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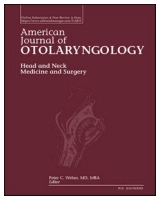

# Meniere's disease: Medical management, rationale for vestibular preservation and suggested protocol in medical failure

Laura H. Christopher [a,*], Eric P. Wilkinson [b,1]

[a] Division of Neurotology, House Ear Clinic, United States of America
[b] House Ear Clinic, House Institute Foundation, United States of America

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ABSTRACT

Meniere's disease is a peripheral audiovestibular disorder characterized by vertigo, hearing loss, tinnitus, and aural fullness. Management of these symptoms includes medical and surgical treatment. Many patients with Meniere's disease can be managed using nonablative therapy, such as intratympanic steroids and endolymphatic shunt surgery, prior to ablative techniques such as intratympanic gentamicin. Recognition of concurrent migraine symptoms may aid in medical therapy and also underscore the importance of preserving vestibular function where possible. The goal of this review is to explain the importance of nonablative therapy options and discuss treatment protocols after medical failure.

Meniere's disease is an idiopathic peripheral audiovestibular disorder characterized by episodic vertigo, unilateral fluctuating hearing loss, tinnitus, and aural fullness. In 1861, Prosper Meniere noted that symptoms of vertigo and hearing loss may be attributable to an inner ear disorder [1]. Meniere's disease (MD) affects approximately 50–200 per 100,000 adults [2]. An approximately 2:1 female gender predilection exists, and onset of symptoms is typically during ages 40 through 60 years [3].

The American Academy of Otolaryngology—Head and Neck Surgery (AAO-HNS) has created strict diagnostic criteria to facilitate diagnosis and management of MD. No definitive test for MD exists, therefore criteria for diagnosis involve categories based on symptoms. Definite MD, as defined by AAO-HNS includes two or more episodes of vertigo, each lasting 20 min to 12 h, audiometrically confirmed low frequency sensorineural hearing loss associated with vertigo, and fluctuating aural symptoms in the affected ear [5]. Typical aural symptoms unilateral tinnitus, subjective hearing loss, and aural fullness. The final criterion for "definite MD" is to exclude other causes of these symptoms. It is important to distinguish MD from other common causes of vertigo which may also present with hearing loss, tinnitus, or aural fullness, such as autoimmune inner ear disease, vestibular migraine, vestibular schwannoma, otosyphilis, vestibular neuritis, and acute labyrinthitis.

Meniere's disease is a clinical diagnosis with significant variation in presentation [6]. Patients tend to have attacks that are random and may have periods of remission lasting months to years. Therefore, an accurate diagnosis may take months, even in ideal circumstances with an experienced neurotologist [6].

The pathophysiology of Meniere's disease is not well understood, and several theories have been proposed over the years to explain the classic symptoms. The most long-standing and well accepted etiology is endolymphatic hydrops (ELH), a term used to describe an increase in endolymph within the membranous labyrinth resulting in episodic inner ear symptoms. In Schuknecht's rupture theory, the endolymph space becomes distended and eventually ruptures Reissner's membrane. Cochlear hair cells and the audiovestibular nerve are then exposed to toxic, potassium rich endolymph, responsible for episodic spinning vertigo and changes in hearing [7,8]. Additional mechanisms suggested to cause hydrops involve excess endolymph production, decreased endolymph resorption, altered secretions of the endolymphatic sac, and altered immune function of the endolymphatic sac [1].

Regardless of the mechanism, endolymphatic hydrops is the ultimate result and has been pathologically confirmed [9]. The hallmark of endolymphatic hydrops seems to be present in all patients with MD, but not all patients with ELH have MD [10]. Histopathology records from Massachusetts Eye and Ear Infirmary show that many patients with ELH have secondary hydrops, or hydrops associated with diseases other than MD. These results suggest that "ELH may be necessary but not sufficient for MD development" [5].

* Corresponding author at: House Ear Clinic, 2100 West Third Street, Los Angeles, CA 90057, United States of America.
*E-mail addresses:* lchristopher@houseclinic.com (L.H. Christopher), ewilkinson@houseclinic.com (E.P. Wilkinson).
[1] House Ear Clinic, 2100 West Third Street, Los Angeles, CA 90057.

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Although the clinical presentation of MD is variable, true "spinning" vertigo is a necessary criterion for diagnosis [5]. Patients may use the word "dizziness" to describe vertigo, lightheadedness, disequilibrium, or balance problems in general. This is particularly relevant in elderly patients, with multiple medical comorbidities. Determining whether the patient is experiencing the false sense of self movement or movement of his or her surroundings is critical to diagnosing MD [11].

The natural course of MD is variable and unpredictable. Typically, MD presents with sudden attacks of vertigo, unilateral hearing loss, tinnitus, and aural fullness [1]. Vertigo is often severe, with associated nausea and vomiting, lasting for hours. Frequency of attacks may range from 6 to 11 attacks per year [6]. These attacks may increase in number for several years and then gradually decline over time. Periods of remission may last months to years, with recurrences occurring even 20 years following diagnosis [12]. The usual course of MD is gradual decline and eventual cessation of vertiginous attacks. Green et al. reported absence of vertigo in 54% and decrease in vertigo in 30% of 108 patients with MD followed for 9 years [13].

Hearing loss in MD tends to mimic the course of vertigo, in that hearing worsens over time with eventual "burn out". Low frequency sensorineural hearing loss is typical in the early disease stages, with eventual high frequency SNHL over time. Hearing loss is usually unilateral and fluctuating and progressively worsens to a flat loss of over 50 dB [14]. A 20-year longitudinal study reported moderate to severe hearing loss in 82% of MD patients over time [14].

