W. Arpornchayanon, et al., **Complete Recovery Following Electroacupuncture Therapy in Refractory Unilateral Sensorineural Hearing Loss**. J Acupunct Meridian Stud, 2019. 12(3): p. 95-101. Role of electroacupuncture (EA) in refractory unilateral sensorineural hearing loss (SNHL) remains unclear but might be promising for the Meniere's disease. Two cases of unilateral SNHL who were unresponsive to conventional treatment of sudden SNHL showed complete recovery after receiving EA therapy. The first case was a 46-year-old woman who received EA in the seventh month after the acute onset of sudden right hearing loss and tinnitus. She had mild-to-moderate degree of SNHL at high frequencies in the right ear with episodic vertigo. The second case was a 55-year-old woman who received EA in the sixth year after developing sudden SNHL in the right ear. Before the EA began, her pure tone average of the affected ear was 45 dB and the phonetically balanced score was 88%. The regimen for both patients included 12 sessions of EA over four weeks at the main acupoints (Tinggong (SI 19), Ermen (TE 21), Qimai (TE 18) and Yifeng (TE 17) on the affected ear and the adjuvant acupoints (Zhongzhu (TE 3), Hegu (LI 4), Qihai (CV 6), Guanyuan (CV 4), Taixi (KI 3), and Taichong (LIV 3)). Both patients regained their normal hearing thresholds three weeks after the first EA. No adverse events were observed. Hence, EA may be a useful additional therapy in unilateral SNHL, even at the late phase when other treatments have failed because the possibility of Meniere's disease cannot be excluded.

A. Ayub, et al., **A systematic review and meta-analysis of extratympanic electrocochleography in Meniere's disease diagnosis**. Int J Audiol, 2019. 58(9): p. 533-540. Objective: Determine whether a combination of electrocochleography determined summating/action potential (SP/AP) ratio and other audiological measurements has greater sensitivity and specificity than that achieved with electrocochleography SP/AP ratio alone in diagnosing definite Meniere's Disease. Design: Systematic review and meta-analysis. Study sample: Pubmed, Cochrane Library, and Web of Science were searched using search terms "electrocochleography", "ECochG, ,"ECoG", "Meniere's Disease", and "Idiopathic Endolymphatic Hydrops". Inclusion criteria were extratympanic electrocochleography methodology, English language publication between January 2002 and December 2017, and the 1995 American Academy of Otolaryngology and Head and Neck Surgery Meniere's disease diagnostic criteria. Five articles satisfied inclusion criteria and were sufficiently detailed for aggregate quantitative analysis of SP/AP ratio (315 subjects) and combination audiological measures (113 subjects). Results: The diagnostic sensitivity and specificity of the SP/AP amplitude ratio was 47.6% and 83.8% and of combination diagnostic measures 63.5% and 89.3%, respectively. Point estimates of sensitivity ($p = 0.248$) and specificity ($p = 0.969$) and the summary Receiver Operator Characteristic Curve ($p = 0.407$) were not statistically significant. Conclusion: Statistically, combination diagnostic measures do not result in greater accuracy of definite Meniere's disease diagnosis compared to the SP/AP amplitude ratio alone. However, given the small sample size further studies are recommended to arrive at a definitive conclusion.

D. Bachinger, et al., **Immunolocalization of calcium sensing and transport proteins in the murine endolymphatic sac indicates calciostatic functions within the inner ear**. Cell Tissue Res, 2019. An exceptionally low calcium (Ca(2+)) concentration in the inner ear endolymph ([Ca(2+)]endolymph) is crucial for proper auditory and vestibular function. The endolymphatic sac (ES) is believed to critically contribute to the maintenance of this low [Ca(2+)]endolymph. Here, we investigated the immunohistochemical localization of proteins that are presumably involved in the sensing and transport of extracellular Ca(2+) in the murine ES epithelium. Light microscopic and fluorescence immunolabeling in paraffin-embedded murine ES tissue sections (male C57BL/6 mice, 6-8 weeks old) demonstrated the presence of the calcium-sensing receptor CaSR, transient receptor potential cation channel

subtypes TRPV5 and TRPV6, sarco/endoplasmic reticulum Ca(2+)-ATPases SERCA1 and SERCA2, Na(+)/Ca(2+) exchanger NCX2, and plasma membrane Ca(2+) ATPases PMCA1 and PMCA4 in ES epithelial cells. These proteins exhibited (i) membranous (apical or basolateral) or cytoplasmic localization patterns, (ii) a proximal-to-distal labeling gradient within the ES, and (iii) different distribution patterns among ES epithelial cell types (mitochondria-rich cells (MRCs) and ribosome-rich cells (RRCs)). Notably, in the inner ear membranous labyrinth, CaSR was exclusively localized in MRCs, suggesting a unique role of the ES epithelium in CaSR-mediated sensing and control of [Ca(2+)]endolymph. Structural loss of the distal ES, which is consistently observed in Meniere's disease, may therefore critically disturb [Ca(2+)]endolymph and contribute to the pathogenesis of Meniere's disease.

D. Bachinger, et al., **Vestibular Aqueduct Morphology Correlates With Endolymphatic Sac Pathologies in Meniere's Disease-A Correlative Histology and Computed Tomography Study**. Otol Neurotol, 2019. 40(5): p. e548-e555. HYPOTHESIS: The vestibular aqueduct (VA) in Meniere's disease (MD) exhibits different angular trajectories depending on the presenting endolymphatic sac (ES) pathology, i.e., 1) ES hypoplasia or 2) ES degeneration. BACKGROUND: Hypoplasia or degeneration of the ES was consistently found in inner ears affected by MD. The two etiologically distinct ES pathologies presumably represent two disease "endotypes," which may be associated with different clinical traits ("phenotypes") of MD. Recognizing these endotypes in the clinical setting requires a diagnostic tool. METHODS: 1) Defining the angular trajectory of the VA (ATVA) in the axial plane. 2) Measuring age-dependent normative data for the ATVA in postmortem temporal bone histology material from normal adults and fetuses. 3) Validating ATVA measurements from normative CT imaging data. 4) Correlating the ATVA with different ES pathologies in histological materials and CT imaging data from MD patients. RESULTS: 1) The ATVA differed significantly between normal adults and MD cases with ES degeneration, as well as between fetuses and MD cases with ES hypoplasia; 2) a strong correlation between ATVA measurements in histological sections and CT imaging data was found; 3) a correlation between the ATVA, in particular its axial trajectory in the opercular region (angle alphaexit), with degenerative (alphaexit < 120 degrees) and hypoplastic ES pathology (alphaexit > 140 degrees) was demonstrated. CONCLUSION: We established the ATVA as a radiographic surrogate marker for ES pathologies. CT-imaging-based determination of the ATVA enables endotyping of MD patients according to ES pathology. Future studies will apply this method to investigate whether ES endotypes distinguish clinically meaningful subgroups of MD patients.

B. Buki, et al., **The Price of Immune Responses and the Role of Vitamin D in the Inner Ear**. Otol Neurotol, 2019. 40(6): p. 701-709. OBJECTIVE: In this review the authors discuss evidence from the literature concerning vitamin D and temporal bone diseases (benign paroxysmal positional vertigo [BPPV], Meniere's disease [MD], vestibular neuritis, idiopathic facial paralysis, idiopathic acute hearing loss). Common features shared by Meniere's disease, glaucoma, and the possible influence by vitamin D are briefly discussed. DATA SOURCES, STUDY SELECTION: Publications from 1970 until recent times have been reviewed according to a keyword search (see above) in PubMed. CONCLUSIONS: MD, BPPV, vestibular neuritis, idiopathic facial paralysis, idiopathic acute hearing loss may all have several etiological factors, but a common feature of the current theories is that an initial viral infection and a subsequent autoimmune/autoinflammatory reaction might be involved. Additionally, in some of these entities varying degrees of demyelination have been documented. Given the immunomodulatory effect of vitamin D, we postulate that it may play a role in suppressing an eventual postviral autoimmune reaction. This beneficial effect may be enhanced by the antioxidative activity of vitamin D and its potential in stabilizing

endothelial cells. The association of vitamin D deficiency with demyelination has already been established in other entities such as multiple sclerosis and experimental autoimmune encephalitis. Mice without vitamin D receptor show degenerative features in inner ear ganglia, hair cells, as well as otoconia. The authors suggest further studies concerning the role of vitamin D deficiency in diseases of the temporal bone. Additionally, the possible presence and degree of demyelination in these entities will have to be elucidated more systematically in the future.

A. Cakir Cetin, et al., **Wide-Band Tympanometry Results during an Acute Episode of Meniere's Disease**. Audiol Neurootol, 2019: p. 1-6. BACKGROUND: Wide-band tympanometry (WBT) was introduced as a beneficial diagnostic test for Meniere's disease (MD) almost 15 years ago. However, an acute episode of MD has not been evaluated by using WBT yet. OBJECTIVE: To investigate WBT findings in patients with MD during acute attacks. METHOD: Thirty definite MD patients with unilateral acute low-tone sensorineural hearing loss and aural fullness, and thirty age- and sex-matched control subjects were enrolled prospectively in a tertiary referral center. Ears were divided into three groups as follows: (1) affected ears of MD patients, (2) contralateral ears of MD patients, (3) control ears. Individuals underwent WBT. The resonance frequency (RF), mean absorbance value, mean low- and high-frequency absorbance values (LF-A and HF-A), and double peak width at 2 kHz of conductance tympanometry (2-kHz PW) were assessed. RESULTS: Seventy percent in group 1, 66.7% in group 2, and 78.3% in group 3 demonstrated double peaks at 2 kHz. The mean 2-kHz PW values were 157.52 +/- 79.19, 177.40 +/- 79.14, and 139.64 +/- 87.501 daPa for groups 1, 2, and 3, respectively. There were no significant differences between groups with respect to 2-kHz PW, RF, absorbance, LF-A, and HF-A. CONCLUSION: This was the first study that evaluated the effects of acute Meniere attacks on WBT findings. An acute Meniere attack was found to have no significant effect on the 2-kHz PW and other variables measured using WBT.

Z. Cao, et al., **Different medications for the treatment of Meniere's disease by intratympanic injection: A systematic review and network meta-analysis**. Clin Otolaryngol, 2019. 44(4): p. 619-627. BACKGROUND: It is generally accepted that intratympanic injection provides an effective approach to manage severe vertigo in Meniere's disease. Although there are several medications available, that which is the most effective is still subject to debate. OBJECTIVE: To assess the effectiveness and safety of the different medications used in the treatment of Meniere's disease by intratympanic injection using a network meta-analysis. METHODS: PubMed, EMBASE, CINAHL and CENTRAL were searched. Only randomised controlled trials that compared the effectiveness of medications used for intratympanic injection to treat Meniere's disease with each other or a placebo were included. The primary outcome assessed was the effectiveness of medication in the management of vertigo symptoms. The effectiveness was expressed in terms of risk ratio (RR) with a 95% credible interval (CrI) for individual studies analysed. Network meta-analyses were performed by Stata version 15.0 using the network package. RESULTS: Nine studies involving 314 patients treated with five different medications were included in the present analysis. A number of injections given varied from 1 to 10 and the follow-up time from 3 to 28 months. When compared to each other or to a placebo, Gentamicin was found to be the most efficacious medication, followed by Methylprednisolone, Latanoprost, Dexamethasone and Ganciclovir in order of effectiveness. However, no significant difference in efficacy was found between Gentamicin and Methylprednisolone when outcomes from studies with a follow-up time equal to or more than 24 months were analysed. It was not possible to conduct subgroup and sensitivity analysis because of the limited number of studies that were included. CONCLUSION: All medications are more effective than a placebo

in the treatment of Meniere's disease by intratympanic injection. According to the SUCRA, Gentamicin ranked the most effective, with Gentamicin and Methylprednisolone equally effective in the long-term effect. When the potential risk of hearing loss induced by Gentamicin is taken into consideration, Methylprednisolone may be the best choice for the treatment of Meniere's disease by intratympanic injection.

G. M. Cioffi, et al., **A Case of Binocular Vertical Diplopia after Intratympanic Gentamicin Therapy**. Eur J Case Rep Intern Med, 2019. 6(8): p. 001187. Intratympanic gentamicin therapy is a useful alternative treatment for refractory Meniere's disease and is generally well tolerated. Visual disturbances as side effects of this treatment are rarely reported in the literature. In this report we describe the case of a 52-year-old woman with refractory Meniere's disease who developed binocular vertical diplopia following intratympanic gentamicin therapy. Spontaneous resolution of diplopia occurred within 2 weeks. The development of diplopia should be discussed as a potential complication with patients undergoing intratympanic gentamicin therapy. LEARNING POINTS: Meniere's disease is an inner ear disorder which can cause vertigo and hearing loss.As medical treatment sometimes fails, other therapeutic options should be considered.Gentamycin chemical labyrinthectomy can be administered as an alternative treatment, but the development of diplopia should be discussed as a potential side effect.

G. Conte, et al., **Audiovestibular Phenotypes and Advanced Magnetic Resonance Imaging Features of Cochlin Gene Mutation Carriers**. Audiol Neurootol, 2019. 24(4): p. 166-173. OBJECTIVE: To describe clinical and imaging findings in a group of patients affected by nonsyndromic deafness A9 (DFNA9), using advanced magnetic resonance imaging (MRI) with 3-dimensional (3D) fluid-attenuated inversion recovery (FLAIR) sequence. METHOD: A retrospective case review was conducted in a tertiary referral center in Italy. Four sequential adult DFNA9-affected patients, who had undergone MRI at our Department between January 2017 and June 2018, were enrolled (male = 2, female = 2; median age: 65.6 years; 8 diseased ears analyzed). Three patients were relatives; the fourth was unrelated. The main outcome measures - age, sex, records of audiological and vestibular testing, genetic assessment, MRI findings - were analyzed. RESULTS: All subjects suffered from bilateral progressive sensorineural hearing loss, more severely at the high frequencies and with a typical clinical pattern of bilateral chronic degenerative cochleovestibular deficit. Aural fullness was reported at the onset of the disease. All patients revealed a pathogenic heterozygous mutation in the Limulus factor C, Coch-5b2 and Lgl1 domain of cochlin. None of the patients showed a significant vestibular and cochlear endolymphatic hydrops at MRI, while high bilateral contrast enhancement on 4-h delayed postcontrast 3D FLAIR sequence was observed in all ears. CONCLUSIONS: Increased perilymph enhancement on 4-h delayed postcontrast 3D FLAIR sequence is the common imaging feature of DFNA9 ears, suggesting that blood-labyrinthine barrier breakdown may play the main role in the pathophysiology of this disease. Significant hydrops has been excluded by MRI. This finding might be clinically useful in differentiating DFNA9 disease from other pathologies with similar clinical findings like Meniere's disease.

I. S. Curthoys, et al., **A review of mechanical and synaptic processes in otolith transduction of sound and vibration for clinical VEMP testing**. J Neurophysiol, 2019. 122(1): p. 259-276. Older studies of mammalian otolith physiology have focused mainly on sustained responses to low-frequency (<50 Hz) or maintained linear acceleration. So the otoliths have been regarded as accelerometers. Thus evidence of otolithic activation and high-precision phase locking to high-frequency sound and vibration appears to be very unusual. However, those results are exactly in accord with a substantial body of knowledge of otolith function in fish

and frogs. It is likely that phase locking of otolith afferents to vibration is a general property of all vertebrates. This review examines the literature about the activation and phase locking of single otolithic neurons to air-conducted sound and bone-conducted vibration, in particular the high precision of phase locking shown by mammalian irregular afferents that synapse on striolar type I hair cells by calyx endings. Potassium in the synaptic cleft between the type I hair cell receptor and the calyx afferent ending may be responsible for the tight phase locking of these afferents even at very high discharge rates. Since frogs and fish do not possess full calyx endings, it is unlikely that they show phase locking with such high precision and to such high frequencies as has been found in mammals. The high-frequency responses have been modeled as the otoliths operating in a seismometer mode rather than an accelerometer mode. These high-frequency otolithic responses constitute the neural basis for clinical vestibular-evoked myogenic potential tests of otolith function.

