* 2008; **7:** 164–67.
65 Viirre ES, Baloh RW. Migraine as a cause of sudden hearing loss. *Headache* 1996; **36:** 24–28.
66 Susac JO, Egan RA, Rennebohm RM, Lubow M. Susac's syndrome: 1975-2005 microangiopathy/autoimmune endotheliopathy. *J Neurol Sci* 2007; **257:** 270–72.
67 Merchant SN, Adams JC, Nadol JB Jr. Pathophysiology of Meniere's syndrome: are symptoms caused by endolymphatic hydrops? *Otol Neurotol* 2005; **26:** 74–81.
68 Yehudai D, Shoenfeld Y, Toubi E. The autoimmune characteristics of progressive or sudden sensorineural hearing loss. *Autoimmunity* 2006; **39:** 153–58.
69 Lunardi C, Bason C, Leandri M, et al. Autoantibodies to inner ear and endothelial antigens in Cogan's syndrome. *Lancet* 2002; **360:** 915–21.
70 Bitner-Glindzicz M. Hereditary deafness and phenotyping in humans. *Br Med Bull* 2002; **63:** 73–94.
71 Janecke AR, Hirst-Stadlmann A, Günther B, et al. Progressive hearing loss, and recurrent sudden sensorineural hearing loss associated with GJB2 mutations—phenotypic spectrum and frequencies of GJB2 mutations in Austria. *Hum Genet* 2002; **111:** 145–53.
72 Keilmann A, Hajioff D, Ramaswami U; FOS Investigators. Ear symptoms in children with Fabry disease: data from the Fabry Outcome Survey. *J Inherit Metab Dis* 2009; **32:** 739–44.
73 Casano RA, Johnson DF, Bykhovskaya Y, Torricelli F, Bigozzi M, Fischel-Ghodsian N. Inherited susceptibility to aminoglycoside ototoxicity: genetic heterogeneity and clinical implications. *Am J Otolaryngol* 1999; **20:** 151–56.
74 Matthies C, Samii M. Management of 1000 vestibular schwannomas (acoustic neuromas): clinical presentation. *Neurosurgery* 1997; **40:** 1–9.
75 Inoue Y, Kanzaki J, Ogawa K. Vestibular schwannoma presenting as sudden deafness. *J Laryngol Otol* 2000; **114:** 589–92.
76 Aarnisalo AA, Suoranta H, Ylikoski J. Magnetic resonance imaging findings in the auditory pathway of patients with sudden deafness. *Otol Neurotol* 2004; **25:** 245–49.
77 Cadoni G, Cianfoni A, Agostino S, et al. Magnetic resonance imaging findings in sudden sensorineural hearing loss. *J Otolaryngol* 2006; **35:** 310–16.
78 Dalmau J, Porta-Etessam J. Paraneoplastic cerebral syndromes with oto-neuro-ophthalomologic manifestations. *Rev Neurol* 2000; **31:** 1213–19.
79 Uppal HS, Ayshford CA, Wilson F. Sudden onset bilateral sensorineural hearing loss: a manifestation of occult breast carcinoma. *J Laryngol Otol* 2001; **115:** 907–10.
80 Acar GO, Acioğlu E, Enver O, Ar C, Sahin S. Unilateral sudden hearing loss as the first sign of chronic myeloid leukemia. *Eur Arch Otorhinolaryngol* 2007; **264:** 1513–16.
81 Segal S, Eviatar E, Berenholz L, Vaiman M, Kessler A, Shlamkovitch N. Hearing loss after direct blunt neck trauma. *Otol Neurotol* 2003; **24:** 734–37.
82 Hardin MF, Barker M, Neis PR. Sensorineural hearing loss as the result of cliff jumping. *J Ark Med Soc* 2003; **99:** 327–30.
83 Rozsasi A, Sigg O, Keck T. Persistent inner ear injury after diving. *Otol Neurotol* 2003; **24:** 195–200.
84 Patterson JH Jr, Hamernik RP. Blast overpressure induced structural and functional changes in the auditory system. *Toxicology* 1997; **121:** 29–40.
85 Escada PA, Capucho C, Madeira da Silva JF. Sudden sensorineural hearing loss following intramuscular administration of penicillin. *J Laryngol Otol* 2004; **118:** 143–45.
86 Hultcrantz M, Simonoska R, Stenberg AE. Estrogen and hearing: a summary of recent investigations. *Acta Otolaryngol* 2006; **126:** 10–14.
87 Maddox PT, Saunders J, Chandrasekhar SS. Sudden hearing loss from PDE-5 inhibitors: a possible cellular stress etiology. *Laryngoscope* 2009; **119:** 1586–89.
88 Formann E, Stauber R, Denk DM, et al. Sudden hearing loss in patients with chronic hepatitis C treated with pegylated interferon/ribavirin. *Am J Gastroenterol* 2004; **99:** 873–77.