The differential diagnosis for patients presenting with vertigo in addition to hearing loss, aural fullness, and tinnitus includes autoimmune ear disease, otosyphilis, perilymphatic fistula, vestibular schwannoma, endolymphatic sac tumors, end stage otosclerosis, and labyrinthitis. For many patients, response to treatment may be needed to confirm the diagnosis. For these reasons, delay in diagnosis is common. A Finnish study reported a diagnostic delay of greater than or equal to five years in 20% of patients with MD [15].

The relationship between vestibular migraine (VM) and MD is important to note, particularly relevant in patients that do not present with hearing loss. There is significant overlap in the clinical features of VM and MD, and these diseases may occur concurrently, with some studies estimating a 35% rate of VM in MD patients [16]. Although the precise pathophysiology involved between these entities is unknown, some suggest that the inner ear pathology related to MD may trigger migraines. This "neural triggering" may exacerbate migraine symptoms in patients with concurrent MD and VM. The recently published AAO-HNS Clinical Practice Guidelines highlight this overlap and recommend that clinicians determine if patients meet diagnostic criteria for vestibular migraine when assessing for Meniere's disease.

Treatment of patients with concurrent VM and MD is complex, in that avoidance of destructive or ablative therapy is important. Therefore, effective long-term treatment using nondestructive therapy is ideal. Endolymphatic sac surgery along with dietary and medical management of migraine symptoms are the treatments of choice in these patients. Migraine patients may also be more prone to cervicogenic dizziness, in which neck movements or muscle tension may precipitate symptoms. These symptoms are related to the vestibulocollic reflex, which causes neck movement in response to head movement sensed by the vestibular system via the medial vestibulospinal tract. The pathophysiology involved is beyond the scope of this paper, but manual neck physical therapy may be a useful additional treatment for these symptoms, if present.

Medical management of vestibular migraine is complex and includes abortive and preventative therapy. Treatment of acute symptoms in VM includes antinausea medications and short-term vestibular suppressants. In patients with concurrent MD and VM, treatment is most often focused on managing chronic symptoms using preventative medications. Diet modifications similar to those of MD have been recommended, including limiting caffeine intake. Supplementation with B2, Magnesium glycinate, and Coenzyme Q have shown some benefit in patients with migraine [17]. The majority of medications for prevention of vestibular migraine are those used for migraine headache and include the following: beta blockers, topiramate, calcium channel blockers, tricyclic antidepressants (amitriptyline, nortriptyline), selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors (venlafaxine), and benzodiazepines [18]. In a 2015 prospective, randomized, controlled clinical trial, venlafaxine and propranolol were both effective in reducing vestibular symptoms for VM patients. Venlafaxine provided additional anti-depressant benefits [19].

Botox is an additional option for VM patients. Botox and topiramate are the current available chronic migraine treatments with more than one high quality randomized controlled trial supporting their use [20]. Recent literature suggests that topiramate may be particularly beneficial for patients with concurrent VM and MD. A recent retrospective review from UC Irvine showed improvement in low frequency sensorineural hearing loss in patients receiving adjuvant migraine medication, specifically nortriptyline and topiramate, in addition to oral and transtympanic steroids, compared to those receiving only oral and transtympanic steroids [21]. The hearing improvement seen with the addition of topiramate may be explained by the medication's ability to lower intracranial pressure. In vivo studies using rats demonstrated a significant reduction of intracranial pressure following both subcutaneous and oral administration of topiramate [22].

Calcitonin gene related peptide (CGRP) is a neuropeptide expressed in trigeminal neurons and involved in pain perception. Much of the current migraine literature is focusing on CGRP and its role in migraine. CGRP receptor antagonists and anti-CGRP monoclonal antibodies have emerged as new and effective treatment options for chronic migraine [20]. Although its role in vestibular migraine is unclear, recent studies suggest that targeting CGRP may change the paradigm for migraine treatment.

Treatment of Meniere's disease is complex and involves both medical and surgical management and destructive and nondestructive options. A wide variety of treatment options exist, partially due to the lack of understanding regarding the pathophysiology of MD and the multiple proposed etiologies. Additionally, randomized controlled trials to study treatment options are difficulty to carry out because of the fluctuating nature of the disease and subjective symptoms. Therefore, anecdotal evidence and opinion are used to guide management of MD.

The goals of treatment are to reduce the severity and frequency of vertigo attacks, preserve hearing, alleviate aural fullness and tinnitus, and improve quality of life. The episodic and unpredictable nature of the disease complicates treatment, due to the difficulty of distinguishing asymptomatic periods of the disease versus treatment benefit.

The purpose of this paper is to highlight the advantages of nondestructive treatment options such as medical management, intratympanic dexamethasone, and endolymphatic shunt surgery prior to the ablative measures including intratympanic gentamicin and labyrinthectomy. Many patients improve using these less invasive measures and are able to avoid potentially morbid treatment options and sacrifice of hearing.

Medical management includes treatment of acute attacks and prophylaxis. Acute attacks are managed using central vestibular suppressants [23]. These medications include first generation antihistamines, benzodiazepines, and anticholinergics, which work through different pathways to alleviate vertigo and nausea. Commonly used first generation antihistamines include meclizine, dimenhydrinate, and diphenhydramine. Promethazine is a commonly used phenothiazine with antihistamine properties. Scopolamine is an anticholinergic that is commonly prescribed in its transdermal form. The AAO-HNS recommends the use of any of the above-mentioned vestibular suppressants, citing similar efficacies [24,25]. Physician and patient preference tend to guide which medication is prescribed. These medications are used only for acute attacks, as chronic use may prevent vestibular compensation.