E. Degerman, et al., **Endolymphatic hydrops induced by different mechanisms responds differentially to spironolactone: a rationale for understanding the diversity of treatment responses in hydropic inner ear disease***.* Acta Otolaryngol, 2019. 139(8): p. 685-691. Background: The exact pathophysiological mechanism(s) underlying endolymphatic hydrops (EH) remain elusive. We have previously shown that chronic administration of vasopressin and inhibitors of the cAMP/cGMP degrading enzymes (PDE3, PDE4, PDE5) results in the development of EH to mice. Aims/objectives: Evaluate the ability of spironolactone, an aldosterone antagonist, to prevent EH, when induced by different pathways. Material and methods: Mice were treated for 4 weeks with vasopressin, the PDE3 inhibitor cilostamide and the PDE4 inhibitor rolipram in the presence or absence of spironolactone. EH was assessed using high resolution 9.4T MRI. The expression of proteins in human saccule sensory epithelium was studied with immunohistochemistry. Results: Spironolactone prevents EH induced by vasopressin and rolipram, but not hydrops induced by cilostamide. The aldosterone target ENaC and the mineralocorticoid receptor were expressed in the human saccule sensory epithelium. Conclusions: The effect of spironolactone on EH appears to be pathway-dependent and may provide explanations why certain drugs may be effective in some patients with hydropic ear disease while not in others. Significance: Extrapolating this finding to the clinic supports that a personalized medicine approach is probably necessary in the treatment of diseases involving EH, as different pathways may be needed to be targeted for treatment.

L. Devantier, et al., **Intratympanic Steroid for Meniere's Disease: A Systematic Review***.* Otol Neurotol, 2019. 40(6): p. 806-812. OBJECTIVES: To investigate the beneficial effects and safety of intratympanic steroid installation compared with placebo in patients with Meniere's disease. METHODS: We performed a systematic literature search in MEDLINE and EMBASE for existing systematic reviews and individual randomized controlled trials (RCTs). Studies were included if they investigated the usage intratympanic steroids in patients aged 18 and above, with definite or probable Meniere's disease. The quality of the identified existing reviews was assessed using the AMSTAR tool. The risk of bias in RCTs was assessed using the Cochrane Risk of Bias Tool and overall quality of the individual outcomes was evaluated using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) method. RESULTS: The literature search provided four systematic reviews, from which one yielded a sufficient AMSTAR evaluation and subsequently provided three RCTs relevant for inclusion. Due to the lack of sufficient reporting of the data, quantitative synthesis was not applicable. In the qualitative synthesis for the primary outcome, the results from the RCTs showed that there was a slight indication of steroid treatment reducing the frequency of vertiginous attacks. No serious adverse events were reported. Based on the GRADE approach the quality for both findings is very low. No studies

reported on the secondary outcomes. CONCLUSION: The effect of intratympanic steroid treatment in Meniere's disease is questionable. There is a great need for further research to sufficiently assess whether steroid treatment may be considered as a safe and effective treatment for patients with Meniere's disease.

L. Devantier, et al., **Positive pressure device treatment for Meniere's disease: an overview of the current evidence and a meta-analysis**. Eur Arch Otorhinolaryngol, 2019. 276(5): p. 1263-1273. OBJECTIVE: The objective was to critically assess the current evidence investigating the efficacy of using a positive pressure device in patients with definite or probable Meniere's disease. METHODS: We performed a systematic literature search in MEDLINE, EMBASE and PsycINFO up to February 2018. We included both systematic reviews and primary literature [randomized controlled trials (RCTs)] investigating positive pressure treatment, in patients (>/= 18 years of age), with Meniere's disease. We assessed the internal validity of systematic reviews using the AMSTAR tool and risk of bias of primary studies using the Cochrane Risk of bias tool. We performed a meta-analysis for each outcome based on the identified studies. The overall certainty of evidence for the outcomes was assessed using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE). RESULTS: The search for systematic reviews identified four relevant reviews. These all included the same four RCTs. An updated search identified one additional RCT. In total, five RCTs were included in the data synthesis. Our data synthesis showed no effect of positive pressure treatment on primary nor secondary outcomes. No serious adverse events were reported. The overall certainty of evidence ranged from very low to low, due to the serious risk of bias and imprecision. CONCLUSION: The current available evidence does not support positive pressure device treatment in patients with Meniere's disease. However, the limitations of the current literature hinder the possibility of any solid conclusion. There remains a need for randomized controlled trials of high quality to fully access the utility of this treatment.

L. Devantier, et al., **Current state of evidence for endolymphatic sac surgery in Meniere's disease: a systematic review**. Acta Otolaryngol, 2019. 139(11): p. 953-958. Background: Endolymphatic sac surgery is an invasive procedure recommended to patients with Meniere's disease. Aims/Objectives: To provide an overview and quality assessment of the existing evidence and to provide an updated assessment of the utility of endolymphatic sac surgery in Meniere's disease. Material and Methods: We performed a systematic literature search for systematic reviews and randomized controlled trials (RCTs). The AMSTAR tool was used to assess the quality of systematic reviews and the Cochrane risk of bias tool for RCTs. The overall certainty of effects for the individual outcomes was evaluated using the GRADE approach. Results: One systematic review of high quality matched the inclusion criteria, and included three RCTs. An updated literature search from the last search date of the included review provided no further relevant RCTs. The identified RCTs individually reported a positive effect of both the placebo and active treatment groups following surgery, strongly indicative of a placebo effect. The overall certainty of the effect was very low. Conclusions and significance: There is still a lack of high-quality research suggesting that endolymphatic sac surgery provides a significant amount of symptomatic relief for Meniere's patients.

S. H. Dong, et al., **Expression of aquaporins in inner ear disease**. Laryngoscope, 2019. The inner ear is responsible for hearing and balance and consists of a membranous labyrinth within a bony labyrinth. The balance structure is divided into the otolith organ that recognizes linear acceleration and the semicircular canal that is responsible for rotational movement. The cochlea is the hearing organ. The external and middle ear are covered with skin and mucosa, respectively, and the space is filled with air, whereas the inner ear is

composed of endolymph and perilymph. The inner ear is a fluid-filled sensory organ composed of hair cells with cilia on the upper part of the cells that convert changes in sound energy and balance into electric energy through the hair cells to transmit signals to the auditory nerve through synapses. Aquaporins (AQPs) are a family of transmembrane proteins present in all species that can be roughly divided into three subfamilies according to structure and function: 1) classical AQP, 2) aquaglyceroporin, and 3) superaquaporin. Currently, the subfamily of mammalian species is known to include 13 AQP members (AQP0-AQP12). AQPs have a variety of functions depending on their structure and are related to inner ear diseases such as Meniere's disease, sensorineural hearing loss, and presbycusis. Additional studies on the relationship between the inner ear and AQPs may be helpful in the diagnosis and treatment of inner ear disease. Laryngoscope, 2019.

M. Flook, et al., **Differential Proinflammatory Signature in Vestibular Migraine and Meniere Disease**. Front Immunol, 2019. 10: p. 1229. Vestibular Migraine (VM) and Meniere's Disease (MD) are episodic vestibular syndromes defined by a set of associated symptoms such as tinnitus, hearing loss or migraine features during the attacks. Both conditions may show symptom overlap and there is no biological marker to distinguish them. Two subgroups of MD patients have been reported, according to their IL-1beta profile. Therefore, considering the clinical similarity between VM and MD, we aimed to investigate the cytokine profile of MD and VM as a means to distinguish these patients. We have also carried out gene expression microarrays and measured the levels of 14 cytokines and 11 chemokines in 129 MD patients, 82 VM patients, and 66 healthy controls. Gene expression profile in peripheral blood mononuclear cells (PBMC) showed significant differences in MD patients with high and low basal levels of IL- 1beta and VM patients. MD patients with high basal levels of IL- 1beta (MDH) had overall higher levels of cytokines/chemokines when compared to the other subsets. CCL4 levels were significantly different between MDH, MD with low basal levels of IL- 1beta (MDL), VM and controls. Logistic regression identified IL- 1beta, CCL3, CCL22, and CXCL1 levels as capable of differentiating VM patients from MD patients (area under the curve = 0.995), suggesting a high diagnostic value in patients with symptoms overlap.

M. Fukushima, et al., **Vertical head impulse and caloric are complementary but react opposite to Meniere's disease hydrops**. Laryngoscope, 2019. 129(7): p. 1660-1666. OBJECTIVES/HYPOTHESIS: Meniere's disease (MD) patients can show normal head impulses despite poor caloric test results. This study aimed to investigate the discrepancy in the vestibulo-ocular reflex (VOR) in MD patients and whether endolymphatic hydrops (EH) influence the VOR. STUDY DESIGN: Prospective, cross-sectional observational study. METHODS: Ninety MD patients were enrolled. Neuro-otological testing, including a video head impulse test (vHIT) of all semicircular canals (SCs), and gadolinium-enhanced inner ear magnetic resonance imaging were performed. The vestibular EH volume was quantitatively evaluated by processing magnetic resonance images. RESULTS: Abnormal vHIT results in MD patients were found most frequently in the posterior (44.4%) SCs, followed by the horizontal (13.3%) and anterior (10%) SCs. Canal paresis (CP) was assessed using the vHIT and the caloric test, and results were not significant when vHIT responses were assessed as CP only using the horizontal SC. The difference in the vestibular EH between the presence and absence of CP was not significant if assessed using the vHIT (P = .5591), but it was statistically different if assessed using the caloric test (P = .0467). CONCLUSIONS: The contradictory reaction of VOR in MD patients may result from the high specificity but low sensitivity of CP in the horizontal vHIT. EH volume in the vestibule affects the caloric response but does not affect the vHIT response. LEVEL OF EVIDENCE: 2b Laryngoscope, 129:1660-1666, 2019.

A. Gallego-Martinez, et al., **Enrichment of damaging missense variants in genes related with axonal guidance signalling in sporadic Meniere's disease**. J Med Genet, 2019. INTRODUCTION: Meniere's disease (MD) is a rare inner ear disorder with a significant genetic contribution defined by a core phenotype: episodic vertigo, sensorineural hearing loss and tinnitus. It has been mostly described in sporadic cases, familial cases being around 10% of the observed individuals. It is associated with an accumulation of endolymph in the inner ear, but the molecular underpinnings remain largely unknown. The main molecular pathways showing higher differentially expressed genes in the supporting cells of the inner ear are related to cochlea-vestibular innervation, cell adhesion and leucocyte extravasation. In this study, our objective is to find a burden of rare variants in genes that interact with the main signalling pathways in supporting cells of the inner ear in patients with sporadic MD. METHODS: We designed a targeted-sequencing panel including genes related with the main molecular pathways in supporting cells and sequenced 860 Spanish patients with sporadic MD. Variants with minor allele frequencies <0.1 in the gene panel were compared with three independent reference datasets. Variants were classified as loss of function, missense and synonymous. Missense variants with a combined annotation-dependent depletion score of >20 were classified as damaging missense variants. RESULTS: We have observed a significant burden of damaging missense variants in few key genes, including the NTN4 gene, associated with axon guidance signalling pathways in patients with sporadic MD. We have also identified active subnetworks having an enrichment of rare variants in sporadic MD. CONCLUSION: The burden of missense variants in the NTN4 gene suggests that axonal guidance signalling could be a novel pathway involved in sporadic MD.

I. P. Hannigan, et al., **Dissociation of caloric and head impulse tests: a marker of Meniere's disease**. J Neurol, 2019. A retrospective analysis of the horizontal video head impulse test (vHIT) results and caloric testing results was undertaken on 644 patients who attended a neuro-otology outpatient facility. Presenting symptoms included spontaneous vertigo, positional vertigo, imbalance or chronic subjective dizziness. For 570 patients, the results of vHIT and caloric testing were concordant. Both tests were normal in 500 subjects with an average vHIT gain = 0.92 +/- 0.09 (L); 0.98 +/- 0.10 (R) and canal paresis (CP) = 7.88 +/- 6.12; (range 0-28%). 54 had concordant asymmetries, average ipsilesional vHIT gain = 0.56 +/- 0.15, average contralesional vHIT gain = 0.88 +/- 0.12. CP = 68.02 +/- 24.38 (range 31-100%). 16 subjects had bilateral vestibular hypofunction with average vHIT gains of 0.42 +/- 0.20 (L); 0.41 +/- 0.19 (R), peak slow phase velocity (SPV) on warm caloric testing = 2.68 +/- 2.08, range 0-6 degrees /s (L) and 3.75 +/- 3.43 range, 0-10 degrees /s (R). 36 patients showed a dissociation of results between the two tests. In these subjects, the vHIT gain was normal (0.93 +/- 0.06 left and 0.98 +/- 0.07 right) and the caloric test showed a CP > 30% (48 +/- 13.8%). Their final diagnoses included clinically definite Meniere's disease (MD) (n = 27), vestibular schwannoma (VS) (n = 2) vestibular migraine (VM) (n = 1), vestibular neuritis (VN) (n = 5) and unknown (n = 1). No patient with abnormal HSCC gain on vHIT had a normal caloric result. The caloric test complements the vHIT in the assessment of vestibular disorders and is most useful in suspected endolymphatic hydrops. Asymmetric caloric function in the presence of normal horizontal head impulse tests is most commonly associated with Meniere's disease and may function as a diagnostic marker.

K. Higashi-Shingai, et al., **Change in endolymphatic hydrops 2 years after endolymphatic sac surgery evaluated by MRI**. Auris Nasus Larynx, 2019. 46(3): p. 335-345. OBJECTIVE: This study was performed to determine whether endolymphatic sac surgery improves vestibular and cochlear endolymphatic hydrops 2 years after sac surgery and to elucidate the relationship between the degree of improvement of endolymphatic hydrops and the changes in vertigo symptoms, the hearing level, and the summating potential/action

potential ratio (-SP/AP ratio) by electrocochleography (ECochG) in patients with Meniere's disease (MD). METHODS: Twenty-one patients with unilateral MD who underwent sac surgery were included in this study. All patients underwent gadolinium-enhanced magnetic resonance imaging (Gd-MRI) before and 2 years after sac surgery. We evaluated the difference in vestibular and cochlear endolymphatic hydrops between before and after surgery in both ears and compared these findings with the frequency of vertigo attacks, hearing level, and ECochG findings. RESULTS: In affected ears, the presence of vestibular endolymphatic hydrops and the frequency of vertigo attacks significantly decreased after surgery. However, affected ears showed no significant improvement in the presence of cochlear endolymphatic hydrops or the -SP/AP ratio by ECochG; there was also no significant improvement or deterioration in the hearing level. CONCLUSION: The present findings suggest that sac surgery reduces vestibular endolymphatic hydrops and prevents aggravation of cochlear endolymphatic hydrops, and these changes lead to a reduction of vertigo attacks and suppress the progression of hearing impairment associated with vertigo attacks.

J. Hornibrook, et al., **Tone burst electrocochleography disproves a diagnosis of Meniere's disease treated aggressively**. Hno, 2019. Reliable confirmation of the presence or absence of endolymphatic hydrops is essential to avoid confusing vestibular migraine with Meniere's disease. MRI inner ear imaging is a promising new method to confirm hydrops, avoiding both unnecessary invasive or destructive inner ear treatments, but it is not universally available. Tone burst electrocochleography is an older simple, quick, safe, and sensitive test that is potentially available, with existing (or minorly upgraded) equipment at most tertiary medical centers. In Meniere's disease hydrops remains after intratympanic treatments. A case is presented of a 45 year-old man with a long history of recurrent vertigo attacks who, due to an erroneous diagnosis of Meniere's disease, was given five intratympanic treatments with no effect. He was subsequently found by tone burst electrocochleography to have no hydrops and was differentially diagnosed with probable vestibular migraine. Response to treatment confirms this diagnosis. This patient's electrocochleographic findings are compared with two other patients with definite Meniere's disease, one of whom had demonstrable hydrops despite intratympanic gentamycin treatments.