89 Federspil P. Drug-induced sudden hearing loss and vestibular disturbances. *Adv Otorhinolaryngol* 1981; **27:** 144–58.
90 Yorgason JG, Fayad JN, Kalinec F. Understanding drug ototoxicity: molecular insights for prevention and clinical management. *Expert Opin Drug Saf* 2006; **5:** 383–99.
91 Stenner M, Stürmer K, Beutner D, Klussmann JP. Sudden bilateral sensorineural hearing loss after intravenous cocaine injection: a case report and review of the literature. *Laryngoscope* 2009; **119:** 2441–43.
92 Young YH, Lou PJ. Post-irradiation sudden deafness. *J Laryngol Otol* 1999; **113:** 815–87.
93 Punj J, Pandey R, Darlong V. Sensorineural hearing loss after general anaesthesia: 52 cases reported until now! *Anaesthesia* 2009; **64:** 226.
94 Glasscock ME, De Souza C, eds. Otosclerosis and stapedectomy: diagnosis, management, and complications. New York: Thieme Medical Publishers, 2003: 137–40.
95 de Seze J, Assouad R, Stojkovic T, Desaulty A, Dubus B, Vermersch P. Hearing loss in multiple sclerosis: clinical, electrophysiologic and radiological study. *Rev Neurol (Paris)* 2001; **157:** 1403–09.
96 Barratt HJ, Miller D, Rudge P. The site of the lesion causing deafness in multiple sclerosis. *Scand Audiol* 1988; **17:** 67–71.
97 Miller DH, Rudge P, Johnson G, et al. Serial gadolinium enhanced magnetic resonance imaging in multiple sclerosis. *Brain* 1988; **111:** 927–39.
98 Sugaya F, Shijubo N, Takahashi H, Abe S. Sudden hearing loss as the initial manifestation of neurosarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis* 1996; **13:** 54–56.
99 Ban JH, Jin SM. A clinical analysis of psychogenic sudden deafness. *Otolaryngol Head Neck Surg* 2006; **134:** 970–74.
100 Ioannis P, Georgios K, Alexandra K, Dimitrios D, Michael T. Pseudohypacusis: the most frequent etiology of sudden hearing loss in children. *Eur Arch Otorhinolaryngol* 2009; **266:** 1857–61.
101 Hiraumi H, Tsuji J, Kanemaru S, Fujino K, Ito J. Non-organic hearing loss. *Acta Otolaryngol Suppl* 2007; **557:** 3–7.
102 Hollanders D. Sensorineural deafness—a new complication of ulcerative colitis? *Postgrad Med J* 1986; **62:** 753–55.
103 Bachmeyer C, Leclerc-Landgraf N, Laurette F, et al. Acute autoimmune sensorineural hearing loss associated with Crohn's disease. *Am J Gastroenterol* 1998; **93:** 2565–67.
104 Sil A, Chatrath P, Gatland DJ. Deafness in Vogt-Koyanagi-Harada syndrome. *J Laryngol Otol* 2006; **120:** 416–18.
105 Hore I, Mitchell RB, Radcliffe G, Quiney R, Walker T. Langerhans' cell histiocytosis—a rare cause of sudden onset unilateral sensorineural hearing loss. *J Laryngol Otol* 1999; **113:** 1098–100.
106 Pawlak-Osinska K, Burduk PK, Kopczynski A. Episodes of repeated sudden deafness following pregnancies. *Am J Obstet Gynecol* 2009; **200:** e7–9.
107 Gluth MB, Baratz KH, Matteson EL, Driscoll CL. Cogan syndrome: a retrospective review of 60 patients throughout a half century. *Mayo Clin Proc* 2006; **81:** 483–88.
108 Cundiff J, Kansal S, Kumar A, Goldstein DA, Tessler HH. Cogan's syndrome: a cause of progressive hearing deafness. *Am J Otolaryngol* 2006; **27:** 68–70.
109 Davies R. Bedside neuro-otological examination and interpretation of commonly used investigations. *J Neurol Neurosurg Psychiatry* 2004; **75** (suppl 4): 32–44.
110 Hendrix RA, DeDio RM, Sclafani AP. The use of diagnostic testing in asymmetric sensorineural hearing loss. *Otolaryngol Head Neck Surg* 1990; **103:** 593–98
111 Aarnisalo AA, Suoranta H, Ylikoski J. Magnetic resonance imaging findings in the auditory pathway of patients with sudden deafness. *Otol Neurotol* 2004; **25:** 245–49.

112 Ramos HV, Barros FA, Yamashita H, Penido Nde O, Souza AC, Yamaoka WY. Magnetic resonance imaging in sudden deafness. *Braz J Otorhinolaryngol* 2005; **71:** 422–26.