Prophylactic treatment for MD focuses on lifestyle modifications and management of potential triggers prior to medication use. Limiting salt,

caffeine, and alcohol is recommended, as these may be triggers for attacks. Salt intake is thought to affect the endolymph fluid in the inner ear, and the recommendations for a sodium-restriction diet are based on the American Heart Association's work [26]. Additional triggers include stress and allergy. Studies have shown that stress hormones in the endolymphatic sac are increased in MD patients, and stress reduction techniques have shown to improve symptoms [27–29]. Stress reduction, well balanced, regular meals, and allergy management are all recommended for control of symptoms. Observational studies have shown improvement in symptoms of vertigo and dizziness with salt and caffeine restrictions [30]. Additionally, most patients are willing and able to try these methods prior to medication or surgery [30]. Although there are no randomized controlled trials to support their use, these dietary/lifestyle modifications have been advocated for decades and improve symptoms in many patients.

Oral pharmacotherapy is used for maintenance therapy in patients in whom diet and lifestyle changes do not control symptoms. As stated previously, the ultimate result of endolymphatic hydrops may be caused by multiple etiologies, including viral infection, ion imbalance, diet, autoimmune factors, vascular abnormalities, and allergy [31–33]. Diuretics and betahistine, the most commonly recommended medications for MD, target these etiologies. Through different mechanisms of actions, diuretics are thought to affect the electrolyte balance of the endolymph in the inner ear and thereby reduce the amount of endolymph. Thiazide diuretics, with or without a potassium sparing diuretic, and the carbonic anhydrase inhibitor acetazolamide (Diamox) are the most commonly prescribed diuretics for MD [23]. Studies have shown improvement in vertigo symptoms with diuretic use [34].

Betahistine is an additional oral pharmacotherapy option used for MD. It is a histamine analogue thought to cause increased vasodilation to the inner ear. Since its exact mechanism of action is unclear, there is no Food and Drug Administration (FDA) approval for its use in MD. However, this drug has been used worldwide for peripheral vertigo treatment for many years. Conflicting evidence exists regarding its effect on vertigo in clinical trials. A 2016 Cochrane found that 60% of patients had an improvement in vertigo after taking betahistine compared to placebo [35]. However, a recent double-blind RCT (BEMED trial) did not show a change in the number of vertigo attacks in MD patients compared to placebo [36]. The MD Clinical Practice Guidelines recommend betahistine as an "option" for maintenance therapy to reduce symptoms or prevent attacks [5].

At the House Ear Clinic, betahistine has been offered to MD patients for around 10 years with good results. Betahistine is not approved by the FDA in the United States. As such, it can be difficult to obtain for patient use. The reader is referred to the discussion on Dr. Timothy Hain's web page regarding legal issues and availability of this drug: http://www.dizziness-and-balance.com/treatment/drug/SERC%20sources.htm and http://www.dizziness-and-balance.com/treatment/drug/serc.html. Compounding pharmacies may be able to supply betahistine in certain situations. Physicians seeking to counsel their patients on the use of Betahistine should refer to local and federal laws regarding supplements and medications that are not FDA approved and also have informed consent discussions with their patients regarding the advantages and disadvantages of using non-FDA approved therapies.

For many, diet and lifestyle modifications in addition to betahistine offer long term control of symptoms. Side effects are minor and include headache, nausea, and upper gastrointestinal symptoms [35]. At the House Ear Clinic, we have found that most patients tolerate this medication quite well with symptom relief.

Additional prophylactic treatments include allergy treatment, immunosuppressants, migraine treatment, antivirals, oral steroids, and low dose benzodiazepines. Significant crossover exists between allergy, migraine, and MD. Some suggest that allergy may, in fact, be the link between MD and migraine [37]. Limited data exists regarding the efficacy of oral steroids and MD, but some studies show improvement in vertigo symptoms [38]. At the House Ear Clinic, prednisone tapers are used frequently for symptoms of increased vertigo or significant changes in hearing. Most patients tolerate this medication well and show improvement in vertigo and hearing. Additionally, low dose benzodiazepines have been used at our institution for symptom control. The low dose prescribed tends to minimize the side effects such as sedation and provides relief from vertigo.

In summary, there are many oral pharmacotherapy options available for MD patients to control symptoms. Of note, trial of the above-mentioned medication options for several months may be necessary to show effect. Strict adherence to a low salt, low caffeine diet in addition to the prescribed medication is needed in order determine whether patients will benefit. At the House Ear Clinic, many patients are able to find a regimen that controls symptoms.

For some patients, however, attacks of vertigo are not controlled with these medications used as maintenance therapy. In patients without symptom control using noninvasive techniques who have serviceable hearing, the next step is intratympanic dexamethasone. The mechanism of action is thought to involve anti-inflammatory effects and ion homeostasis [39]. The AAO-HNS clinical practice guidelines for MD offer intratympanic (IT) steroid therapy as an "option" for patients with active MD not responsive to noninvasive techniques. Randomized control trials and systematic reviews have shown improvement in vertigo, tinnitus, hearing, and aural fullness with intratympanic steroids [40,41]. Other studies have shown lack of statistically significant changes in vertigo rates [42].