J. Hu, et al., **Recovery of ocular and cervical vestibular evoked myogenic potentials after treatment of inner ear diseases**. Int J Neurosci, 2019. 129(10): p. 1004-1012. Purpose: This study aimed to assess the clinical value of ocular vestibular evoked myogenic potential (oVEMP) and cervical vestibular evoked myogenic potential (cVEMP) for monitoring the rehabilitation of vestibular function in patients treated for peripheral vertigo. Materials and methods: Fifteen patients who had been diagnosed with peripheral vertigo and showed no VEMP response on the affected side but exhibited symptom alleviation and VEMP responses after therapies were retrospectively enrolled. We analyzed the restoration and parameters of their VEMP response. Results: After treatment, six patients with sudden sensorineural hearing loss showed VEMP recovery, including two with both oVEMP and cVEMP recovery, three with oVEMP recovery only, and one with cVEMP recovery only. Two patients with Meniere's disease (MD) showed cVEMP recovery, while the other three MD patients showed oVEMP recovery. Three patients with herpes zoster oticus exhibited cVEMP recovery. One patient with vestibular neuritis exhibited cVEMP recovery. Among the patients with cVEMP and/or oVEMP restoration, most patients presented normal VEMP parameters; however, some patients showed abnormal VEMP parameters after treatment. Conclusion: Combined oVEMP and cVEMP are objective tools for assessing vestibular otolithic end organ function during dynamic functional recovery from vestibular diseases.

R. Hulse, et al., **[Prevalence of peripheral vestibular diseases in children in Germany]**. Hno, 2019. INTRODUCTION: Dizziness is a common complaint among patients; however, a lack of valid data concerning age and gender distribution of dizziness disorders among children under the age of 15 years can preclude effective diagnosis and treatment. The goal of this study was to describe the prevalence and gender distribution of three classical peripheral vestibular disorders; benign paroxysmal positional vertigo (BPPV), vestibular neuritis (VN), and Meniere's disease (MD) as well as unspecific dizziness (UV) in children between 0 and 15 years of age, using state sponsored health insurance data. METHODS: A population-based epidemiological survey based on confirmed International Classification of Diseases (ICD) 10 codes of all persons aged 0-15 years in a national population was performed. Outcome measures were age and gender distribution and prevalence of BPPV, VN, and MD in this population. RESULTS: Dizziness diagnosed as being of peripheral vestibular origin was found in 1414 patients. The prevalence of peripheral vestibular disorders was found to be 15.16 per 100,000 individuals. The BPPV was coded most frequently with a prevalence of 10.21 per 100,000 individuals, followed by VN with a prevalence of 3.5 per 100,000 and MD at 1.54 per 100,000. CONCLUSION: Peripheral vestibular disorders can occur in childhood and the prevalence increases with age. In childhood, girls and boys are similarly affected. Peripheral vestibular disorders should be taken into consideration when a young child presents with vertigo or dizziness and are even more important when a child presents with unclear symptoms, as very young children might not be able to adequately verbalize dizziness and vertigo. For that reason peripheral vestibular disorders in childhood are probably underdiagnosed.

D. Huppert, et al., **Risk of traffic accidents after onset of vestibular disease assessed with a surrogate marker**. J Neurol, 2019. 266(Suppl 1): p. 3-8. OBJECTIVES: To determine if the risk of traffic accidents increases after disease onset in patients with acute vestibular disorders. That could provide a valid rationale for guidelines on driving restrictions. METHODS: 5,260,054 patient data (> 18 years of age) from a statutory health insurer were used to identify traffic injuries in incident cases of Meniere's disease (MD) and vestibular neuritis (VN) in 2010-2013. Incident diagnoses were defined as the absence of such diagnoses in the preceding 5 years. Comparators were insured individuals with no such diagnoses throughout 2005-2017. The surrogate for traffic injuries were whiplash injuries coded in ICD-10 as diagnosis of sprain of ligaments of the cervical spine without structural changes. RESULTS: We identified 4509 incident patients with Meniere's disease and 25,448 with vestibular neuritis and 5,102,655 controls with no such diagnoses throughout the observation period. The incidence of traffic injuries was increased for both vestibular disorders prior to the time point of diagnosis-MD 0.72 [0.47; 0.97] and VN 0.66 [0.56; 0.76] compared to controls (0.46 [0.46; 0.47]). The temporal course of incidence in whiplash injuries showed no increase and was 0.64 [0.41; 0.88] for MD at diagnosis and 0.73 [0.48; 0.98] after diagnosis, for VN it was 0.81 [0.70; 0.92] at diagnosis and 0.65 [0.55; 0.74] after diagnosis. CONCLUSIONS: Although these data were not originally collected to address the research question, they provide a valid body of evidence. There is no rationale for driving restrictions, which substantially interfere with the individuals' quality of life, in patients with incident MD and VN.

H. Inui, et al., **Magnetic resonance imaging of the endolymphatic space in patients with acute low-tone sensorineural hearing loss**. Auris Nasus Larynx, 2019. 46(6): p. 859-865. OBJECTIVE: The aim of this study was to measure the volume of the endolymphatic space (ELS) and to investigate prognosis in patients with acute low-tone sensorineural hearing loss (ALHL). METHODS: A total of 61 ALHL patients participated; 47 were definite while 14 were probable ALHL cases. The definite ALHL patients were classified into three groups: A, "Cure"; B, "No cure"; and C, "Recurrence." Also, nine patients for whom diagnosis changed from

ALHL to cochlear Meniere's disease (cMD) without vertigo (ALHL-cMD group). Images of the inner ear fluid space, positive perilymph, and positive endolymph were acquired using a 3T magnetic resonance scanner. Three-dimensional (3D) images were semi-automatically reconstructed using anatomical and tissue information to fuse the 3D images of the inner ear fluid space with the 3D ELS images. RESULTS: Patients in the no cure group showed a significantly higher ELS/total fluid space (TFS) volume ratio in the affected cochlear region than the patients of the other groups. Additionally, the affected vestibular ELS/TFS volume ratio in the cure group was significantly lower than that in the recurrence group. There were significantly higher cochlear and vestibular ELS/TFS ratios in ALHL-cMD patients than in control subjects. CONCLUSIONS: These results indicate that the cochlear ELS/TFS volume ratio should be considered when investigating the extent of recovery, while the extended ELS in the vestibule should be considered when investigating cases of recurrence. Thus, our study suggests that the severe extended ELS appeared likely to change to cMD and that the prognostic determination of ALHL is possible.

H. Inui, et al., **Magnetic resonance-based volumetric measurement of the endolymphatic space in patients with Meniere's disease and other endolymphatic hydrops-related diseases**. Auris Nasus Larynx, 2019. 46(4): p. 493-497. OBJECTIVE: To employ magnetic resonance imaging (MRI) to measure the volume of the inner ear endolymphatic space (ELS) in patients with acute low-tone sensorineural hearing loss (ALHL), sudden deafness (SD), cochlear Meniere's disease (cMD), and unilateral MD (uMD) compared with control subjects (CS) with chronic rhinosinusitis. METHODS: Forty-one patients with ALHL, 82 with SD, 48 with cMD, 72 with uMD, and 47 CS participated in the study. With the exception of all uMD patients, none of the subjects had vertigo. Images of the inner ear fluid space, positive perilymph signal, and positive endolymph signal were acquired using a 3-T MRI scanner. Three-dimensional images were reconstructed semi-automatically by using anatomical and tissue information to fuse the inner ear fluid space images and the ELS images. RESULTS: The cochlear ELS/total fluid space (TFS) volume ratio was 10.2+/-6.7% (mean+/-standard deviation) in the CS group, 12.1+/-5.7% in ALHL patients, 15.2+/-8.7% in SD patients, 18.1+/-8.2% in cMD patients, and 21.9+/-16.4% in uMD patients. The vestibular ELS/TFS volume ratio was 17.7+/-10.2% in the CS group, 18.9+/-8.3% in ALHL patients, 19.9+/-11.3% in SD patients, 22.5+/-13.7% in cMD patients, and 35.7+/-24.1% in uMD patients. The cochlear ELS/TFS volume ratio in patients with uMD was similar to that in the cMD group and significantly higher than that in the CS, ALHL, and SD groups (CS=ALHL<SD<cMD=uMD: $p<0.05$ for CS vs. SD and $p<0.01$ for CS vs. cMD). The vestibular ELS/TFS volume ratio in patients with uMD was significantly higher than that in the CS and all other patient groups (CS=ALHL=SD=cMD<uMD: $p<0.01$ for uMD vs. all other groups). CONCLUSION: The cochlear ELS volume of patients with MD and other endolymphatic hydrops-related diseases differed from that of CS. Our results suggest that ALHL may not be caused by endolymphatic hydrops. We confirmed the presence of extended ELS in patients with SD.

T. Ito, et al., **Relationship between changes in hearing function and volumes of endolymphatic hydrops after endolymphatic sac drainage**. Acta Otolaryngol, 2019. 139(9): p. 739-746. Background: Endolymphatic sac drainage (ELSD) may have a positive effect on endolymphatic hydrops (EH) and may help to preserve inner ear function. However, the relationship between changes in EH volumes and hearing function after ELSD has not been described. Objectives: We aimed to reveal the factors related to changes in hearing and EH following ELSD. Material and Methods: Twenty-one patients who received ELSD were enrolled. Pure tone audiometry and 3-T magnetic resonance imaging (MRI) 4 h after intravenous injection of gadolinium enhancement were performed just before surgery and 2 years later. To characterize the endolymphatic space (ELS), we measured the volume of the

total fluid (TFS) and ELS and calculated the ratio of ELS to TFS (ELS ratio). Results: The ELS ratio of the patients who showed hearing improvement was 18.5 +/- 11.4% before surgery and 23.9 +/- 14.3% after. For those with no change, it was 29.7 +/- 10.8% before and 29.4 +/- 9.5% after, and in patients with worsened hearing function it was 22.7 +/- 7.5% before and 27.2 +/- 13.4% after. Conclusion: We found no correlation between the changes in hearing function and the volume of EH after ELSD.

G. P. Jacobson, et al., **Development and Preliminary Findings of the Dizziness Symptom Profile**. Ear Hear, 2019. 40(3): p. 568-576. OBJECTIVES: Dizziness, vertigo, and unsteadiness are common complaints of patients who present to primary care providers. These patients often are referred to otology for assessment and management. Unfortunately, there are a small number of specialists to manage these patients. However, there are several dizziness disorders that can be successfully managed by primary care providers if the disorder is properly identified. To assist in the identification of several of the most common dizziness disorders, we developed the dizziness symptom profile (DSP). The DSP is a self-report questionnaire designed to generate one or more differential diagnoses that can be combined with the patient's case history and physical examination. DESIGN: This report describes three investigations. Investigations 1 and 2 (i.e., exploratory and confirmatory investigations, N = 514) describe the development of the DSP. Investigation 3 (N = 195) is a validation study that describes the level of agreement between the DSP completed by the patient, and, the differential diagnosis of the otologist. RESULTS: The final version of the DSP consists of 31 items. Preliminary findings suggest that the DSP is in agreement with the differential diagnoses of ear specialists for Meniere's disease (100% agreement), vestibular migraine (95% agreement), and benign paroxysmal positional vertigo (82% agreement). CONCLUSIONS: Early results suggest that DSP may be useful in the creation of differential diagnoses for dizzy patients that can be evaluated and managed locally. This has the potential to reduce the burden on primary care providers and reduce delays in the diagnosis of common dizziness and vertigo disorders.

T. Kamakura, et al., **Rat Model of Meniere's Attack: Intratympanic Injection of Potassium Chloride Produces Direction-Changing Spontaneous Nystagmus and Hearing Fluctuations**. Audiol Neurootol, 2019: p. 1-7. The major symptoms of Meniere's disease are episodic vertigo, fluctuating hearing loss, and tinnitus. Direction-changing spontaneous nystagmus is a characteristic vestibular finding in Meniere's disease. In the acute stage, spontaneous nystagmus beating to the affected side (irritative nystagmus) is often observed, while paralytic nystagmus beating to the healthy side is found in the chronic stage. This direction-changing nystagmus can be reproduced in guinea pigs by increasing the potassium ion concentration in the perilymph. The objectives of the present study were to examine the effects of increasing the potassium ion concentration of the rat perilymph on hearing and nystagmus. Under isoflurane anesthesia, 22 rats received intratympanic injection of different concentrations of potassium chloride (KCl) solution or distilled water: groups 1, 2, 3, and 4 received saturated (3.4 M) KCl solution, 2 M KCl, 1 M KCl, and distilled water, respectively. The nystagmus direction and number per 15 s were monitored for 150 min. In the other 8 rats, hearing was monitored 30 min and 20 h after intratympanic injection of 2 M KCl (group 5) or distilled water (group 6) using the auditory brainstem responses. Rats in groups 1 and 2 showed spontaneous irritative nystagmus beating to the affected ear followed by paralytic nystagmus beating to the contralateral side. In group 3, irritative nystagmus occurred but paralytic nystagmus was rarely observed. Rats in group 4 showed no nystagmus. Rats in group 5 showed significant hearing impairment 30 min after KCl injection that recovered 20 h later. Control animals in group 6 showed no significant changes in hearing. The reversible hearing impairment with direction-changing spontaneous

nystagmus induced by potassium injection into the tympanic cavity in rats was quite similar to that observed in acute Meniere's attacks. This rat model could be used for basic research investigating the pathophysiological mechanisms underlying Meniere's attacks.

R. G. Kanegaonkar, et al., **Meniere's disease treated by grommet insertion**. Ann R Coll Surg Engl, 2019: p. 1-4. INTRODUCTION: Meniere's disease (MD) is an uncommon cause of sudden profound vertigo. A variety of medical and surgical treatments have been used to manage this condition. This study reviewed the outcomes of patients treated with grommet insertion and transtympanic steroid injection. METHODS: Patients diagnosed with MD between 2007 and 2017 were identified, and case notes and audiological data were retrieved for those managed by grommet (ventilation tube) insertion with and without transtympanic steroid injection. RESULTS: Thirty-three patients were identified as being diagnosed with MD. Grommet insertion resulted in cessation or improvement of attacks in 91% of cases. The mean follow-up duration was 33.8 months (median: 29 months). The mean hearing threshold across the low frequencies improved from 57.2dBHL to 49.4dBHL (p=0.031). Following the intervention, improved tinnitus was reported in 80% of cases. Twelve patients (36%) reported aural fullness prior to grommet insertion; all reported improved symptoms following the procedure. CONCLUSIONS: Early grommet insertion with transtympanic steroid injection, combined with customised vestibular physiotherapy, may provide an alternative first-line strategy for MD, preventing further true MD attacks. In some patients, it may significantly improve hearing thresholds.

E. Kharkheli, et al., **Correlation between Vestibular Evoked Myogenic Potentials and Disease Progression in Meniere's Disease**. ORL J Otorhinolaryngol Relat Spec, 2019. 81(4): p. 193-201. OBJECTIVE: To assess the relationship between ocular (oVEMPs) and cervical (cVEMPs) vestibular evoked myogenic potentials and audiometrically determined clinical stage in Meniere's disease (MD). METHODS: Thirty-four unilateral MD patients and 30 healthy volunteers were included in the study. Pure-tone hearing levels, oVEMPs, cVEMPs, and videonystagmography results were analyzed and compared between the groups. RESULTS: Both oVEMPs and cVEMPs were highly reproducible in the control group. At the early stages of MD, cVEMPs were particularly disturbed, while at the advanced stages both oVEMPs and cVEMPs were altered pathologically. In the study group, oVEMP and cVEMP amplitudes and interaural amplitude difference (IAD) statistically differed from those in the control sample. oVEMPs were absent in 7.7% of stage III and in 44.5% of stage IV MD patients, while cVEMPs were absent in 15.4% of stage III and in 54.5% of stage IV MD patients, respectively. In stage III and IV MD patients in whom oVEMPs and cVEMPs were obtained, IADs were increased. Caloric asymmetry was found in 64.7% of MD patients. Caloric weakness was more prominent in cases with advanced MD. CONCLUSION: VEMPs can be used for objective validation of the stage of MD.