113 Vernooij MW, Ikram MA, Tanghe HL, et al. Incidental findings on brain MRI in the general population. *N Engl J Med* 2007; **357:** 1821–28.
114 British Association of Otolaryngologists—Head and Neck Surgeons. Clinical effectiveness guidelines: acoustic neuroma (vestibular schwanoma). BAO-NHS Document 5. Spring 2002. http://www.entuk.org/members/publications/ceg_acousticneuroma.pdf (accessed June 11, 2009).
115 Moon IS, Kim J, Lee SY, Choi HS, Lee WS. How long should the sudden hearing loss patients be followed after early steroid combination therapy? *Eur Arch Otorhinolaryngol* 2009; **266:** 1391–95.
116 Mattox DE, Simmons FB. Natural history of sudden sensorineural hearing loss. *Ann Otol Rhinol Laryngol* 1977; **86:** 463–80.
117 Guyot JP, Thielen K. Evolution of sudden deafness without treatment. *Schweizerische Medizinische Wochenschrift* 2000; **116:** 93S-96S.
118 Wilson WR, Byl FM, Laird N. The efficacy of steroids in the treatment of idiopathic sudden hearing loss. A double-blind clinical study. *Arch Otolaryngol* 1980; **106:** 772–76.
119 Plontke SK, Bauer M, Meisner C. Comparison of pure-tone audiometry analysis in sudden hearing loss studies: lack of agreement for different outcome measures. *Otol Neurotol* 2007; **28:** 753–63.
120 Garcia Berrocal JR, Ramirez-Camacho R. Immune response and immunopathology of the inner ear: an update. *J Laryngol Otol* 2000; **114:** 101–07.
121 Mort DJ, Bronstein AM. Sudden deafness. *Curr Opin Neurol* 2006; **19:** 1–3.
122 Wei BP, Mubiru S, O'Leary S. Steroids for idiopathic sudden sensorineural hearing loss. *Cochrane Database Syst Rev* 2006; **1:** CD003998.
123 Conlin AE, Parnes LS. Treatment of sudden sensorineural hearing loss: II. A Meta-analysis. *Arch Otolaryngol Head Neck Surg* 2007; **133:** 582–86.
124 Chen CY, Halpin C, Rauch SD. Oral steroid treatment of sudden sensorineural hearing loss: a ten year retrospective analysis. *Otol Neurotol* 2003; **24:** 728–33.
125 Free RH, Smale ND, De Kleine E, Van Der Laan BFAM. Side effects of oral dexamethasone pulse therapy for idiopathic sudden sensorineural hearing loss. *Otol Neurotol* 2009; **30:** 691.
126 Huy PT, Sauvaget E. Idiopathic sudden sensorineural hearing loss is not an otologic emergency. *Otol Neurotol* 2005; **26:** 896–902.
127 Hughes GB, Kinney SE, Barna BP, Calabrese LH. Practical versus theoretical management of autoimmune inner ear disease. *Laryngoscope* 1984; **94:** 758–67.
128 Parnes LS, Sun AH, Freeman DJ. Corticosteroid pharmacokinetics in the inner ear fluids: an animal study followed by clinical application. *Laryngoscope* 1999; **109:** 1–17.
129 Battaglia A, Burchette R, Cueva R. Combination therapy (intratympanic dexamethasone + high-dose prednisone taper) for the treatment of idiopathic sudden sensorineural hearing loss. *Otol Neurotol* 2008; **29:** 453–60.
130 Ho HG, Lin HC, Shu MT, Yang CC, Tsai HT. Effectiveness of intratympanic dexamethasone injection in sudden-deafness patients as salvage treatment. *Laryngoscope* 2004; **114:** 1184–89.
131 Plontke SK, Löwenheim H, Mertens J, et al. Randomized, double blind, placebo controlled trial on the safety and efficacy of continuous intratympanic dexamethasone delivered via a round window catheter for severe to profound sudden idiopathic sensorineural hearing loss after failure of systemic therapy. *Laryngoscope* 2009; **119:** 359–69.
132 Lee HS, Kim JM, Kim YJ, Chung DH, Seo BS, Kim SH. Results of intratympanic dexamethasone injection as salvage treatment in idiopathic sudden hearing loss. *J Otolaryngol Head Neck Surg* 2008; **37:** 263–68.
133 Ahn JH, Yoo MH, Yoon TH, Chung JW. Can intratympanic dexamethasone added to systemic steroids improve hearing outcome in patients with sudden deafness? *Laryngoscope* 2008; **118:** 279–82.
134 Hamid M, Trune D. Issues, indications, and controversies regarding intratympanic steroid perfusion. *Curr Opin Otolaryngol Head Neck Surg* 2008; **16:** 434–40.