The AAO-HNS Clinical Practice Guidelines note that IT steroid therapy provides less control of vertigo than intratympanic gentamicin (43–90% of patients versus 70–87% of patients, respectively) [43–46]. The guidelines go on to state that "IT gentamicin therapy may provide superior vertigo control in patients with severe or recurrent vertigo or advanced MD." This is intuitive, as gentamicin is vestibulotoxic, and IT gentamicin may be considered a chemical labyrinthectomy. IT gentamicin and other ablative techniques such as labyrinthectomies do offer a higher likelihood of vertigo control. However, this comes at a cost: the sacrifice of hearing. In patients without serviceable hearing, the decision to proceed with IT gentamicin prior to IT steroids may be appropriate. The low dose transtympanic gentamicin protocol developed by the Mayo Clinic recommends injecting approximately 0.75 mL of a 40 mg/mL gentamicin solution into the middle ear [47].This dose may be repeated at one month for continued symptoms and may be diluted to 20 mg/mL in patients older than 65 years. Reported incidences of sensorineural hearing loss following transtympanic gentamicin injections vary. Using their low dose protocol, the Mayo Clinic results show no major changes in hearing [47]. A meta-analysis comparing techniques of intratympanic gentamicin administration reported an overall hearing loss rate of 25% [48]. Higher rates of hearing loss were seen with multiple daily dosing regimens.

In the large subset of patients with good or serviceable hearing, destructive therapies should be avoided until all nondestructive therapies have been exhausted. Therefore, it is our practice to advocate for nonablative techniques prior to ablative or destructive techniques. Emphasis is also placed on ruling out concurrent vestibular migraine. Specifically, patients should be managed with oral pharmacotherapy, IT steroids, or endolymphatic shunt surgery prior to destructive techniques such as IT gentamicin.

The risks associated with IT steroids are minimal and avoid the systemic side effects of oral steroids. Tympanic membrane perforation is cited as a risk factor, with some studies reporting a nearly 40% risk of perforation [49]. In our experience, permanent tympanic membrane perforation following IT therapy is rare. Cost, time for treatment, and patient discomfort have been cited as additional "risks". We have found that patients tolerate the procedure well. IT steroid treatment is most commonly offered for patients with active Meniere's disease and has a relatively quick onset of action. This is particularly desirable for patients whose quality of life is poor due to vertigo and additional inner ear symptoms. The additional time and cost are far outweighed by the

improvement in symptoms, hearing preservation, and lack of systemic side effects.

IT steroids may be administered multiple times, depending on patient symptoms. For some, maintenance therapy using oral medications with intermittent IT steroid injections for flareups provides lifelong control of symptoms. In patients without a good response to IT steroid injections or those desiring a more long-term solution for vertigo control, endolymphatic sac surgery is recommended.

Endolymphatic sac (ELS) surgery has been a controversial subject in neurotology for many years, with conflicting evidence in the literature regarding its efficacy. Since its initial description in 1927 by Portmann, four types of surgical techniques have evolved: endolymphatic sac incision, endolymphatic-subarachnoid shunt, endolymphatic-mastoid shunt, and endolymphatic sac decompression [50]. William House is recognized for his description of the endolymphatic subarachnoid shunt. However, the House Clinic now consistently performs the endolymphatic-mastoid shunt using silastic sheeting, with a reduced risk for intracranial complications and hearing decline.

The Danish Sham Study, published by Thomsen et al. in 1981, sparked controversy regarding the efficacy of ELS surgery, reporting no difference in vertigo control when comparing ELS surgery to "placebo" mastoidectomy [51]. Critics, including Pillsbury, Welling, and Nagaraja, reviewed the data and reported statistically significant improvement in vertigo with ELST surgery [2,52]. A review of the current literature supports that 80–90% of MD patients have vertigo control for 2 years after surgery, decreasing to approximately 60% at 5 years [53–55]. Hearing is preserved, with a less than 2% incidence of total SNHL, based on the recent AAO-HNS Clinical Practice Guidelines [5].

In response to the controversy surrounding the efficacy of ELS surgery and the recent emphasis in the medical community regarding cost effective treatment options, Pensak et al. reported a five-year control rate for vertigo of 68–92% in patients undergoing ELS surgery [56]. A follow up study in 2008 demonstrated a 78% control rate of vertigo using ELS surgery, emphasizing the surgery's long-term efficacy using evidence-based results in contrast to transtympanic steroids' unknown long-term results [57]. Convert et al. studied long term quality of life results after undergoing endolymphatic sac decompression for MD. Using a 40 item MD Outcome Questionnaire, the authors reported a 71% control rate for vertigo at 2 years following surgery. Additionally, hearing was improved or stable at three months after surgery [58].

Despite these results, the recently released AAO-HNS Clinical Practice Guidelines do not make a recommendation for or against ELS surgery for MD. At the House Ear Clinic, ELS surgery is routinely offered to patients with good hearing and uncontrolled symptoms despite maximal medical management. This procedure offers an additional long-term treatment option prior to destructive management. The surgery is a low risk procedure, and elderly patients tolerate the procedure well [59]. We have found that most patients opt for ELS surgery prior to undergoing any kind of destructive treatment, highlighting the value placed on hearing preservation by patients. Revision ELS surgery may also be provided, with significant improvement in vertigo control in 76–95% of patients [60,61]. ELS surgery is particularly important in patients with bilateral disease at risk of bilateral hearing loss. Attempting to treat unilateral MD without ablative therapy may avoid the complex treatment situation of an only hearing ear in the future. The literature suggests that ELS surgery may limit the need for destructive treatment to approximately 2% in some estimates [2].