J. Y. Kim, et al., **Association of Obstructive Sleep Apnea With the Risk of Meniere's Disease and Sudden Sensorineural Hearing Loss: A Study Using Data From the Korean National Health Insurance Service**. J Clin Sleep Med, 2019. STUDY OBJECTIVES: Several studies have reported an association between obstructive sleep apnea (OSA) and neuro-otologic diseases, such as Meniere's disease or sudden sensorineural hearing loss (SSNHL). However, the exact relationship between OSA and those diseases has not been fully evaluated. Therefore, the aim of this study was to investigate the prospective link between OSA and Meniere's disease or SSNHL. METHODS: We used a nationwide cohort sample of data for 2002-2013 representing approximately 1 million patients. The OSA group (n = 942) included patients diagnosed between 2004 and 2006; the comparison group was selected using propensity score matching (n = 3,768). We investigated Meniere's disease and SSNHL events over a 9-

year follow-up period. Survival analysis, log-rank test, and Cox proportional hazards regression models were used to calculate incidence, survival rate, and hazard ratios for each group. RESULTS: In the OSA group, the incidences of Meniere's disease and SSNHL were 7,854.4 and 7,876.3 person-years, respectively. Cox proportional hazards analysis revealed no overall association between patients with OSA and the risk of subsequent Meniere's disease or SSNHL. In a subgroup analysis, female and middle-aged patients with OSA were independently associated with a two-fold higher incidence of subsequent Meniere's disease, compared to those without OSA. However, we could not find any significant association between patients with OSA and SSNHL even in the subgroup analysis. CONCLUSIONS: Our findings suggest that female or middle-aged patients with OSA are associated with an increased incidence of Meniere's disease. However, there was no association between OSA and SSNHL.

S. H. Kim, et al., **Pathophysiologic Findings in the Human Endolymphatic Sac in Endolymphatic Hydrops: Functional and Molecular Evidence**. Ann Otol Rhinol Laryngol, 2019. 128(6_suppl): p. 76s-83s. BACKGROUND: The endolymphatic sac (ES) is a cystic structure situated on the posterior fossa dura and is connected to the luminal space of the vestibular organ through the endolymphatic duct, which branches into the utricular and saccular ducts. Unlike the cochlea and vestibule, the ES does not contain sensory epithelium in its luminal space, and a single layer of epithelial cells line the luminal surface area. The ES in the inner ear is thought to play a role in the regulation of inner ear homeostasis, fluid volume, and immune reaction. If these functions of the ES are disrupted, dysfunction of the inner ear may develop. The most well-known pathology arising from dysfunction of the ES is endolymphatic hydrops, characterized by an enlarged endolymphatic space due to the accumulation of excessive endolymphatic fluid. Although, molecular identities and functional evidence for the roles were identified in animal studies, basic studies of the human ES are relatively uncommon compared with those using animal tissues, because of limited opportunity to harvest the human ES. METHODS: In this study, molecular and functional evidence for the role of the human ES in the development of endolymphatic hydrops are reviewed. RESULTS AND CONCLUSIONS: Although evidence is insufficient, studies using the human ES have mostly produced findings similar to those of animal studies. This review may provide a basis for planning further studies to investigate the pathophysiology of disorders with the finding of endolymphatic hydrops.

S. Y. Kim, et al., **Migraine increases the proportion of sudden sensorineural hearing loss: A longitudinal follow-up study**. Auris Nasus Larynx, 2019. 46(3): p. 353-359. OBJECTIVE: The aim of the present study was to investigate the proportion of sudden sensorineural hearing loss (SSNHL) patients in a representative population cohort with migraine. METHODS: The Korean National Health Insurance Service-National Sample Cohort was collected from 2002 to 2013. A total of 45,114 migraine participants (the migraine group) were matched according to age, sex, income, region of residence, hypertension, diabetes, and dyslipidemia with 180,456 controls (the control group). The migraine group included participants diagnosed with migraine (International Classification of Disease [ICD]-10: G43) who underwent treatment >/=2 times. The SSNHL was investigated based on the ICD-10 (H912) code and confirmed by an audiometry exam and steroid treatment. Histories of hypertension, diabetes, dyslipidemia, ischemic heart disease, stroke, depression, Meniere's disease, and tinnitus were evaluated using ICD-10 codes. Crude (simple) and adjusted hazard ratios (HRs) of SSNHL associated with migraine were analyzed using the Cox proportional hazards model. Subgroup analyses were conducted according to age and sex. RESULTS: In total, 0.9% (399/44,714) of the migraine patients and 0.6% (1,169/179,287) of the controls were diagnosed with SSNHL (P<0.001). The adjusted HR of migraine for SSNHL was 1.34

(95% confidence interval [CI]=1.19-1.50, P<0.001). Both patient age subgroups (20-59years old and >/=60years old) showed high adjusted HRs for SSNHL. Both the men and women presented an elevated proportion of SSNHL cases. CONCLUSION: Migraine patients had a higher likelihood of SSNHL. All age and sex migraine subgroups showed an elevated proportion of SSNHL cases.

V. Kirsch, et al., **A probabilistic atlas of the human inner ear's bony labyrinth enables reliable atlas-based segmentation of the total fluid space**. J Neurol, 2019. 266(Suppl 1): p. 52-61. Intravenous contrast agent-enhanced magnetic resonance imaging of the endolymphatic space (ELS) of the inner ear permits direct, in-vivo, non-invasive visualization of labyrinthine structures and thus verification of endolymphatic hydrops (ELH). However, current volumetric assessment approaches lack normalization. The aim of this study was to develop a probabilistic atlas of the inner ear's bony labyrinth as a first step towards an automated and reproducible volume-based quantification of the ELS. The study included three different datasets: a source dataset (D1) to build the probabilistic atlas and two testing sets (D2, D3). D1 included 24 right-handed patients (12 females; mean age 51.5 +/- 3.9 years) and D2 5 patients (3 female; mean age 48.8 +/- 5.01 years) with vestibular migraine without ELH or any measurable vestibular deficits. D3 consisted of five patients (one female; mean age 46 +/- 5.2 years) suffering from unilateral Meniere's disease and ELH. Data processing comprised three steps: preprocessing using an affine and deformable fusion registration pipeline, computation of an atlas for the left and right inner ear using a label-assisted approach, and validation of the atlas based on localizing and segmenting previously unseen ears. The three-dimensional probabilistic atlas of the inner ear's bony labyrinth consisted of the internal acoustic meatus and inner ears (including cochlea, otoliths, and semicircular canals) for both sides separately. The analyses showed a high level of agreement between the atlas-based segmentation and the manual gold standard with an overlap of 89% for the right ear and 86% for the left ear (measured by dice scores). This probabilistic in vivo atlas of the human inner ear's bony labyrinth and thus of the inner ear's total fluid space for both ears represents a necessary step towards a normalized, easily reproducible and reliable volumetric quantification of the perilymphatic and endolymphatic space in view of MR volumetric assessment of ELH. The proposed atlas lays the groundwork for state-of-the-art approaches (e.g., deep learning) and will be provided to the scientific community.

K. Kitano, et al., **Results in caloric test, video head impulse test and inner ear MRI in patients with Meniere's disease**. Auris Nasus Larynx, 2019. OBJECTIVE: Our aim was to elucidate relationships between results from the caloric test (c-test), video Head Impulse Test (vHIT) and inner ear gadolinium-enhanced MRI (ieMRI) in patients with endolymphatic hydrops (EH), especially patients with Meniere's disease (MD). METHODS: We managed 1789 successive patients at the Vertigo/Dizziness Center in Nara Medical University from May 2014 to December 2018. After providing informed consent for vertigo/dizziness examinations, 281 patients were hospitalized to check their inner ear function for proper diagnosis and treatment. Then 76 participants underwent the c-test, vHIT and ieMRI. Among these 76 cases, 20 were diagnosed with MD (20/76; 26.3%) and 56 were non-MD (56/76; 73.7%) according to the 2015 diagnostic guideline of the International Classification of Vestibular Disorders. The MD group included 15 unilateral and 5 bilateral cases. The non-MD group included 22 benign paroxysmal positional vertigo, 10 vestibular neuritis, 8 sudden deafness with vertigo, 6 orthostatic dysregulation, 4 vestibular neuropathy and 6 others. Results in these examinations in the side of an active lesioned inner ear were representative in each peripheral case. RESULTS: Twenty-nine of the 76 patients (38.1%) showed discrepant results between the c-test (outside of normal range) and vHIT (within normal range).

Twenty-two of 76 patients (28.9%) had a positive EH sign on ieMRI. The c-test/vHIT discrepancy percentage in MD (14/20; 70.0%) was significantly higher than that in non-MD (15/56; 26.8%) (p=0.00179). The positive EH sign in ieMRI percentage in MD (15/20; 75.0%) was significantly higher than that in non-MD (7/56; 12.5%) (p=0.0015). There was a significant positive relationship between the c-test/vHIT discrepancy and the positive EH sign (p=0.00058) in all 76 cases combined. However, there was no significant relationship between c-test/vHIT discrepancy and positive EH sign (p=0.13) in the 20 MD cases. Considering the 15 unilateral and 5 bilateral MD cases, the c-test/vHIT discrepancy was observed in 14 of the 25 affected ears. Positive signs of vestibular EH herniation into the cupula in the lateral semicircular canal was seen in 14 of the 25 MD ears. There was significant relationship between the c-test/vHIT discrepancy and EH herniation (p=0.0012) in MD ears. CONCLUSION: The present results suggest that patients with MD could have inner ear EH significantly more often than those with non-MD. In cases with MD, a positive EH sign on ieMRI did not always indicate a c-test/vHIT discrepancy; both findings may occur due to herniation of vestibular EH adjacent to the lateral semicircular canal.

M. A. Kutlubaev, et al., **Benign paroxysmal positional vertigo in Meniere's disease: systematic review and meta-analysis of frequency and clinical characteristics**. J Neurol, 2019. There is a recognized association of Meniere's disease (MD) and benign paroxysmal positional vertigo (BPPV). However, the frequency and clinical characteristics of BPPV in MD are unclear. The aim of this review was to determine the mean frequency and clinical features of BPPV in MD. Three databases were searched: MEDLINE, PubMed and Google Academia. Studies reporting the frequency of BPPV in MD were pooled. A total of 4198 references were identified, of which 20 studies were considered eligible. The pooled frequency of BPPV in MD was 14% (95% CI 9-18%). It was 38% (95% CI 26-49%) in longitudinal studies and 8% (95% CI 6-11%) in cross-sectional ones. BPPV comorbid with MD was mostly observed in the ear affected by hydrops, in females, in patients with more advanced disease. Canalolithiasis of the horizontal semicircular canal was more common in patients with BPPV associated with MD than in idiopathic BPPV. BPPV in MD was more prone to recurrence and required more canal repositioning maneuvers.

J. Lee, et al., **Quantitative analysis of cochlear signal intensity on three-dimensional and contrast-enhanced fluid-attenuated inversion recovery images in patients with Meniere's disease: Correlation with the pure tone audiometry test**. J Neuroradiol, 2019. 46(5): p. 307-311. PURPOSE: The purpose of this study was to correlate the quantitative analysis of cochlear signal intensity (SI) on 3-dimensional fluid-attenuated inversion recovery (3D-FLAIR) and contrast-enhanced (CE) 3D-FLAIR images with results of the pure tone audiometry (PTA) test in patients with Meniere's disease (MD). MATERIALS AND METHODS: Over a 3-year period, 123 patients with MD underwent 3-Tesla (3 T) temporal magnetic resonance imaging (MRI), including 3D-FLAIR and CE-FLAIR sequences. The SI of membranous labyrinth of the cochlea in both ears of each patient was measured by drawing a region of interest (ROI) with a seed growing technique. The correlation between measured cochlear SIs on 3D-FLAIR and CE-FLAIR images, contrast enhancement index (CEI), and contrast enhancement ratio (CER) and clinical findings and pre- and post-treatment PTA results were assessed. RESULTS: Cochlear signal ratios of symptomatic ears on 3D-FLAIR and CE-FLAIR images were significantly higher than those of asymptomatic ears ($P < 0.001$). The area under the curve, from the receiver operating characteristic curve of cochlear SIs on 3D-FLAIR and CE-FLAIR images for discrimination between symptomatic and asymptomatic ears, was 0.729 and 0.728, respectively. Cochlear SIs on 3D-FLAIR and CE-FLAIR images were significantly correlated with patients' sex ($P < 0.05$ and $P < 0.01$, respectively), symptomatic ear (both $P < 0.0001$), and pre-treatment PTA ($P < 0.0001$ and $P < 0.005$, respectively), but were not

significantly correlated with patients' age, post-treatment PTA or hearing threshold level at 0.5, 1.0, 2.0, or 4.0 kHz. CONCLUSION: Quantitative analysis of cochlear SI on 3D-FLAIR and CE-FLAIR images may be a helpful diagnostic adjunct for MD, but may be of little value in predicting the prognosis of MD.

J. Y. Lee, et al., **Peripheral Vestibulopathy Presenting as Acute Vertigo and Spontaneous Nystagmus with Negative Video Head Impulse Test***.* Otolaryngol Head Neck Surg, 2019. 160(5): p. 894-901. OBJECTIVE: To analyze acute vertigo showing spontaneous nystagmus with negative video head impulse test (vHIT). STUDY DESIGN: Retrospective chart analysis. SETTING: Tertiary referral hospital. SUBJECTS AND METHODS: Over 16 months, 155 patients were identified with acute vertigo with spontaneous nystagmus. Of these 155, 30 (19.4%) were enrolled in this study because they did not show gain loss or catch-up saccades in both sides of the horizontal vHIT. Results of vestibular function tests (videonystagmography, horizontal vHIT, caloric test, and cervical vestibular-evoked myogenic potential [cVEMP]) and pure tone audiometry were analyzed. For all cases, magnetic resonance imaging with diffusion-weighted imaging was checked. RESULTS: Patients consisted of 17 with Meniere's disease and 7 with sudden sensorineural hearing loss with vertigo (SSNHL_V), and only 3 patients were finally diagnosed as having acute vascular stroke. Except for the loss of hearing on the lesion side, the direction of nystagmus or cVEMP asymmetry showed very different results. All 7 patients with SSNHL_V did not have canal paresis in the caloric test, but cVEMP amplitude was smaller on the lesion side for 6 patients. CONCLUSIONS: For patients with acute vertigo presenting spontaneous nystagmus with negative horizontal vHIT, it is important not only to focus on the diagnosis of acute vascular stroke but also to evaluate hearing because of the high possibility of Meniere's disease or SSNHL_V.

S. U. Lee, et al., **Intralabyrinthine Schwannoma: Distinct Features for Differential Diagnosis***.* Front Neurol, 2019. 10: p. 750. Objectives: The aim of this study was to delineate the clinical and laboratory features suggestive of intralabyrinthine schwannoma (ILS). Methods: We compared the clinical features of 16 patients with ILS, who had been diagnosed at the Seoul National University Bundang Hospital from 2003 to 2018, with those of 18 patients with symptomatic unilateral intracanalicular schwannoma and randomly selected 20 patients with definite or probable unilateral Meniere's disease (MD). Results: Patients with ILS presented with either recurrent spontaneous dizziness/vertigo combined with auditory symptoms (n = 8), isolated auditory symptoms without dizziness/vertigo (n = 7), or recurrent spontaneous dizziness/vertigo without auditory symptoms (n = 1). Most patients reported no improvement (n = 11) or worsening (n = 1) of the symptoms despite medical treatments including intratympanic (n = 5) or intravenous steroids (n = 2). Conventional brain MRIs failed to detect ILS in about a half of the patients (7/16, 44%). However, ILS showed a filling defect on 3-dimensional (3D) heavily T2-weighted MRIs (n = 12), and nodular enhancement on 3D contrast-enhanced T1 (n = 15) or FLAIR MRIs (n = 13) targeted for the inner ear. Compared to MD or intracanalicular schwannoma, ILS showed mostly abnormal head-impulse tests (HITs, p = 0.001). In contrast, the incidence of canal paresis did not differ among the groups (p = 0.513). Conclusion: ILS may mimic MD by presenting recurrent dizziness/vertigo and auditory symptoms. ILS should be suspected in patients with recurrent audiovestibulopathy especially when (1) the duration of the dizziness is not typical for MD, (2) the patients do not respond to medical treatments, or (3) HITs are abnormal.