135 Plontke SK, Meisner C, Caye-Thomasen P, Parnes L, Agrawal S, Mikulec T. Intratympanic glucocorticoids for sudden sensorineural hearing loss (Protocol). *Cochrane Database Syst Rev* 2009; **4:** CD008080.
136 Harris JP, Weisman MH, Derebery JM, et al. Treatment of corticosteroid-responsive autoimmune inner ear disease with methotrexate: a randomized controlled trial. *JAMA* 2003; **290:** 1875–83.
137 Broughton SS, Meyerhoff WE, Cohen SB. Immune-mediated inner ear disease: 10-year experience. *Semin Arthritis Rheum* 2004; **34:** 544–48.
138 Grasland A, Pouchot J, Hachulla E, Bletry O, Papo T, Vinceneux P. Typical and atypical Cogan's syndrome: 32 cases and review of the literature. *Rheumatology (Oxford)* 2004; **43:** 1007–15.
139 Touma Z, Nawwar R, Hadi U, Hourani M, Arayssi T. The use of TNF-alpha blockers in Cogan's syndrome. *Rheumatol Int* 2007; **27:** 995–96.
140 Yue WL, Li P, Qi PY, Li HJ, Zhou H. Role of low-molecular-weight heparins in the treatment of sudden hearing loss. *Am J Otolaryngol* 2003; **24:** 328–33
141 Mora R, Dellepiane M, Mora F, Jankowska B. The use of recombinant tissue-type plasminogen activator for the treatment of sudden and chronic hearing loss. *Int Tinnitus J* 2005; **11:** 181–84.
142 Wiles NM, Hunt BJ, Callanan V, Chevretton EB. Sudden sensorineural hearing loss and antiphospholipid syndrome. *Haematologica* 2006; **91:** ECR46.
143 Conlin AE, Parnes LS. Treatment of sudden sensorineural hearing loss: I. A systematic review. *Arch Otolaryngol Head Neck Surg* 2007; **133:** 573–81.
144 Zhuo XL, Wang Y, Zhuo WL, Zhang XY. Is the application of prostaglandin E1 effective for the treatment of sudden hearing loss? An evidence-based meta-analysis. *J Int Med Res* 2008; **36:** 467–70.
145 Agarwal L, Pothier DD. Vasodilators and vasoactive substances for idiopathic sudden sensorineural hearing loss. *Cochrane Database Syst Rev* 2009; **4:** CD003422.
146 Cook TG, de Sanctis CA, Plaza JA, Sawyer DD. Stellate ganglion block for sudden profound hearing loss. *Anesthesiology* 1981; **54:** 421–23.
147 Bennett MH, Kertesz T, Yeung P. Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus. *Cochrane Database Syst Rev* 2007; **1:** CD004739.
148 Nageris BI, Ulanovski D, Attias J. Magnesium treatment for sudden hearing loss. *Ann Otol Rhinol Laryngol* 2004; **113:** 672–75.
149 Cinamon U, Bendet E, Kronenberg J. Steroids, carbogen or placebo for sudden hearing loss: a prospective double-blind study. *Eur Arch OtoRhinoLaryngol* 2001; **258:** 477–80.
150 Ni Y, Zhao X. Carbogen combined with drugs in the treatment of sudden deafness. [in Chinese]. *Lin Chuang Er Bi Yan Hou Ke Za Zhi* 2004; **18:** 414–15.
151 Luo RH, Zhou J, Huang YS, Xu K. Observation on therapeutic effect of electroacupuncture for treatment of sudden hearing loss. *Zhongguo Zhenjiu* 2009; **29:** 185–87.
152 Zhang S, Wu XF, Yuan Y, Yue LC, Tai XH. Dialectical types of traditional Chinese medicine and pure tone test indexes in patients with sudden hearing lossæ. *Chin J Clin Rehabil* 2006; **27:** 22–24.
153 Shi J, Zheng Z. Ocular needling for treatment of sudden deafness in 40 cases. *Tradit Chin Med* 2004; **24:** 44–45.
154 Maier W, Fradis M, Kimpel S, Schipper J, Laszig R. Results of exploratory tympanotomy following sudden unilateral deafness and its effects on hearing restoration. *Ear Nose Throat J* 2008; **87:** 438–51.
155 Gedlicka C, Formanek M, Ehrenberger K. Analysis of 60 patients after tympanotomy and sealing of the round window membrane after acute unilateral sensorineural hearing loss. *Am J Otolaryngol* 2009; **30:** 157–61.
156 Schein JD, Miller MH. Sudden deafness, part 2: rehabilitation. *Geriatrics Ageing* 2005; **8:** 67–69.
157 Herraiz C, Hernandez FJ, Toledano A, Aparicio JM. Tinnitus retraining therapy: prognosis factors. *Am J Otolaryngol* 2007; **28:** 225–29.