Delayed endolymphatic hydrops is defined by new onset of MD symptoms following a previous unilateral severe hearing loss and is a form of bilateral Meniere's disease [1]. A longitudinal follow up study of Meniere's patients estimated up to a 45% incidence of bilateral MD [13]. Results showed that a larger percentage of patients with bilateral MD continued to require medical treatment at 14 year follow up, compared to patients with unilateral MD [13]. A 2006 retrospective review at our institution found a 25% prevalence of bilateral involvement [62]. Contralateral ear involvement may occur up to decades after unilateral MD, therefore, long term follow up for MD patients is imperative [62]. Bilateral vestibular loss may occur in patients with bilateral MD. The bilateral vestibular loss in these patients may be present with symptoms of imbalance, as opposed to spinning vertigo [62]. Additionally, these patients may have difficulty with oscillopsia, further complicating their imbalance. In summary, the decision to proceed with ablative therapy for unilateral disease is made complicated by the risk of developing contralateral disease.

Patients may not have immediate results after ELS surgery, however, at our institution we recommend waiting two to three months before proceeding with any additional changes to therapy or ablative therapy. This allows time to assess the efficacy of the ELS surgery. During this time, intratympanic steroids may be used for additional symptom control. The addition of IT steroids as a "boost" therapy postoperatively is not uncommon [54]. Some surgeons may recommend cessation of medical therapy (i.e. diuretics and betahistine) post operatively. We recommend that patients continue all medications for several months following ELS surgery, with a gradual tapering as symptoms improve. Again, this allows the ELS surgery time to prove effective.

Vestibular nerve section (VNS) is considered a hearing preservation technique but is a vestibular ablative technique in that the vestibular input is destroyed. Patients with contralateral disease are not candidates for this procedure. Videonystagmography must be performed in the contralateral ear preoperatively to avoid creating bilateral vestibular loss, resulting in oscillopsia. Studies have reported vertigo control rates from >90% after vestibular nerve section [63–65]. Some surgeons favor VNS over ELS surgery. However, VNS carries a higher risk of SNHL as the cochlear nerve fibers are sometimes difficult to dissect from the vestibular nerve. The surgery is more invasive than ELS surgery and adds the risks of a craniotomy. Finally, complete vertigo control may not be attained if residual nerve fibers are left intact [66].

Vestibular nerve sectioning was first described in the early 1900s using a suboccipital approach [67]. Since that time, additional approaches to VNS have been described, including retrolabyrinthine, middle fossa, and combined retrolabyrinthine/retrosigmoid approaches. The retrolabyrinthine approach was first described in 1978 by Drs. Brackmann and Hitselberger and is the preferred approach at the House Clinic today. Benefits of the retrolabyrinthine approach include hearing preservation, reduced cerebellar retraction, direct view of the vestibulocochlear and facial nerves, and consistent outcomes for symptom relief [67]. One indication for proceeding directly to VNS rather than medical management or ELS surgery is drop attacks. Due to the potentially morbid risks associated with drop attacks, ablative techniques may be indicated [68].

While the goal of this paper is to emphasize attempting nondestructive therapy in MD, ablative techniques certainly play a role in management. Patients with uncontrolled vertigo despite medical management, IT steroids, and ELS shunt are candidates for ablative therapy (Fig. 1). Destructive therapy options include IT gentamicin and labyrinthectomy. Patients with nonserviceable hearing may be offered these options early during management, as these options provide good control of symptoms. Prior to initiation of IT gentamicin, particularly in patients with class A or B hearing, patients should be tested for a specific mitochondrial mutation which is well known to cause aminoglycoside sensitivity, resulting in rapid onset severe to profound hearing loss, even with small doses [69]. Saint Francis Health System offers testing for this genotype, *MT-RNR1*, and the resulting mutation, m.1555A > G, using a simple blood test (St. Francis Laboratory, St. Louis, MO). This testing is particularly important in patients who have any serviceable hearing [69].

Elderly patients with MD are unique in that they may have delayed or failed vestibular compensation following ablative therapies [70,71]. Surgical procedures for ablative therapy and also nonablative therapies, such as ELS surgery, may not be possible due to medical comorbidities. In these cases, intratympanic gentamicin is the procedure of choice. Dilution of gentamicin or titrating the dosage may be useful in the