Y. Li, et al., **Comprehensive comparison of MR image quality between intratympanic and intravenous gadolinium injection using 3D real IR sequences***.* Acta Otolaryngol, 2019. 139(8): p. 659-664. Background: Intratympanic and intravenous gadolinium administration is

used to visualise endolymphatic hydrops. Aims/objectives: The goal of this study was to compare the image quality between intratympanic (IT-method) and intravenous (IV-method) gadolinium administration using three-dimensional inversion recovery with real reconstruction (3D real IR) sequences. Materials and methods: A number of 152 patients with Meniere's disease were included. The 3D real IR sequence was performed 24 h after IT administration or 4 h after IV administration. The detection rate of endolymphatic hydrops, signal-to-noise ratio (SNR), and contrast-to-noise ratio (CNR) of the two methods were compared. Specifically, the average image scores of the two methods were evaluated by two radiologists. Results: The SNRROI and CNRs of the IT-method were higher than those of the IV-method, whereas no significant difference between the IT-method and IV-method with regard to the SNRB was found. The average image scores were 3.49 +/- 0.12 and 3.30 +/- 0.12 for the IT-method and IV-method, respectively (p = .229). No statistically significant difference was found between two methods in terms of the detection rate of endolymphatic hydrops. Conclusions and significance: IT-method images can display endolymphatic hydrops more precisely than IV-method images. The IV-method can be used as an alternative to the IT-method in clinical applications to some extent.

H. C. Lin, et al., **Proteome of normal human perilymph and perilymph from people with disabling vertigo**. PLoS One, 2019. 14(6): p. e0218292. The vast majority of hearing loss, the most common sensory impairment, and vertigo, which commonly causes falls, both reflect underlying dysfunction of inner ear cells. Perilymph sampling can thus provide molecular cues to hearing and balance disorders. While such "liquid biopsy" of the inner ear is not yet in routine clinical practice, previous studies have uncovered alterations in perilymph in patients with certain types of hearing loss. However, the proteome of perilymph from patients with intact hearing has been unknown. Furthermore, no complete characterization of perilymph from patients with vestibular dysfunction has been reported. Here, using liquid-chromatography with tandem mass spectrometry, we analyzed samples of normal perilymph collected from three patients with skull base meningiomas and intact hearing. We identified 228 proteins that were common across the samples, establishing a greatly expanded proteome of the previously inferred normal human perilymph. Further comparison to perilymph obtained from three patients with vestibular dysfunction with drop attacks due to Meniere's disease showed 38 proteins with significantly differential abundance. The abundance of four protein candidates with previously unknown roles in inner ear biology was validated in murine cochleae by immunohistochemistry and in situ hybridization: AACT, HGFAC, EFEMP1, and TGFBI. Together, these results motivate future work in characterizing the normal human perilymph and identifying biomarkers of inner ear disease.

F. Liu, et al., **Clinical long-term effects of surgical treatment for intractable Meniere's disease: a more than 13-year follow-up after pressure treatment and further surgical treatment for intractable vertigo**. Acta Otolaryngol, 2019: p. 1-5. Background: Meniere's disease appears to be a complex inner ear disorder and also remains a controversial and often difficult disease as regards determination of diagnosis, pathogenesis and especially optimal treatment. Aims/objectives: To investigate the long-term effects of progressive surgical treatment in the management of the vertigo attacks of intractable Meniere's disease. Material and methods: Eighteen patients with medically intractable and active Meniere's disease were opted to try Meniett pulse generator (Meniett), endolymphatic sac decompression (ESD) and triple semicircular canal occlusion (TSCO) in order to control the attacks of vertigo. Patients were indicated on the symptom report card the maximum level of vertigo, activity and stress. Results: Of 18 patients with medically intractable and active Meniere's disease during mean 165-month follow-up, the attacks of vertigo were effectively

controlled in 14 patients by Meniett (77.78%), 2 patients by Meniett and ESD (11.11%), 2 patients by Meniett, ESD and TSCO (11.11%). Conclusions and significance: It is of great importance for intractable Meniere's disease to select surgically combined treatment process including Meniett, ESD and TSCO to effectively control the attacks of vertigo and a long-term follow-up.

H. Liu, et al., **Fluctuating Sensorineural Hearing Loss**. Audiol Neurootol, 2019. 24(3): p. 109-116. BACKGROUND: Several otologic conditions can present with fluctuating sensorineural hearing loss, including Meniere's disease, autoimmune inner ear disease, and enlarged vestibular aqueduct. Although these 3 etiologies vary greatly, distinguishing between these conditions at initial presentation can be challenging. Furthermore, initial treatment of these conditions is often similar. In this review, we discuss historical and current perspectives on diagnosis and treatment of these conditions. SUMMARY: A literature search was performed regarding fluctuating hearing loss, and current treatment of these etiologies of fluctuating hearing loss was summarized. Immediate measures at the onset of acute hearing loss include corticosteroid therapy, while preventative and chronic therapies, which can limit disease severity and frequency, vary based on the specific condition treated. Key Messages: Fluctuating hearing loss can represent a range of pathologies, but the precise etiology may not be clear at initial presentation. Timely treatment and long-term follow-up, along with appropriate diagnostics, are necessary to optimize long-term hearing.

Y. F. Liu, et al., **Quantification of Cognitive Dysfunction in Dizzy Patients Using the Neuropsychological Vertigo Inventory**. Otol Neurotol, 2019. 40(7): p. e723-e731. OBJECTIVE: Currently available patient reported outcomes questionnaires for dizzy patients give limited insight into the cognitive dysfunction patients often report. Using the newly developed English version of the neuropsychological vertigo inventory (NVI), we aimed to quantify the cognitive impairment of dizzy patients. STUDY DESIGN: Prospective cohort study. SETTING: Tertiary neurotology clinic. PATIENTS: Adults with vestibular diagnoses seen between June 2018 and October 2018. Patients with neurologic disorders affecting cognition were excluded. INTERVENTIONS: None. MAIN OUTCOME MEASURE: NVI score. Secondary measures: dizziness handicap inventory (DHI) score, cognitive failure questionnaire (CFQ) score, 20-item short form health survey scores (SF20). RESULTS: Of 67 subjects, 13 had BPPV, 11 had Meniere's disease (MD), and 20 had vestibular migraine (VM). VM patients were significantly younger (43.5 versus 61.1 yrs, $p = 0.016$), and had significantly higher NVI (67.5 versus 51.0, $p = 0.040$) scores than BPPV patients. MD patients had significantly higher CFQ scores (44.8 versus 23.4, $p = 0.015$) than BPPV patients. NVI scores were similar between MD (67.3) and VM (67.5) patients ($p = 1.000$). DHI scores were similar for all patients ($p = 0.102$). NVI scores were highly correlated to CFQ scores ($r = 0.864$, $p < 0.001$). CONCLUSIONS: VM patients have levels of cognitive dysfunction similar to MD patients, but greater than BPPV patients. A lack of difference in DHI scores among these patients reflects its limitation in assessing the cognitive domain.

Y. P. Liu, et al., **[The prognostic value of glycerol test of electrocochleography on the effects of endolymphatic sac decompression surgery in patients with unilateral Meniere's disease]**. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi, 2019. 33(6): p. 485-488. Objective:To determine whether the preoperative results of glycerol test of electrocochleography and hearing stage have a prognostic value on the effects of endolymphatic sac decompression surgery in patients with unilateral Meniere's disease. Method:A retrospective study was conducted of 58 unilateral Meniere's disease patients who underwent endolymphatic sac decompression surgery. The correlation between the preoperative results of glycerol test of electrocochleography hearing stage and vertigo

control was analyzed by Kendall test. Result:Patients in the positive glycerol test of electrocochleography group had better vertigo control after the decompression of the lymphatic sac than the negative group(P=0.029). Preoperative hearing staging was significantly associated with vertigo control after endolymphatic sac decompression(P=0.028). The better the preoperative hearing, the higher the control rate of vertigo after endolymphatic sac decompression. The stage patients were 91.7%, the stage patients were 78.1%, and the third stage patients were 57.1%, respectively. Conclusion:Our findings suggested that the positive preoperative results of glycerol test of electrocochleography and better hearing stage may indicate a better effects of endolymphatic sac decompression surgery in patients with unilateral Meniere's disease.

I. A. Lopez, et al., **Otopetrin-2 Immunolocalization in the Human Macula Utricle**. Ann Otol Rhinol Laryngol, 2019. 128(6_suppl): p. 96s-102s. BACKGROUND: In the present study, we investigated the localization of otopetrin-2-a member of the otopetrin family that encodes proton-selective ion channels-in the human macula utricle using immunohistochemistry. METHODS: Macula utricle were acquired at surgery from patients who required transmastoid labyrinthectomy for intractable vertigo due to Meniere's disease (MD; n = 3) and/or vestibular drops attacks (VDA; n = 2) and from temporal bones (n = 2) acquired at autopsy from individuals with no balance disorders. Immunofluorescence staining with otopetrin-2 (rabbit affinity purified polyclonal antibody) and GFAP (mouse monoclonal antibody) to identify vestibular supporting cells was made in formalin fixed cryostat sections or whole microdissected utricle (for flat mount preparations). Secondary antibodies against rabbit and mouse were used for the identification of both proteins. Digital fluorescent images were obtained using a high-resolution laser confocal microscope. RESULTS: Using cryostat sections and flat mount preparations otopetrin-2 immunofluorescence was seen as punctated signal throughout the supporting cells cytoplasm. GFAP immunofluorescence was present in the supporting cell cytoplasm. The distribution of otopetrin-2 was similar in the macula utricle obtained from MD, VDA, or autopsy normative patients. CONCLUSIONS: Otopetrin-2 was localized in supporting cells in a similar fashion that otopetrin-1 previously reported in the mouse macula utricle. The differential expression of otopetrin-2 in the supporting cells of the human macula utricle suggest an important role in the vestibular sensory periphery homeostasis and otolith maintenance.

T. C. Lu, et al., **Evolution of Meniere's Disease from MD 1.0, via MD 1.5, to MD 2.0**. Acta Otolaryngol, 2019. 139(9): p. 747-752. Background: Elder Meniere's disease (MD) patients ultimately lose their vestibular function. Objective: This study utilized an inner ear test battery to investigate evolution of MD. Methods: Total 278 elder MD patients aged >65 years were divided into three groups. Ninety-four patients with bilateral MD (188 ears) were assigned to Group A. The remaining 184 patients with unilateral MD were further divided into two groups. Group B consisted of 20 affected ears with normal vestibular function on the opposite ears, while Group C indicated 184 unaffected ears. All patients underwent an inner ear test battery. Results: Inner ear deficits in Group B declined from the cochlea via the saccule, utricle to semicircular canals. In contrast, Groups A and C did not significantly differ in the abnormality rates of cervical vestibular-evoked myogenic potential (cVEMP), ocular VEMP and caloric tests, indicating that Group C (unaffected ears) may partly share the same mechanism like Group A (affected ears), namely aging and hydropic effects. Conclusion and significance: Evolution of MD may progress from unilateral MD (MD 1.0), via unilateral MD coupled with asymptomatic hydrops on opposite ear (MD 1.5), toward bilateral MD (MD 2.0), where the number 1.0-2.0 means the number of clinically affected ears.

J. K. Mattingly, et al., **Intraoperative Electrocochleography in Patients With Meniere's Disease Undergoing Endolymphatic Sac Decompression and Shunt Surgery**. Otol Neurotol, 2019. 40(9): p. 1208-1216. HYPOTHESIS: Objective physiologic changes measured using electrocochleography at the round window (ECOG) are observable during endolymphatic sac decompression and shunt surgery (ELS). BACKGROUND: Limited effective treatment options are available to patients with Meniere's disease (MD) who have failed conservative management, experience persistent vertigo symptoms, and have substantial residual hearing. ELS is a feasible therapeutic option for these patients. However, the efficacy of this procedure has been questioned, and objective measures assessing inner ear physiologic alterations are lacking. METHODS: ECOG was measured in patients with MD undergoing ELS. Stimuli consisted of tone bursts (250, 500, 1000, 2000, 4000 Hz) and 100 mus broadband clicks at various intensities (60-90 dB nHL). Cochlear microphonic (CM), summation potential (SP), compound action potential (AP), SP:AP ratio, and CM harmonic distortions were measured. RESULTS: ECOG was completed in 18 patients. The mean SP magnitude at 500 Hz changed significantly from -7.1 muV before to -5.1 muV after ELS ($p < 0.05$). However, the mean SP:AP ratio in those tested ($n = 13$) did not significantly change after ELS. CM harmonic magnitudes remained unchanged from pre- to post-ELS ($n = 12$) across all frequencies. CONCLUSION: ECOG allows detection of acute electrophysiological changes in the cochlea. However, our results indicate only small objective changes in the low-frequency SP magnitude (500 Hz) immediately after ELS, but not in other frequencies or measures tested (CM, SP:AP, CM harmonic distortions). These results suggest minimal electrophysiological changes occur in the cochlea as a result of ELS.

R. Mittal, et al., **Nanoparticle-based drug delivery in the inner ear: current challenges, limitations and opportunities**. Artif Cells Nanomed Biotechnol, 2019. 47(1): p. 1312-1320. Hearing loss is the most common neurosensory impairment worldwide. While conductive hearing loss can be managed by surgery, the management of sensorineural hearing loss (SNHL), related to the damage of sensory cells of the inner ear is more challenging to manage medically. Many causes of SNHL such as sudden idiopathic SNHL, Meniere's disease, noise-induced hearing loss, autoimmune hearing loss or hearing loss from exposure to ototoxic substances can benefit from delivery of otoprotective drugs to the inner ear. However, systemic drug delivery through oral, intravenous and intramuscular methods leads to undesirable side effects due to the inner ear's limited blood supply and the relatively poor penetration of the blood-inner ear barrier (BLB). Therefore, there has been an increased interest for the targeted drug delivery to the inner ear using nanoparticles. Drug delivery through nanoparticles offers several advantages including drug stabilization for controlled release and surface modification for specific targeting. Understanding the biocompatibility of nanoparticles with cochlea and developing novel non-invasive delivery methods will promote the translation of nanoparticle-mediated drug delivery for auditory disorders from bench to bedside.

A. Molnar, et al., **Intratympanically administered steroid for progressive sensorineural hearing loss in Meniere's disease**. Acta Otolaryngol, 2019. 139(11): p. 982-986. Background: Meniere's disease is characterised by episodic rotational vertigo, sensorineural hearing loss, tinnitus, and vegetative symptoms. Objectives: The aim of our study is to follow-up the effects of the intratympanic steroid treatment of hearing loss in MD. Material and methods: A group of 105 clinically diagnosed MD patients were enrolled in this investigation. Long-term follow-up was carried out, and pure tone speech audiometry results of the subjects before and after application of steroid were contrasted. Statistical analysis was carried out using the IBM SPSS V24 software. Results: Based on the audiograms in this population, all stages of hearing loss were presented (from slight to profound). In most of the cases

(68.6%), after intratympanic dexamethasone treatment, stagnation in the hearing profile was achieved. Moreover, there was a smaller group demonstrating hearing improvement after the treatment (12.4%). According to logistic regression [p = .001; Odds ratio: 2.75 (95% CI 1.068-4.442,)], there was a strong correlation between hearing improvement and dexamethasone treatment (all patients were treated with intratympanic dexamethasone, while improvement without steroid treatment could never be attained). Conclusions and significance: Intratympanically administered dexamethasone is a potent agent to prevent the progression of hearing loss in MD.

A. Moodley, et al., **Could there be any merit in lumping primary open-angle glaucoma, idiopathic intracranial hypertension and Meniere's disease into a novel and discrete category of fluid tension disorders?** Med Hypotheses, 2019. 132: p. 109361. Open-angle glaucoma, idiopathic intracranial hypertension, and Meniere's disease are disorders managed by different specialties in medicine viz. ophthalmology, neurology, and otorhinolaryngology respectively. By working in silos, the similarity of these disorders is overlooked. Close inspection of these disorders reveals the presence of signs and symptoms triggered by fluid under high pressure within relatively closed chambers. There is a similarity in the capillary production of fluid, which then circulates and drains into the venous system. Management practices that reduce fluid production, decrease fluid pressure or enhance fluid drainage are employed for the treatment of all three disorders. A search for a unifying mechanism explaining the pathophysiology of all three disorders may unlock effective and perhaps curative measures for these disorders.

K. S. Noij, et al., **Predicting Development of Bilateral Meniere's Disease Based on cVEMP Threshold and Tuning**. Otol Neurotol, 2019. OBJECTIVE: To investigate if the cervical vestibular evoked myogenic potential (cVEMP) is predictive for developing bilateral Meniere's disease (MD). STUDY DESIGN: Retrospective cohort study. SETTING: Tertiary care center. PATIENTS: Records of 71 patients previously diagnosed with unilateral MD at our institution who underwent cVEMP testing between 2002 and 2011 were screened. INTERVENTION: Patients were contacted to answer a questionnaire to identify which patients had developed bilateral disease. Based on questionnaires and medical charts, 49 patients with a follow-up time of at least 5 years were included. The 49 originally asymptomatic ears are referred to as "study ears." Previously reported cVEMP criteria (original criteria) applied to study-ear cVEMPs separated them into Meniere-like and normal-like groups. MAIN OUTCOME MEASURE: The main purpose was to determine if previously obtained cVEMP thresholds and tuning ratios of unilateral MD patients could predict who develops bilateral disease. RESULTS: From the 49 included patients, 12 developed bilateral disease (24.5%). The study ears characterized by original cVEMP criteria as Meniere-like were significantly more likely to develop bilateral disease compared with the normal-like study ears. The original criteria predicted development of bilateral disease with a positive predictive value (PPV) and negative predictive value (NPV) of 58.3% and 86.5% respectively. ROC curves were used to revise cVEMP criteria for predicting the progression to bilateral disease. A revised criterion combining three cVEMP metrics, reached a PPV and NPV of 85.7% and 93.7%. CONCLUSION: cVEMP threshold and tuning in unilateral MD patients are predictive of which patients will develop bilateral disease.

F. S. Obeidat, et al., **Comparing the sensitivity and specificity of cervical vestibular-evoked myogenic potentials and electrocochleography in the diagnosis of Meniere's disease**. Int J Audiol, 2019. 58(11): p. 738-746. Objective: To compare the sensitivity and specificity of objective cervical vestibular-evoked myogenic potential (cVEMP) tuning curves and electrocochleography (ECochG) for the diagnosis of Meniere's disease (MD). Design:

Sensitivity and specificity were calculated from 95% normative ranges of 500 Hz cVEMP threshold and ECochG SP/AP amplitude ratios. Measures: Extra-tympanic ECochG testing to 90 dB nHL clicks and cVEMP threshold tuning curves (250-1000 Hz). Study sample: We tested 15 patients (30 ears) diagnosed with definite bilateral MD based on the clinical criteria proposed by the American Academy of Otolaryngology Head and Neck surgery, 1995 (assumed gold standard) and 20 controls. Results: 500 Hz cVEMP threshold was the most promising parameter to differentiate MD ears from controls. cVEMP and ECochG showed high specificity (83.3 and 100%, respectively) and low to moderate sensitivity (22.2 and 71.4%) for long term MD. ECochG sensitivity increased to 89% during a symptomatic period, compared to 33% for cVEMP. However, ECochG can be difficult to schedule during symptomatic periods. Sensitivity of cVEMP for the diagnosis of MD appears limited. Conclusions: ECochG has higher sensitivity than cVEMP in the diagnosis of Meniere's patients, but the ECochG SP/AP amplitude ratio measure is not perfect for the diagnosis of MD.

F. S. Obeidat, et al., **Objective methods to measure vestibular evoked myogenic potential response saccular tuning curves**. Int J Audiol, 2019. 58(11): p. 724-732. Objective: To detect cervical vestibular evoked myogenic potential (cVEMP) responses using objective statistical approaches and to apply this approach to estimate saccular frequency-tuning curves in volunteers and Meniere's disease (MD) patients. Design: Estimates of cVEMP threshold were carried out by 3 expert raters at 500 Hz and compared to objective threshold estimates (using Hotelling's T(2) [HT(2)] and Fsp). Saccular tuning curves were objectively estimated. Study sample: Objective and subjective estimates of cVEMP response thresholds were compared for 13 normal hearing adults. Objective measurement of saccular tuning curves was explored in 20 healthy adults and 15 patients with MD. Results: Significant variability was seen between subjective estimates of cVEMP thresholds. Objective analysis with the HT(2) test was more sensitive than 2 of 3 experts in detecting responses. The measurement time of cVEMP was considerably reduced with the HT(2) test. Objective saccular tuning curves in volunteers showed strongest responses at 500 Hz. A flatter tuning curve was seen for MD patients. Conclusions: There is significant variability in subjective estimations of cVEMP thresholds. Objective analysis methods are more sensitive than subjective analysis, can detect responses rapidly and have potential to reduce variability in threshold estimates, hence they appear well suited to measure cVEMP tuning curves.

K. Ozturk, et al., **Intratympanic mixture gentamicin and dexamethasone versus dexamethasone for unilateral Meniere's disease**. Am J Otolaryngol, 2019. 40(5): p. 711-714. OBJECTIVE: This study aimed to determine the effectiveness of an intratympanic (IT) injection of a mixture of gentamicin and dexamethasone compared with intratympanic dexamethasone (ITD) for controlling vertigo and protecting the hearing level of Meniere's disease patients who have persistent vertigo attacks, despite medical treatment. METHODS: Thirty eight patients with intractable Meniere's disease were included in this study. Twenty-one patients were treated with IT mixture gentamicin and dexamethasone injection; seventeen patients were treated with ITD. Pre- and post-treatment audiograms were compared with pure-tone averages. Control of vertigo was classified according to the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) vertigo control index. RESULTS: In the mixture group single IT injection was administered in 18 patients (85.7%), 2 injections were administered in 2 patients (9.5%) and 3 injections were administered in one patient (4.8%). In the ITD group IT injection was performed 3 times (days 1,3,5) at intervals. The mean number of intervals per patient was 3,41 (range 1-6). Two years after IT treatment there was better control of vertigo in mixture group than in ITD group; 81% of mixture group and 70,6% of the ITD group achieved satisfactory control of

vertigo (p=0,0286). Audiology results of mixture group showed 20 patients (95,24%) with unchanged hearing and 1 patient (4,76%) with only 10-decibel deteriorated hearing. There was no worsening of hearing in the ITD group. CONCLUSION: The results of this study showed that an IT injection of a mixture of gentamicin and dexamethasone in intractable Meniere's disease cases is more effective than ITD for vertigo control.

B. Pang, et al., **Incidence of Developing Contralateral Meniere's Disease in Patients Undergoing Transmastoid Labyrinthectomy for Unilateral Meniere's Disease**. Ear Nose Throat J, 2019: p. 145561319854744. OBJECTIVES: To analyze the incidence of developing contralateral Meniere's disease (MD) in patients who undergo labyrinthectomy for vestibular dysfunction in unilateral MD. STUDY DESIGN: Retrospective chart review. PARTICIPANTS AND METHODS: Adult patients with a diagnosis of MD who underwent surgical labyrinthectomy with minimum follow-up of 12 months were included. Patients who experienced chemical labyrinthectomy, surgical labyrinthectomy for a diagnosis other than MD, contralateral ear surgery, or bilateral MD before the labyrinthectomy were excluded. The key outcome measure is whether symptoms of MD developed in the contralateral ear post-labyrinthectomy. Statistical analysis was performed using chi(2) (Fisher exact) test for discrete variables and the Student t test for continuous variables. A P value < .05 was considered significant. RESULTS: Of the140 patients who underwent labyrinthectomy for intractable vertigo due to unilateral MD, 84 had at least 1 year follow-up appointments. Twelve percent (10/84) of these patients developed contralateral MD, which was diagnosed by a neuro-otologist based on symptoms consistent with MD, including low-frequency sensorineural hearing loss. Average age in years is 63.12 (10.83; mean [SD]) at time of surgery. Average follow-up was 35.57 (15.89) months (range: 12-69 months). CONCLUSION: The incidence of contralateral MD development in patients who underwent labyrinthectomy for unilateral MD is 12%. The current literature states that MD has a 30% bilateral involvement rate. Our incidence is significantly lower when compared to the current literature.

P. Perez-Carpena, et al., **A Tinnitus Symphony in 100 Patients With Meniere's Disease**. Clin Otolaryngol, 2019. Tinnitus is a heterogeneous condition in Meniere's Disease. The type of tinnitus in Meniere's Disease ranged from pure tones to noise-like tinnitus (white, brown and pink noise). Meniere's Disease patients with tonal tinnitus present higher scores in Tinnitus Handicap Inventory compared to Meniere's Disease patients with noise-like tinnitus. There is a positive correlation between Tinnitus Handicap Inventory and Visual Analogue Scale, with a stronger association in patients with bilateral Meniere's Disease. Tinnitus extreme phenotype (TEP) in Meniere's Disease showed Tinnitus Handicap Inventory scores of 80 out of 100, with lower age of onset for both Meniere's Disease and tinnitus.

I. Pyykko, et al., **Association between Meniere's disease and vestibular migraine**. Auris Nasus Larynx, 2019. 46(5): p. 724-733. OBJECTIVE: The aim of the present study was to evaluate complaints in people with Meniere's disease (MD) with and without migraine and headache to study the association between MD and Vestibular Migraine (VM). We believe this will help us understand if these two disorders represent a disease continuum in that they may share a common aetiology. METHODS: The study used a retrospective design and included data of 911 patients with MD from the Finnish Meniere Federation database. The study participants had a mean age of 60.2 years, mean duration of disease of 12.6 years, and 78.7% of the participants were females. The questionnaire data comprised of both disease specific and impact related questions. The data were analyzed using the Mann-Whitney U test, the Kruskal Wallis H test, logistic regression analyses, and decision tree analysis. RESULTS: Migraine and headache was reported by 190 subjects (20.9%) and 391 subjects

(42.9%) respectively. We found that patients that could be classified as VM in the study (i.e., those with frequent vertigo spells associated with migraine) more often reported complaints of severe MD symptoms, had reduced health-related quality of life, suffered more from anxiety, had more neurological complaints, and experienced a reduced sense of coherence than the non-migraneous patients with MD. However, neither the decision tree analysis nor the logistic regression analysis could reliably discriminate VM from MD patients. CONCLUSION: Our study results confirm that MD is frequently associated with headache and migraine. In addition, results also indicate that migraine provokes the severity of MD. We suggest that MD and VM may share similar pathophysiological mechanisms. Hence, the future MD classification systems should include a category referred to as 'MD with migraine' that will include patients with VM.

I. Pyykko, et al., **Driving Habits and Risk of Traffic Accidents among People with Meniere's Disease in Finland**. J Int Adv Otol, 2019. 15(2): p. 289-295. OBJECTIVES: The study evaluated the driving habits and risk of traffic accidents among people with Meniere's disease (MD) in Finland. MATERIALS AND METHODS: The study used a cross-sectional survey design. Members of the Finnish Meniere Federation (FMF) were contacted and requested to participate in an online survey. In total, 558 FMF members (58.7% response rate) responded to the survey. RESULTS: People with MD were responsible for significantly fewer traffic accidents (0.8%) annually than individuals in the general population (1.7%). In addition, the lifetime risk of car accidents was lower among subjects with MD (8.3%) than that among individuals in the general population (24 to 28%). Nearly half of the total participants had either reduced the frequency of driving or had given up driving because of their condition. Factors such as gender, balance problems, visual problems with visual aura, and syncope during vestibular drop attacks can help explain the reasons for giving up car driving. One third (35.9%) of the participants were able to anticipate the MD attack before they decided to drive a car. Participants with falls during a vestibular drop attack, attacks of rotary vertigo, syncope during vestibular drop attacks, and those who were of a younger age were at a higher risk of experiencing a vertigo attack while driving a car. The most common strategies to avoid car accidents were selective driving and not driving when symptoms appeared. CONCLUSION: The results show that people with MD are at a lower risk of traffic accidents than individuals in the general population, which can be explained by selective driving.

D. Qin, et al., **Histamine H4 receptor gene polymorphisms: a potential contributor to Meniere disease**. BMC Med Genomics, 2019. 12(1): p. 71. BACKGROUND: The immune system is likely involved in the pathophysiology of Meniere's disease (MD). However, its role of patients with MD has not been well studied. Given that histamine H4 receptors are highly expressed in immune system, we tested the hypothesis that histamine H4 receptor gene polymorphisms are a potential contributor to the risk of MD. METHODS: A group of patients was enrolled with a diagnosis of definite MD based on the American Academy of Otolaryngology-Head and Neck Surgery Committee on Hearing and Equilibrium guidelines and a control group of patients without any vestibular disease. We selected one SNP, rs77485247 in HRH4 and conducted an exploratory investigation of its correlations with the symptoms of vertigo and proinflammatory cytokines levels in MD patients. RESULTS: HRH4 rs77485247 polymorphism may be associated with the risk of MD. Furthermore, basal levels of proinflammatory cytokines, such as IL-1beta and TNF-alpha, in PBMCs are increased in patients with MD compared to control patients. This increased basal level of proinflammatory cytokines is prominent in MD patients with the A allele. CONCLUSIONS: These suggested that HRH4 rs77485247 polymorphism may be an important mediator in regulating proinflammatory cytokines, which are involved in the pathogenesis of MD.

N. Quaranta, et al., **Therapeutic strategies in the treatment of Meniere's disease: the Italian experience**. Eur Arch Otorhinolaryngol, 2019. 276(7): p. 1943-1950. PURPOSE: Meniere's disease (MD) is an inner ear disorder of unknown etiology, whose pathological substrate is the endolymphatic hydrops. Different treatments have been proposed; however, evidence of their effectiveness is lacking. The aim of this study was to evaluate by a questionnaire which medical and surgical treatments are used in Italy for the treatment of MD and to compare them with those proposed in other countries. METHODS: An electronic questionnaire of 40 questions was formulated and sent to Italian otolaryngologist (ENT) divided into two groups: Group 1 ("generalists" 60.8%) and Group 2 ("neurotologist- NO" 39.2%). RESULTS: One hundred and twenty five ENT replied. Treatment of the acute phase, apart from symptomatics, was based on diuretics that are prescribed by 83.5% of respondents, steroids, prescribed by 66.7%, and vasodilators, prescribed by 22%. In the intercritical phase, 87.2% of respondents recommended low-salt diet, 78.4% of respondents prescribed betahistine, and 52.8% diuretics. Statistical analysis did not show correlation neither with the declared specialization nor with the number of patients treated. In case of failure of medical treatment, IT gentamicin was suggested by 48.8% of the respondents and IT steroids by 40.8%. Statistical analysis showed that generalists prefer IT steroids and NO IT gentamicin (p 0.019). In case of failure of both medical treatment and IT treatment, vestibular neurectomy was indicated by 58.4% of the respondents, 6.4% indicated endolymphatic sac surgery, and 2.4% surgical labyrinthectomy. CONCLUSION: In Italy, the treatment of MD stand on a gradual approach that starts from the dietary-behavioral changes and a pharmacological therapy based on betahistine. In refractory cases, IT treatment initially with steroids and, therefore, with gentamicin allows the control in vertigo in the majority of cases. In case of failure of IT treatment, VNS is the surgery of choice.

A. R. Rego, et al., **The cardiovascular aspects of a Meniere's disease population - A pilot study**. J Otol, 2019. 14(2): p. 51-56. Introduction: MD is considered a rare disease. An adequate model that explains MD's pathophysiology is not well established. Recently, the vascular theory of the disease has been revived. Objectives: To characterize a MD population according to its cardiovascular risk and correlate it to the MD clinical course. Methods: In this retrospective chart study the data of 31 MD patients observed between January 2017 and April 2018 in a tertiary university hospital were reviewed. Patients included in the study were diagnosed according to the Barany Society criteria. Lost follow-ups, patients with autoimmune disease, atopy or allergy, major psychiatric disease and migraine were excluded. Age, gender, cardiovascular risk factors, audiometric and vestibular parameters, occurrence of MD attacks in the previous 6 months, vestibular medication in course and time course of MD were recorded and compared between groups (with and without cardiovascular risk factors). Results: 31 patients (61.3% females) mean aged 60.3 years (+/-9.7) were studied. 74% of the population had at least one risk factor and 51.6% of patients had attacks in the last 6 months. There was a statistically significant difference in the occurrence of MD attacks in the last 6 months (p=0.014) between MD patients with and without risk factors. Mean PTA thresholds were higher and speech discrimination was lower in individuals with more cardiovascular risk factors. Conclusions: Treatment of MD focusing on vascular risk factors may allow a better control of symptoms and result in a decreased need for ablative procedures in this disorder.