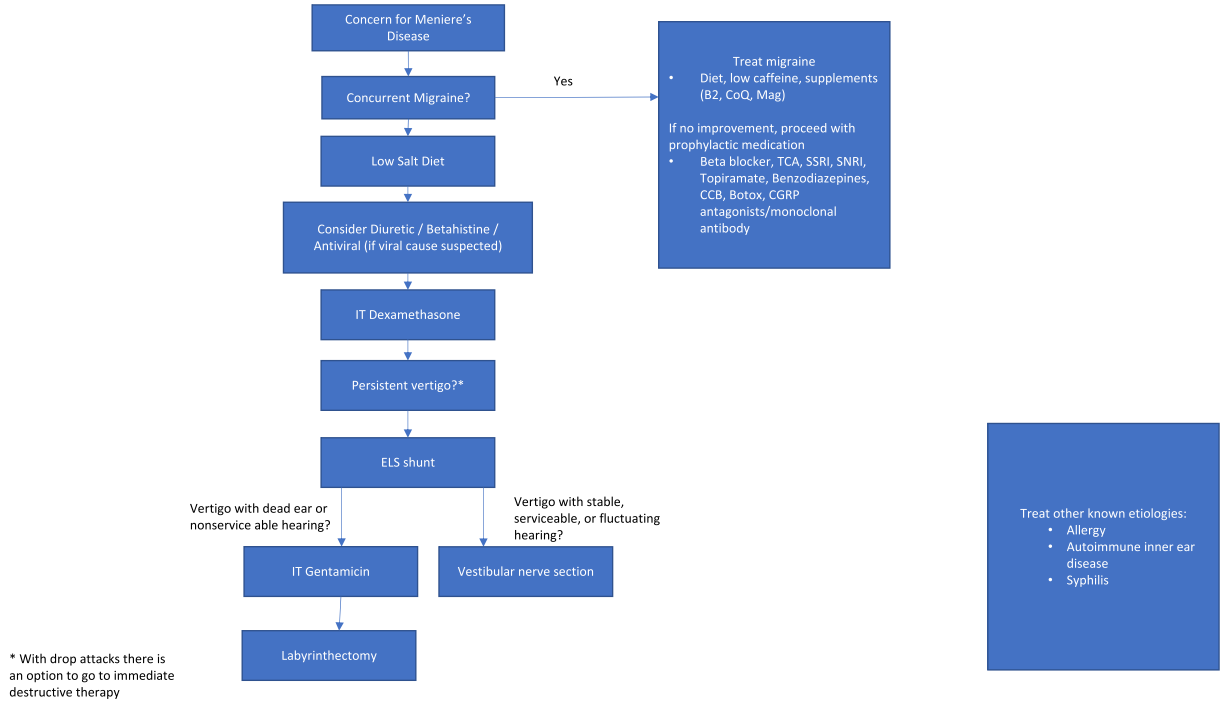


**Fig. 1.** Meniere's disease treatment algorithm.

elderly. Additionally, vestibular rehabilitation therapy in older patients may improve their recovery following ablative techniques [71].

In conclusion, MD patients should be offered nondestructive therapies before proceeding with IT gentamicin or other destructive techniques. Many patients are able to be managed using migraine treatment, MD oral pharmacotherapy, IT dexamethasone, or ELS surgery. Surgical treatment of MD is necessary only in the minority of patients. ELS surgery is a good nonablative option and is routinely offered to patients at our institution prior to vestibular nerve section. The value of these treatment options should be emphasized in MD treatment algorithms.

## Declaration of competing interest

None.

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## References

[1] Antonio SM, Friedman R. Meniere's disease. In: Jackler RK, Brackmann DE, editors. Neurotology. Philadelphia: Elsevier; 2005. p. 621–38.
[2] Packer MD, Welling DB. Surgery of the endolymphatic sac. In: Brackmann DE, Shelton C, Arriaga MA, editors. Otologic surgery. Philadelphia: Elsevier; 2016. p. 362–76.
[3] Harris JP, Alexander TH. Current-day prevalence of Meniere's syndrome. Audiol Neurootol 2010;15(5):318–22.
[5] Basura GJ, Adams ME, Monfared A, et al. Clinical practice guideline: Ménière's disease. Otolaryngol Head Neck Surg 2020;162(2_suppl):S1–55.
[6] Watanabe Y, Mizukoshi K, Shojaku H, Watanabe I, Hinoki M, Kitahara M. Epidemiological and clinical characteristics of Meniere's disease in Japan. Acta Otlaryngol Suppl 1995;519:06–210.
[7] Schuknecht HF, Gulya AJ. Endolymphatic hydrops: an overview and classification. Ann Otol Rhinol Laryngol Suppl 1983;106:1–20.
[8] Oberman BS, Patel VA, Cureoglu S, Isildak H. The aetiopathologies of Meniere's disease: a contemporary review. Acta Otorhinolaryngol Ital 2017;4:250–63.
[9] Paparella MM, Djalilian HR. Etiology, pathophysiology of symptoms, and pathogenesis of Me'nie're's disease. Otolaryngol Clin North Am 2002;35(3):529–45.
[10] Merchant SN, Adams JC, Nadol Jr JB. Pathophysiology of Meniere's syndrome: are symptoms caused by endolymphatic hydrops? Otol Neurotol 2005;26(1):74–81.
[11] Bisdorff A, Von Brevern M, Lempert T, Newman-Toker DE. Classification of vestibular symptoms: towards an international classification of vestibular disorders. J Vestib Res 2009;19:1–2–13.
[12] Havia M, Kentala E, Pyykko I. Prevalence of Meniere's disease in general population of southern Finland. Otolaryngol Head Neck Surg 2005;133(5):762–8.
[13] Green Jr JD, Blum DJ, Harner SG. Longitudinal followup of patients with Menière's disease. Otolaryngol Head Neck Surg 1991;104(6):783–8.
[14] Friberg U, Stahle J, Svedberg A. The natural course of Me'nie're's disease. Acta Otolaryngol Suppl 1984;406:72–7.
[15] Pyykko I, Nakashima T, Yoshida T, Zou J, Naganawa S. Me'nie're's disease: a reappraisal supported by a variable latency of symptoms and the MRI visualisation of endolymphatic hydrops. BMJ Open 2013;3(2).
[16] Shin CH, Kim Y, Yoo MH, et al. Management of Me'nie're's disease: how does the coexistence of vestibular migraine affect outcomes? Otol Neurotol 2019;40(5):666–73.
[17] Gaul C, Diener HC, Danesch U. Migravent® Study Group. Improvement of migraine symptoms with a proprietary supplement containing riboflavin, magnesium and Q10: a randomized, placebo-controlled, double-blind, multicenter trial. J Headache Pain 2015;16:516.
[18] Bisdorff AR. Management of vestibular migraine. Ther Adv Neurol Disord 2011;4(3):183–91.
[19] Salviz M, Yuce T, Acar H, Karatas A, Acikalin RM. Propranolol and venlafaxine for vestibular migraine prophylaxis: a randomized controlled trial. Laryngoscope 2016;126(1):169–74.
[20] Agostoni EC, Barbanti P, Calabresi P, et al. Current and emerging evidence-based treatment options in chronic migraine: a narrative review. J Headache Pain 2019;20(1):92 [Published 2019 Aug 30].
[21] Abouzari M, Goshtasbi K, Chua JT, et al. Adjuvant migraine medications in the treatment of sudden sensorineural hearing loss [published online ahead of print, 2020 Apr 3]. Laryngoscope 2020. https://doi.org/10.1002/lary.28618 [doi: 10.1002/lary.28618].
[22] Scotton WJ, Botfield HF, Westgate CS, et al. Topiramate is more effective than acetazolamide at lowering intracranial pressure. Cephalalgia 2019;39(2):209–18. https://doi.org/10.1177/0333102418776455.
[23] Slattery 3rd WH, Fayad JN. Medical treatment of Meniere's disease. Otolaryngol Clin North Am 1997;30(6):1027–37.
[24] Clissold SP, Heel RC. Transdermal hyoscine (scopolamine): a preliminary review of its pharmacodynamic properties and therapeutic efficacy. Drugs 1985;29(3):189–207.
[25] Hahn A, Sejna I, Stefflova B, Schwarz M, Baumann W. A fixed combination of cinnarizine/dimenhydrinate for the treatment of patients with acute vertigo due to vestibular disorders: a randomized, reference-controlled clinical study. Clin Drug Investig 2008;28(2):89–99.
[26] Cogswell ME, Zhang Z, Carriquiry AL, et al. Sodium and potassium intakes among US adults: NHANES 2003–2008. Am J Clin Nutr 2012;96(3):647–57.
[27] Kitahara T, Doi K, Maekawa C, et al. Meniere's attacks. Occur in the inner ear with excessive vasopressin type-2 receptors. J Neuroendocrinol 2008;20(12):1295–300.