M. Rogha, et al., **Therapeutic Effect of Intratympanic Injection of Dexamethasone plus Hyaluronic Acid on Patients with Meniere's disease**. Iran J Otorhinolaryngol, 2019. 31(105): p. 217-223. Introduction: Intratympanic therapy, as a widely used treatment for inner ear diseases, is regarded as a therapeutic method in controlling the vertigo of the patients with Meniere's disease. This study was designed to evaluate the effect of the Intratympanic

dexamethasone-hyaluronic acid combination on patients suffering from Meniere's disease. Materials and Methods: This study was a clinical trial on patients with Meniere's disease during 2016-2017. Patients received two Intratympanic injections of dexamethasone plus hyaluronic acid as a mixture within a month. Before and 2 weeks after the intervention, pure tone average (PTA) at 0.5, 1, 2, and 4 KHz frequencies, speech discrimination score (SDS), dizziness handicap inventory (DHI), and tinnitus handicap inventory (THI) scores were evaluated for each patient. The obtained scores were statistically analyzed. Results: This study was conducted on a total number of 25 patients with Meniere's disease. The mean age of participants in this study was 44.71+/-4.92 years. Gender distribution among participants revealed that 36% of patients were male. The mean values of PTA, SDS, and THI were not significantly different before and after the intervention. However, the mean score of DHI decreased significantly after the intervention (P<0.001). Conclusion: Intratympanic dexamethasone/hyaluronic acid had a positive effect on the vertigo of the investigated patients without any significant improvement in hearing impairment and tinnitus in the short term.

A. N. Salt, et al., **Comparison of the Pharmacokinetic Properties of Triamcinolone and Dexamethasone for Local Therapy of the Inner Ear**. Front Cell Neurosci, 2019. 13: p. 347. Some forms of triamcinolone may provide alternate options for local therapy of the inner ear in addition to the steroids currently in use. We compared the perilymph pharmacokinetics of triamcinolone-acetonide, triamcinolone, and dexamethasone, each delivered as crystalline suspensions to guinea pigs. Triamcinolone-acetonide is a widely used form of the drug with molecular properties that allow it to readily permeate biological barriers. When applied intratympanically triamcinolone-acetonide entered perilymph rapidly but was also found to be eliminated rapidly from perilymph. The rapid rate of elimination severely limits the apical distribution of the drug when applied locally, making it unsuitable for use in the ear. In contrast, triamcinolone, rather than triamcinolone-acetonide, is a more polar form of the molecule, with higher aqueous solubility but calculated to pass less-readily through biological boundaries. Perilymph concentrations generated with intratympanic applications of triamcinolone were comparable to those with triamcinolone-acetonide but elimination measurements showed that triamcinolone was retained in perilymph longer than triamcinolone-acetonide or dexamethasone. The slower elimination is projected to result in improved distribution of triamcinolone toward the cochlear apex, potentially allowing higher drug levels to reach the speech frequency regions of the human ear. These measurements show that triamcinolone could constitute an attractive additional treatment option for local therapy of auditory disorders.

A. Scarpa, et al., **Low-dose intratympanic gentamicin administration for unilateral Meniere's disease using a method based on clinical symptomatology: Preliminary results**. Am J Otolaryngol, 2019: p. 102289. PURPOSE: There are many therapeutic options for Meniere's disease (MD); intratympanic (IT) gentamicin has been proposed for intractable cases although controversy about dosage and method exists. The purpose of this study was to assess the efficacy and safety of low-dose IT gentamicin on vertigo attacks in MD using a clinical symptomatology-based method in which administration was repeated only if vertigo attacks recurred, with a 2-week interval between injections. MATERIALS AND METHODS: Forty-eight patients with unilateral intractable MD were included in the study. All patients received one to five IT injections with 0.5ml of 10mg of gentamicin (80mg/2ml) with an interval of 2 weeks between injections. Vertigo attacks were evaluated before and after therapy and categorized into classes A-F according to the 2015 Equilibrium Committee criteria. Audiovestibular assessment with pure tone audiometry, vestibular bed-side examination and video head impulse test was performed. RESULTS: Before treatment

patients had an average of 4.4 vertigo attacks/month; after treatment the average number decreased to 0.52. The majority of patients (77%) reached Class A vertigo control with 5 or less gentamicin injections. VOR gain was unaffected in the healthy side and significantly reduced in the affected side. No hearing deterioration was found in all treated patients. CONCLUSIONS: Low-dose IT gentamicin administration based on clinical symptomatology can produce a satisfactory control of vertigo attacks after treatment; such protocol had an effect mainly on the vestibular function as demonstrated by the significant reduction in VOR gain in the affected side avoiding a cochlear damage.

A. Scarpa, et al., **Food-induced stimulation of the antisecretory factor to improve symptoms in Meniere's disease: our results**. Eur Arch Otorhinolaryngol, 2019. PURPOSE: Specially processed cereals (SPC) that increase endogenous antisecretory factor (AF) synthesis have been proposed to improve symptoms of Meniere's disease (MD) with controversial results. The aim of this study was to evaluate the effects of SPC in patients with definite unilateral MD and compare the results to a treatment protocol with intravenous glycerol and dexamethasone. METHODS: Thirteen patients with unilateral MD were treated with SPC and 13 patients were treated with intravenous glycerol and dexamethasone for 12 months. Audio-vestibular evaluation was performed before (T0) and at the end of the treatments (T12). The number of vertigo spells were evaluated before and after therapy and the Efficacy Index (EI) was calculated. Questionnaires for hearing loss (HHIA), tinnitus (THI) and quality of life (TFL) were administered. RESULTS: EI decreased in the SPC group in the second semester compared to the first although not significantly ($p = 0.6323$). There was a significant reduction for THI score in the SPC group at T12 ($p = 0.0325$). No significant differences were found between the two groups at T0 ($p = 0.4723$), while a significant difference was found at T12 ($p = 0.0041$). Quality of life showed an improvement in daily activities in the SPC group compared to infusion therapy group. CONCLUSION: Our study shows a reduced number of vertigo attacks and a positive effect on the discomfort generated by tinnitus and quality of life in patients with unilateral MD treated with SPC and when compared to patients treated with intravenous glycerol and dexamethasone. No effects on hearing thresholds were noted in both groups.

C. Sevilla, et al., **Aural fullness and transtympanic ventilation tubes in Meniere's disease: a scoping review**. J Laryngol Otol, 2019. 133(6): p. 450-456. BACKGROUND: Meniere's disease often presents with aural fullness, for reasons that are currently not well understood. Transtympanic ventilation tube insertion has been historically used for the management of this symptom, though the nature and mechanism of effectiveness is unclear. OBJECTIVE: To give an overview of the data available on the effects of ventilation tube insertion on aural fullness in Meniere's disease. METHODS: The databases PubMed, Embase, Medline, Scopus, Web of Science, Central and Google Scholar were searched to identify relevant records. Records were subsequently analysed and data extracted. RESULTS: Only two studies directly measured the effect of ventilation tube insertion on aural fullness, while three others measured it as a placebo to assess another treatment. Considerable heterogeneity was found amongst the studies, including conflicting conclusions. CONCLUSION: There is a paucity of evidence investigating the effect of grommet insertion on aural fullness in Meniere's disease. This work directs future research into this topic.

S. Shi, et al., **3D-real IR MRI of Meniere's disease with partial endolymphatic hydrops**. Am J Otolaryngol, 2019. 40(4): p. 589-593. OBJECTIVES: A three-dimensional inversion-recovery sequence with real reconstruction (3D-real IR) sequence 4h after intravenous gadolinium injection (IV) has been used to visualize the endolymphatic hydrops (ELH) in Meniere's disease (MD). This study was designed to explore the pathology of MD with partial ELH.

METHODS: We collected 338 patients with definite MD, all of whom underwent the IV method. Patients who were found to have partial ELH (vestibular or cochlear) were enrolled. The hearing thresholds of the enrolled patients were analyzed, the regions of interest of the cochlear perilymph and the cerebellum white matter were determined, and the signal intensity ratio in the former to the latter (CC ratio) for both sides in the patients was subsequently evaluated. RESULTS: Of the 338 collected patients with definite MD, 19 patients (5.6%) had unilateral vestibular ELH (N=18) or cochlear ELH (N=1), and 4 patients (1.2%) with bilateral ELH had contralateral cochlear ELH. The CC ratio of the affected side (1.44+/-0.46) was higher than that of the unaffected side (1.15+/-0.33, P<0.05) in the 19 patients with unilateral ELH. Conversely, there was no difference between the ratio of the contralateral side (1.18+/-0.16) and the unaffected side (P>0.05) in the 4 patients with bilateral ELH. CONCLUSIONS: Partial vestibular ELH was more common than partial cochlear ELH in MD. Moreover, vestibular ELH, rather than cochlear ELH, may correlate with the elevated contrast effect in the affected side, which may better reflect the pathologic mechanism of MD.

C. H. Shin, et al., **Management of Meniere's Disease: How Does the Coexistence of Vestibular Migraine Affect Outcomes?** Otol Neurotol, 2019. 40(5): p. 666-673. OBJECTIVE: To report the incidence of vestibular migraine (VM) in patients with Meniere's disease (MD) and investigate whether management outcomes of MD differ by the association of VM. STUDY DESIGN: Retrospective cohort study. SETTING: Tertiary care academic center. PATIENTS: MD patients (n = 251) with/without VM who were managed for 5 years in a dizziness clinic. MAIN OUTCOME MEASURES: Influence of VM on management outcomes and hearing at the latest follow-up in stepwise management options. RESULTS: Incidence of VM was 35% in MD patients. VM was more common in women than men (40 vs. 22%) and in probable MD than definite MD (43 vs. 29%). Bilateral MD was more frequent with coexistence of VM than without VM in definite MD (14 vs. 0%) as well as probable MD (24 vs. 7%). At the latest follow-up, preventive medications were effective in controlling vertigo in most (80%) patients (74%/90% in definite/probable MD). Additional intratympanic steroids were required in 16% (20%/10% in definite/probable MD) and intratympanic gentamicin or surgeries in 9 (6%) patients with intractable MD. The percentage of intractable MD did not differ with coexistence of VM, though definite MD showed a significantly higher percentage of intractable MD than probable MD (6 vs. 0%, respectively, p = 0.002). Worsening hearing was more frequent in definite MD than probable MD (19 vs. 4%), and association of VM did not influence the incidence of worsening hearing. CONCLUSIONS: Coexistence of VM was about 30 to 40% in definite and probable MD, especially frequent in bilateral MD (77%) and women with probable MD (50%), requiring identification of coexisting VM while managing MD patients. Management outcomes and worsening hearing in MD patients are not dependent on the coexistence of VM, when both are managed.

S. Skarp, et al., **Whole-exome sequencing suggests multiallelic inheritance for childhood-onset Meniere's disease**. Ann Hum Genet, 2019. 83(6): p. 389-396. The genetic background of Meniere's disease (MD) was studied in one patient with childhood-onset MD and his grandfather affected with middle age-onset MD. Whole-exome sequencing was performed and the data were compared to 76 exomes from unrelated subjects without MD. Thirteen rare inner ear expressed variants with pathogenic estimations were observed in the case of childhood-onset MD. These variants were in genes involved in the formation of cell membranes or the cytoskeleton and in genes participating in cell death or gene-regulation pathways. His grandfather shared two of the variants: p.Y273N in HMX2 and p.L229F in TMEM55B. HMX2 p.Y273N was considered the more likely candidate for MD, as the gene is known to affect both hearing and vestibular function. The variant in the HMX2 gene may

affect inner ear development and structural integrity and thus might predispose to the onset of MD. As there was a significant difference in onset between the patients, an accumulation of defects in several pathways is probably responsible for the exceptionally early onset of the disease, and the genetic etiology of childhood-onset MD is most likely multifactorial. This is the first molecular genetic study of childhood-onset MD.

M. J. Suh, et al., **Clinical Characteristics of Bilateral Meniere's Disease in a Single Asian Ethnic Group**. Laryngoscope, 2019. 129(5): p. 1191-1196. OBJECTIVES/HYPOTHESIS: To identify the clinical characteristics of patients with bilateral Meniere's disease (MD) in an Asian population. STUDY DESIGN: Cross-sectional retrospective study. METHODS: We compared the clinical features of bilateral MD (BMD) and unilateral MD (UMD) in 320 Asian patients with single ethnicity. Demographic variables; age of onset; inner ear function; the coexistence of related disorders such as vestibular migraine, delayed MD, systemic autoimmune diseases, and familial MD; and prognoses were analyzed and compared. RESULTS: The overall prevalence of BMD was 5.6%. The mean age of disease onset was 40.3 +/- 14.8 and 47.0 +/- 14.1 years for patients with BMD and UMD, respectively (P = .07). Demographic variables were not significantly different between patients with BMD and UMD (P > .05). Inner ear function, evaluated by hearing thresholds, caloric tests, and cervical vestibular evoked myogenic potentials, was significantly more deteriorated in the first involved ear of patients with BMD than in the second involved ear or the affected side of patients with UMD (P < .05). Among the comorbid conditions, only the prevalence of delayed MD was significantly higher in patients with BMD than in patients with UMD. Systemic autoimmune disease was found in only three patients with UMD. There was no significant prognostic difference between patients with UMD and BMD (P > .05). CONCLUSIONS: A low prevalence of BMD, a higher frequency of delayed MD in BMD patients, and a low frequency of systemic autoimmune diseases in both UMD and BMD patients are significant findings in an Asian population. LEVEL OF EVIDENCE: 4 Laryngoscope, 129:1191-1196, 2019.

S. Sun, et al., **Solute carrier family 4 member 1 might participate in the pathogenesis of Meniere's disease in a murine endolymphatic hydrop model**. Acta Otolaryngol, 2019. 139(11): p. 966-976. Background: To date, the pathogenesis of Meniere's disease (MD) remains unclear. Previous research found that the SLC4A1 gene significantly down-regulated. Aims: This study sought to understand the effect of SLC4A1 on the pathogenesis of MD. ELH C57 mice models were induced by intraperitoneal injection of AVP. Material and methods: The mRNA expression levels of SLC4A1, SLC4A10 and SLC26A4 were monitored by real-time quantitative PCR, the protein expression levels of SLC4A1 were monitored by immunoblotting and immunofluorescence before and after the ELH. DIDS is an inhibitor of SLC4A1. The expression levels of SLC4A1 were also monitored in the AVP + DIDS group. Results: We successfully established the model of ELH after applied AVP. The results of HE staining showed displacement of Reissner's membrane with bulge to scala vestibule in ears of the AVP group. Cochlea/ELS SLC4A1 protein and SLC4A1, SLC4A10, SLC26A4 mRNA expressions were reduced significantly in C57 mice of the AVP group. The SLC4A1 protein expression levels and SLC4A1, SLC4A10, SLC26A4 mRNA expression levels declined more obvious in the cochlea and ELS in C57 mice of the AVP + DIDS group. Conclusions and significance: SLC4A1 was a protective factor in the pathogenesis of MD, but the mechanisms were unknown.