[28] Maekawa C, Kitahara T, Kizawa K, et al. Expression and translocation of aquaporin-2 in the endolymphatic sac in patients with Me'nie're's disease. J Neuroendocrinol 2010;22(11):1157–64.
[29] Yardley L, Kirby S. Evaluation of booklet-based self management of symptoms in Me'nie're disease: a randomized controlled trial. Psychosom Med 2006;68(5):762–9.
[30] Luxford E, Berliner KI, Lee J, Luxford WM. Dietary modification as adjunct treatment in Me'nie're's disease: patient willingness and ability to comply. Otol Neurotol 2013;34(8):1438–43.
[31] Derebery MJ. The role of allergy in Meniere's disease. Otolaryngol Clin North Am 1997;30(6):1007–16.
[32] Vrabec JT. Herpes simplex virus and Me'nie're's disease. Laryngoscope 2003;113(9):1431–8.
[33] Derebery MJ, Rao VS, Siglock TJ, Linthicum FH, Nelson RA. Me'nie're's disease: an immune complex-mediated illness? Laryngoscope 1991;101(3):225–9.
[34] Torok N. Old and new in Me'nie're disease. Laryngoscope 1977;87(11):1870–7.
[35] Murdin L, Hussain K, Schilder AGM. Betahistine for symptoms of vertigo. Cochrane Database Syst Rev 2016;6:CD010696.
[36] Adrion C, Fischer CS, Wagner J, Gurkov R, Mansmann U, Strupp M. Efficacy and safety of betahistine treatment in patients with Me'nie're's disease: primary results of a long term, multicentre, double blind, randomised, placebo controlled, dose defining trial (BEMED trial). BMJ 2016;352:h6816.
[37] Sen P, Georgalas C, Papesch M. Co-morbidity of migraine and Me'nie're's disease—is allergy the link? J Laryngol Otol 2005;119(6):455–60.
[38] Morales-Luckie E, Cornejo-Suarez A, Zaragoza-Contreras MA, Gonzalez-Perez O. Oral administration of prednisone to control refractory vertigo in Me'nie're's disease: a pilot study. Otol Neurotol 2005;26(5):1022–6.
[39] Shirwany NA, Seidman MD, Tang W. Effect of transtympanic injection of steroids on cochlear blood flow, auditory sensitivity, and histology in the guinea pig. Am J Otol 1998;19(2):230–5.
[40] Phillips JS, Westerberg B. Intratympanic steroids for Me'nie're's disease or syndrome. Cochrane Database Syst Rev 2011;7:CD008514.
[41] Garduno-Anaya MA, Couthino De Toledo H, Hinojosa-Gonzalez R, Pane-Pianese C, Rios-Castaneda LC. Dexamethasone inner ear perfusion by intratympanic injection in unilateral Me'nie're's disease: a two-year prospective, placebo controlled, double-blind, randomized trial. Otolaryngol Head Neck Surg 2005;133(2):285–94.
[42] Lambert PR, Carey J, Mikulec AA, LeBel C. Intratympanic sustained-exposure dexamethasone thermosensitive gel for symptoms of Me'nie're's disease: randomized phase 2b safety and efficacy trial. Otol Neurotol 2016;37(10):1669–76.
[43] Casani AP, Piaggi P, Cerchiai N, Seccia V, Franceschini SS, Dallan I. Intratympanic treatment of intractable unilateral Meniere disease: gentamicin or dexamethasone? A randomized controlled trial. Otolaryngol Head Neck Surg 2012;146(3):430–7.
[44] ElBeltagy Y, Shafik A, Mahmoud A, Hazaa N. Intratympanic injection in Me'nie're's disease; symptomatic and audiovestibular; comparative, prospective randomized 1-year control study. Egypt J Otolaryngol 2012;28(3):171–83.
[45] Patel M, Agarwal K, Arshad Q, et al. Intratympanic methylprednisolone versus gentamicin in patients with unilateral Me'nie're's disease: a randomised, double-blind, comparative effectiveness trial. Lancet 2016;388(10061):2753–62.
[46] Sarafraz M, Saki N, Nikakhlagh S, Mashali L, Arad A. Comparison the efficacy of intratympanic injections of methylprednisolone and gentamicin to control vertigo in unilateral Me'nie're's disease. Biomed Pharmacol J 2015;8:705–9.
[47] Harner SG, Kasperbauer JL, Facer GW, Beatty CW. Transtymp.
[48] Chia SH, Gamst AC, Anderson JP, Harris JP. Intratympanic gentamicin therapy for Ménière's disease: a meta-analysis. Otol Neurotol 2004;25(4):544–52. https://doi.org/10.1097/00129492-200407000-00023.