R. Teggi, et al., **Endolymphatic hydrops and ionic transporters: genetic and biohumoral aspects**. J Neurol, 2019. 266(Suppl 1): p. 47-51. Meniere's disease (MD) is an inner ear disorder, characterized by a burden of symptoms, probably arising from the interplay of

genetic and environmental factors. In this brief review, we consider the role of ion channels and transporters in the pathophysiology of MD, focusing on genetic and biohumoral aspects. Pathophysiological mechanisms related to altered concentrations of ions in the endolymph include altered osmotic pressure leading to hydrops and/or immunomodulatory effects of K(+) and Endogenous Ouabain (EO) concentrations in the inner ear. Aquaporins 1-5 (AQPs) have been found in the inner ear; AQP2 is the only isoform controlled by a hormone, namely, vasopressin (antidiuretic hormone, ADH). Genetic studies on AQPs have provided inconclusive results. Recently, two genetic polymorphisms have been associated with MD: rs3746951, a missense variant (Gly180Ser) in the Salt-Inducible Kinase-1 (SIK1) gene and rs487119, an intronic variant of gene SLC8A1 coding for a Na(+),Ca(++) exchanger (NCX-1). EO is a hormone released by the midbrain and adrenal glands. It controls the constitutive capacity of modulating Na(+),K(+)-ATPase activity. Higher plasma levels of EO have been found in MD subjects compared to a control group.

O. J. Ungar, et al., **Optimal Head Position Following Intratympanic Injections of Steroids, As Determined by Virtual Reality**. Otolaryngol Head Neck Surg, 2019: p. 194599819878699. OBJECTIVES: To study optimal head position after intratympanic steroid injections to enhance drug bioavailability. STUDY DESIGN: Application of virtual and in vitro models of the intratympanic anatomy. SETTING: The surgical 3-dimensional printing laboratory of a tertiary academic medical center. SUBJECTS AND METHODS: A high-resolution computerized tomographic scan of healthy temporal bone and surrounding soft tissue was segmented and reconstructed to a 3-dimensional model. The tympanic membrane was perforated in the posterior-inferior quadrant. Methylene blue-stained 10-mg/mL dexamethasone was administered to the middle ear cleft, after which a 3-dimensional rotation in space was performed to hypothesize the optimal position in relation to gravity. The same stereolithography file used for the actual model was used for a digital virtual liquid flow simulation. The optimal head position was defined as the one with the maximum vertical distance between the round window membrane and the plane of the aditus ad antrum and eustachian tube orifice. RESULTS: The virtual model yielded the following position of the head as optimal: 53 masculine rotation away from the injected ear in the vertical axis (yaw), 27 masculine rotation toward the noninjected ear in the longitudinal axis (roll), and 10 masculine neck extension in the transverse axis (pitch). CONCLUSIONS: Virtual imaging determined that 53 masculine and 27 masculine yaw and roll, respectively, away and 10 masculine pitch were the optimal position for drug delivery after intratympanic injection to the middle ear and that an erect head position provided optimal passage of steroids from the middle ear to the inner ear.

P. Wang, et al., **Subcellular Abnormalities of Vestibular Nerve Morphology in Patients With Intractable Meniere's Disease**. Front Neurol, 2019. 10: p. 948. Objective: Few studies so far have focused on the retrocochlear lesions in Meniere's disease (MD). This study aims to investigate pathological alterations in the central portion of the vestibular nerve (VN) in patients with intractable Meniere's disease (MD) and to explore retrocochlear lesions and their relationship with disease severity. Methods: Eight MD patients with refractory vertigo received vestibular neurectomy via a retrosigmoid or translabyrinthine approach. Segments of VN were carefully removed and immediately fixed for histopathological examination. Five VN specimens were examined by light microscopy after hematoxylin/eosin staining; three specimens were extensively analyzed using transmission electron microscopy, to identify VN ultrastructural lesions. Correlations between lesions and patient clinical characteristics were examined. Results: Histopathological examination revealed evidence of various types of chronic VN impairment, including the formation of corpora amylacea (CA), axon atrophy, and severe damage to the myelin sheath. Electron microscopy revealed membranous whorls

within dilated Schmidt-Lanterman incisures, the formation of myeloid bodies, dysmyelination, and demyelination. Unexpectedly, we observed a positive correlation between the density of CA in VN tissue and the duration of disease, as well as the degree of hearing impairment, independent of age. Conclusion: Our findings indicate that deformation of subcellular organelles in the central portion of the VN is one of the key pathological indicators for the progressive severity and intractability of vertigo and support a vestibular nerve degeneration.

M. S. Welgampola, et al., **Dizziness demystified**. Pract Neurol, 2019. Four vestibular presentations caused by six different disorders constitute most of the neuro-otology cases seen in clinical practice. 'Acute vestibular syndrome' refers to a first-ever attack of acute, spontaneous, isolated vertigo and there are two common causes: vestibular neuritis / labyrinthitis and cerebellar infarction. Recurrent positional vertigo is most often caused by benign paroxysmal positional vertigo and less commonly is central in origin. Recurrent spontaneous vertigo has two common causes: Meniere's disease and vestibular migraine. Lastly, chronic vestibular insufficiency (imbalance) results from bilateral, or severe unilateral, peripheral vestibular impairment. These six disorders can often be diagnosed on the basis of history, examination, audiometry, and in some cases, basic vestibular function testing. Here we show that most common neuro-otological problems can be readily managed by general neurologists.

P. H. Wu, et al., **Prediction of Unilateral Meniere's Disease Attack Using Inner Ear Test Battery**. Ear Hear, 2019. OBJECTIVES: In the clinical setting, a variety of inner ear test results are obtained from patients with unilateral Meniere's disease (MD). In this study, the authors use inner ear test results as parameters to illustrate the relationship between inner ear function and vertigo attack frequency. DESIGN: We retrospectively enrolled 50 unilateral MD patients. In addition to clinical symptoms, the results of pure-tone audiometry and caloric, acoustic cervical vestibular-evoked myogenic potential (cVEMP), galvanic cVEMP, vibratory ocular VEMP (oVEMP), and galvanic oVEMP tests were collected via chart review. The multiple linear regression method was used to examine which independent variables have a statistically significant influence on vertigo attacks. RESULTS: In affected ears, the abnormal rate of the caloric, acoustic cVEMP, galvanic cVEMP, vibratory oVEMP, and galvanic oVEMP tests was 74%, 76%, 48%, 34%, and 30%, respectively. According to the regression model, the abnormal galvanic cVEMP response and abnormal galvanic oVEMP response had significantly negative correlations with the frequency of vertigo attacks after logarithmic transformation. A predictive model for disease attack frequency using significant parameters and their regression coefficients was proposed: Log10 (predicted vertigo attack frequency) = 0.25+ 0.56 x (galvanic cVEMP) +0.37 x (galvanic oVEMP). CONCLUSIONS: Using the proposed model with galvanic VEMP, clinicians could develop better strategies to manage vertigo attacks in patients with MD.

W. J. Wu, et al., **[Interpretation of international consensus on treatment of Meniere's disease]**. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi, 2019. 33(6): p. 515-516;524. Summary The international consensus (ICON) on the treatment of Meniere's disease was presented in the last IFOS Congress in 2017. This article interpreted the main contents of the consensus combined with other guidelines of Meniere's disease. It discussed the prinCIples of clinical treatment of Meniere's disease and treatment process, which provided recommendations for the treatment selection.

M. Xu, et al., **[Evaluation of vestibular evoked myogenic potential, caloric test and cochlear electrogram in the diagnosis of Meniere's disease]**. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke

Za Zhi, 2019. 33(8): p. 704-708. Objective:The aim of this study is to evaluate the diagnostic value of vestibular-evoked myogenic potential cVEMP and oVEMP, caloric test, and cochlear electrogram EcochG in patients with Meniere's disease MD and non-Meniere's disease. Method:Sixty-four patients 64 ears with Unilateral Meniere's disease were enrolled in the study group MD group, and 127 cases254 ears of non-Meniere's disease patients as non-MD group, including vertigo migraine in 40 cases, benign paroxysmal positional vertigo in 48 cases, benign recurrent vertigo in 13 cases, vestibular paroxysmia in 3 cases, vestibular neuritis in 5 cases and other undiagnosed vertigo in 18 cases. Both group undertake cVEMP, oVEMP, caloric test and ECochG. Use Medcale software to draw ROC curve of ECochG and calculate the area under curveAUC, Jordan index and optimal diagnostic cut-off points. Make the cut-off point as the point of -SP/AP, then evaluate the sensitivity, specificity, positive predictive valuePPV, negative predictive valueNPV and diagnostic accuracy of cVEMP, oVEMP, caloric test and ECochG in MD group and non-MD group. Result:The AUC of ECochG ROC curve was 0.74, the Jordan index was 0.47 and the cut-off point was 0.4. The sensitivity and specificity of cVEMP62% and 68%, oVEMP61% and 53% and caloric test53% and 57% were all below ECochG65% and 78%. The positive predictive value and of ECochG was the highest61.9%, the negative predictive value of cVEMP was highest87.5%. The diagnostic accuracy of ECochG was highest74%, followed with cVEMP67%, oVEMP55% and caloric test56%. Conclusion:Compared with the vestibular function tests, the sensitivity, specificity, diagnostic accuracy and NPV were all higher in ECochG, and the diagnostic benefit can be maximized when -SP/AP value>0.4. So the value of single vestibular function examination in the diagnosis of Meniere's disease is limited. The diagnosis of MD still requires a comprehensive evaluation in combination with medical history, audiological tests and vestibular function examinations.

H. R. Yu, et al., **[The effect of surgical treatment on Meniere's disease]**. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi, 2019. 33(6): p. 501-504. Objective:To compare functional outcomes after different surgical procedures in treatment of patients with Meniere's disease. Method:Patients with Meniere's disease were categorized into different groups mainly based on pure-tone average and functional level scale. Individualized surgical procedure was provided including endolymphatic sac shunt or decompression (ELSS), vestibular neurectomy (VN), labyrinthectomy (LC), semicircular canals plugging (SCP) and endolymphatic duct blockage (EDB). Result:Vertigo control rate of Grade A and B was 78.4% in patients with ELSS, 100.0% with VN, 100.0% with LC, 87.0% with SCP and 86.4% with EDB, respectively. Hearing was preserved with ELSS, VN and EDB postoperatively (P>0.05). But there was a significant hearing loss after SCP (P<0.05). Postoperatively, the QOL score improved significantly in each group (P<0.01). There were CSF leakage in 4 cases, temporary facial paralysis in 1 case, intracranial infection in 1 case, and abdominal hematoma in 5 cases in VN group after surgeries. None of the above complications occurred in other groups. Conclusion:Surgical Treatment choice for patients with Meniere's disease depends on several factors. The functional outcomes after different surgeries are generally satisfying. Residual hearing can be preserved effectively and the quality of life can be improved greatly. VN can effectively eradicate vertigo and preserve residual hearing, however, there is still a risk of some complications with this procedure. As for VN, retrolabyrinthine approach is more advantageous compared with retrosigmoid sinus approach.

Y. J. Zhou, et al., **Are Meniere's disease patients with otolith organ impairment more likely to have balance dysfunction?** Acta Otolaryngol, 2019. 139(11): p. 977-981. Background: Patients with Meniere's disease (MD) may present with peripheral vestibular end organ dysfunction and balance dysfunction. Objective: This study aimed to compare the results of vestibular evoked myogenic potential (VEMP) tests with those of the sensory organization

test (SOT) in patients with MD to determine whether they are correlated. Material and methods: In total, 132 patients with unilateral MD were evaluated using an audiometric test, the SOT, a caloric test and VEMP tests. Results: Cervical VEMP and ocular VEMP tests were conducted in 132 patients with MD, and the response rates of the affected side were lower than those of the unaffected side. The composite score, C5(ES), and C6(ES) of the SOT were significantly decreased in patients with no VEMP responses compared to those with VEMP responses. Conclusions and significance: MD patients with no VEMP responses are more likely to develop balance impairment than those with VEMP responses. MD patients with otolith organ impairment may therefore have balance disorders, and should exercise caution to prevent falls and subsequent injuries.

R. T. Zhu, et al., **The Interrelations Between Different Causes of Dizziness: A Conceptual Framework for Understanding Vestibular Disorders**. Ann Otol Rhinol Laryngol, 2019. 128(9): p. 869-878. BACKGROUND: According to population-based studies that estimate disease prevalence, the majority of patients evaluated at dizziness clinics receive a single vestibular diagnosis. However, accumulating literature supports the notion that different vestibular disorders are interrelated and often underdiagnosed. OBJECTIVE: Given the complexity and richness of these interrelations, we propose that a more inclusive conceptual framework to vestibular diagnostics that explicitly acknowledges this web of association will better inform vestibular differential diagnosis. METHODS: A narrative review was performed using PubMed database. Articles were included if they defined a cohort of patients, who were given specific vestibular diagnosis. The interrelations among vestibular disorders were analyzed and placed within a conceptual framework. RESULTS: The frequency of patients currently receiving multiple vestibular diagnoses in dizziness clinic is approximately 3.7% (1263/33 968 patients). The most common vestibular diagnoses encountered in the dizziness clinic include benign paroxysmal positional vertigo (BPPV), vestibular migraine, vestibular neuritis, and Meniere's disease. CONCLUSIONS: A review of the literature demonstrates an intricate web of interconnections among different vestibular disorders such as BPPV, vestibular migraine, Meniere's disease, vestibular neuritis, bilateral vestibulopathy, superior canal dehiscence syndrome, persistent postural perceptual dizziness, anxiety, head trauma, and aging, among others.

J. Zou, **Autoinflammatory characteristics and short-term effects of delivering high-dose steroids to the surface of the intact endolymphatic sac and incus in refractory Meniere's disease**. J Otol, 2019. 14(2): p. 40-50. Objective: To investigate immune-related genetic background in intractable Meniere's disease (MD) and the immediate results of a novel therapy by delivering steroids to the surface of the intact endolymphatic sac (ES) and incus in a sustainable manner. Case report and methods: Candidate genes involved in immune regulation were sequenced using a next-generation sequencing method in a patient with intractable MD. Mutations were confirmed using the Sanger sequencing method. The ES was exposed, and gelatin sponge particles were immersed in high-dose methylprednisolone solution and placed onto the surface of ES. "L"-shaped gelatin sponge strips were immersed in dexamethasone solution and served as a guiding device for the steroids by touching the incus and gelatin sponge particles on the surface of the ES. Gelatin sponge particles immersed in dexamethasone solution were placed around the gelatin sponge strips and sealed using fibrin glue. Results: Autoinflammation in the refractory MD case was indicated by genotype, including novel heterozygous mutations of PRF1, UNC13D, SLC29A3, ITCH, and JAK3, as well as phenotype. The vertigo was fully relieved immediately after operation. Tinnitus and aural fullness were resolved 3 weeks after operation, whereas hearing improved in 2 mon postoperation. No recurrence was noted during the 5-monfollow-up, and the final MRI supported the novel therapeutic hypothesis. Conclusion: Autoinflammation

was involved in a refractory MD. This novel therapy, which involves the delivery of steroids to the surface of the intact ES and incus, is effective in relieving vertigo and tinnitus and improves hearing function of refractory MD.

A. Zwergal, et al., **Advances in pharmacotherapy of vestibular and ocular motor disorders**. Expert Opin Pharmacother, 2019. 20(10): p. 1267-1276. INTRODUCTION: Vertigo and dizziness are common chief complaints of vestibular and ocular motor disorders (lifetime prevalence 30%). Treatment relies on physical, pharmacological, psychological and rarely surgical approaches. Eight groups of drugs are currently used in vestibular and ocular motor disorders, namely anti-vertiginous, anti-inflammatory, anti-meniere's, anti-migrainous medications, anti-depressants, anti-convulsants, aminopyridines and agents that enhance vestibular plasticity. AREAS COVERED: The purpose of this review is to summarize the pharmacological characteristics and clinical applications of medications that are used for peripheral, central and functional vestibular and ocular motor disorders. The level of evidence for the respective drugs is described alongside the pathophysiological premises supporting their use. The authors place particular focus on translation and back-translation in vestibular pharmacological research and the repurposing of known drugs for new indications and rare disorders. EXPERT OPINION: The use of drugs in vestibular and ocular motor disorders is often based on open-label, non-controlled studies and expert opinion. In the future, strong evidence derived from RCTs is needed to support the effectiveness and tolerability of these therapies in well-defined vestibular and ocular motor disorders. Vestibular pharmacological research must be guided by a better understanding of the molecular targets relevant in the pathophysiology of vestibular and ocular motor disorders.