[49] Lambert PR, Nguyen S, Maxwell KS, et al. A randomized, double-blind, placebo-controlled clinical study to assess safety and clinical activity of OTO-104 given as a single intratympanic injection in patients with unilateral Me'nie're's disease. Otol Neurotol 2012;33(7):1257–65.
[50] Portmann G. The saccus endolymphaticus and an operation for draining for the relief of vertigo. Proc R Soc Med 1927;20(12):1862–7.
[51] Thomsen J, Bretlau P, Tos M, Johnsen NJ. Placebo effect in surgery for Ménière's disease. A double-blind, placebo-controlled study on endolymphatic sac shunt surgery. Arch Otolaryngol 1981;107(5):271–7.
[52] Welling DB, Nagaraja HN. Endolymphatic mastoid shunt: a reevaluation of efficacy. Otolaryngol Head Neck Surg 2000;122(3):340–5.
[53] Brackmann DE, Nissen RL. Meniere's disease: results of treatment with the endolymphatic subarachnoid shunt compared with the endolymphatic mastoid shunt. Am J Otol 1987;8(4):275–82.
[54] Brinson GM, Chen DA, Arriaga MA. Endolymphatic mastoid shunt versus endolymphatic sac decompression for Meniere's disease. Otolaryngol Head Neck Surg 2007;136(3):415–21.
[55] Telischi FF, Luxford WM. Long-term efficacy of endolymphatic sac surgery for vertigo in Me'nie're's disease. Otolaryngol Head Neck Surg 1993;109(1):83–7.
[56] Pensak ML, Friedman RA. The role of endolymphatic mastoid shunt surgery in the managed care era. Am J Otol 1998;19(3):337–40.
[57] Lee L, Pensak ML. Contemporary role of endolymphatic mastoid shunt surgery in the era of transtympanic perfusion strategies. Ann Otol Rhinol Laryngol 2008;117(12):871–5. https://doi.org/10.1177/000348940811701201.
[58] Convert C, Franco-Vidal V, Bebear JP, Darrouzet V. Outcome-based assessment of endolymphatic sac decompression for Ménière's disease using the Ménière's disease outcome questionnaire: a review of 90 patients. Otol Neurotol 2006;27(5):687–96.
[59] Paparella MM, Fina M. Endolymphatic sac enhancement: reversal of pathogenesis. Otolaryngol Clin North Am 2002;35(3):621–37.
[60] Paparella MM. Revision of endolymphatic sac surgery for recurrent Meniere's disease. Otolaryngol Clin North Am 2002;35(3):607–19.
[61] Schwager K, Baier G, El-Din N, Shehata-Dieler W, Carducci F, Helms J. Revision surgery after saccotomy for Meniere's disease: does it make sense? Eur Arch Otorhinolaryngol 2002;259(5):239–42.
[62] House JW, Doherty JK, Fisher LM, Derebery MJ, Berliner KI. Meniere's disease: prevalence of contralateral ear involvement. Otol Neurotol 2006;27(3):355–61.
[63] Glasscock 3rd ME, Thedinger BA, Cueva RA, Jackson CG. An analysis of the retrolabyrinthine vs. the retrosigmoid vestibular nerve section. Otolaryngol Head Neck Surg 1991;104(1):88–95.
[64] Ortiz Armenta A. Retrolabyrinthine vestibular neurectomy. 10 years' experience. Rev Laryngol Otol Rhinol (Bord) 1992;113(5):413–7.
[65] Silverstein H, Norrell H, Rosenberg S. The resurrection of vestibular neurectomy: a 10-year experience with 115 cases. J Neurosurg 1990;72(4):533–9.
[66] Alarcon AV, Hidalgo LO, Arevalo RJ, Diaz MP. Labyrinthectomy and vestibular neurectomy for intractable vertiginous symptoms. Int Arch Otorhinolaryngol 2017;21(2):184–90.
[67] Barnard ZR, Lekovic GP, Wilkinson EP, Peng KA. Vestibular nerve section via retrolabyrinthine craniotomy. Oper Tech Otolayngol Head Neck Surg 2019;30(3):212–6.
[68] Nevoux J, Barbara M, Dornhoffer J, Gibson W, Kitahara T, Darrouzet V. International consensus (ICON) on treatment of Me'nie're's disease. Eur Ann Otorhinolaryngol Head Neck Dis 2018;135(1s):S29–s32.
[69] Dean L. Gentamicin therapy and *MT-RNR1* genotype. In: Pratt VM, McLeod HL, Rubinstein WS, et al., editors. Medical genetics summaries. Bethesda (MD): National Center for Biotechnology Information (US); 2012.
[70] Blakley BW. Update on intratympanic gentamicin for Meniere's disease. Laryngoscope 2000;110(2 Pt 1):236–40.
[71] Rosenberg SI. Vestibular surgery for Ménière's disease in the elderly: a review of techniques and indications. Ear Nose Throat J 1999;78(6):443–6.