M. Abouzari, et al., **Successful treatment of a child with definite Meniere's disease with the migraine regimen**. Am J Otolaryngol, 2019. Emerging evidence suggests substantial overlap between the symptoms of Meniere's disease (MD) and migraine-related cochlear/vestibular disorders. We report a 5-year-old girl with a 6-month history of left-sided hearing loss followed by daily episodes of vertigo, headache, and vomiting who met the criteria for definite MD. The patient became symptom-free and gained near normal hearing levels after starting on a 6-week migraine diet/lifestyle regimen with riboflavin and magnesium. We believe that the symptoms of MD may be primarily due to a vestibular migraine phenomenon. Pediatric MD patients may benefit from migraine lifestyle/dietary changes with control of both cochlear and vestibular symptoms.

P. L. M. Albernaz, **Meniere's Disease and Disorders of the Carbohydrate Metabolism Involving the Inner Ear**. Int Arch Otorhinolaryngol, 2019. 23(2): p. 218-220. Introduction Meniere's disease was described in 1861, but there are still uncertainties regarding its pathophysiology and treatment. Endolymphatic hydrops is recognized as a fundamental pathological characteristic of the disease, as a result of an inadequate absorption of the endolymph. A milder type of endolymphatic hydrops results from an altered chemical composition of the endolymph, due to disorders of the carbohydrate metabolism. Objective To describe the association of both types of hydrops in patients with Meniere disease. Methods This was a retrospective study of 98 patients with Meniere's disease, 62 of whom also presented disorders of the carbohydrate metabolism, and 5 patients with delayed endolymphatic hydrops, 2 of whom also presented disorders of the carbohydrate metabolism. Results The follow-up of these patients showed that the correction of the metabolic disorders may help in the clinical treatment of Meniere's disease and of delayed endolymphatic hydrops, but this does not happen in the more severe types of the diseases. Conclusion Patients with Meniere's disease may present simultaneous disorders of the carbohydrate metabolism, affecting the inner ear. The correction of these disorders helps the clinical treatment but does not preclude the progression of the more severe cases of Meniere disease.

A. Attye, et al., **The vestibular aqueduct sign: Magnetic resonance imaging can detect abnormalities in both ears of patients with unilateral Meniere's disease**. J Neuroradiol, 2018. BACKGROUND AND PURPOSE: In patients with Meniere's disease (MD), saccular hydrops can only be studied by magnetic resonance imaging (MRI) at a late stage when the disease is already responsible for moderate to severe hearing loss. However, these patients may also present vestibular aqueduct (VA) abnormalities. MATERIALS AND METHODS: In this prospective study (38RC14.428 for healthy subjects/38RC15.173 for patients), imaging was carried out on a 3T MRI scanner. Twenty healthy subjects (13 women, median age 53.5 [52.2-66.7]) and twenty MD patients (9 women, median age 54.5 [52-66.7]) had MRI scans with 3D-FLAIR sequences without injection, then 4 hours after a single intra-venous dose of contrast agent. Two radiologists independently ranked the morphology of the VA in the healthy subjects and in MD patients, using a three-level score (completely visible, discontinuous and not visible). Each subject was then graded, based on both the VA's appearance and on saccular hydrops presence. Inter-reader agreement tests were performed. RESULTS: In controls and patients, VA modifications were symmetrical without significant difference between the symptomatic and asymptomatic ears. The presence of at least one ear with discontinuous VA showed a correlation with clinical MD ($P < 0.001$) with a sensitivity of 90%. Ten patients had saccular hydrops, but only in the symptomatic ears. The evaluation of VA did not differ between MRI, both within MRI series or between the two radiologists (kappa without and with contrast agent = 0.9 and 0.92 respectively). CONCLUSION: Analysis of the vestibular aqueduct by MRI detects abnormalities in both ears of patients with unilateral MD.

D. P. Ballard, et al., **Quality-of-Life Outcomes following Surgical Treatment of Meniere's Disease: A Systematic Review and Meta-analysis**. Otolaryngol Head Neck Surg, 2019. 160(2): p. 232-238. OBJECTIVE: Several surgical interventions are offered to patients with Meniere's disease (MD) who fail medical management. Although outcomes have historically been reported according to American Academy of Otolaryngology-Head and Neck Surgery guidelines, patient-reported outcome measures

(PROMs) are increasingly used to evaluate treatments. This study reviews PROMs used to assess surgical treatments for MD and compares the effect of each intervention based on PROM scores. DATA SOURCES: PubMed, EMBASE, CINAHL, and Web of Science. REVIEW METHODS: This is a systematic review and meta-analysis of English-language studies that reported PROMs for surgical treatments of MD. Two independent investigators assessed study eligibility, rated the quality using Methodological Index for Non-Randomized Studies (MINORS), and abstracted data for comparative analysis. A random-effects model was used for meta-analysis of pooled data. RESULTS: Of 148 unique studies identified, 11 satisfied inclusion criteria. The Meniere's Disease Outcome Questionnaire (MDOQ) was the most commonly used survey. Interventions included intratympanic gentamicin, vestibular nerve section, endolymphatic sac surgery, and labyrinthectomy. Pooled analysis of 8 studies that used the MDOQ instrument demonstrated statistically significant improvements in quality of life but did not identify a difference between destructive and nondestructive procedures. CONCLUSION: Although our review shows significant improvements in PROM scores for both destructive and nondestructive interventions, there was no significant difference noted between treatment types. We cannot draw conclusions regarding the comparative effectiveness of specific interventions, and the results do not account for placebo effects or the natural history of the disease. Further investigation with randomized controlled trials should be considered in future studies.

S. Becker-Bense, et al., **Balanced sex distribution in patients with Meniere's disease**. J Neurol, 2019.

A. Bernaerts, et al., **The value of four stage vestibular hydrops grading and asymmetric perilymphatic enhancement in the diagnosis of Meniere's disease on MRI**. Neuroradiology, 2019. 61(4): p. 421-429. PURPOSE: There is still a clinical-radiologic discrepancy in patients with Meniere's disease (MD). Therefore, the purpose of this study was to investigate the reliability of current MRI endolymphatic hydrops (EH) criteria according to Barath in a larger study population and the clinical utility of new imaging signs such as a supplementary fourth low-grade vestibular EH and the degree of perilymphatic enhancement (PE) in patients with Meniere's disease (MD). METHODS: This retrospective study included 148 patients with probable or definite MD according to the 2015 American Academy of Otolaryngology, Head and Neck Surgery criteria who underwent a 4-h delayed intravenous Gd-enhanced 3D-FLAIR MRI between January 2015 and December 2016. Vestibular EH, vestibular PE, cochlear EH, and cochlear PE were reviewed twice by three experienced readers. Cohen's Kappa and multivariate logistic regression were used for analysis. RESULTS: The intra- and inter-reader reliability for the grading of vestibular-cochlear EH and PE was excellent (0.7 < kappa < 0.9). The two most distinctive characteristics to identify MD are cochlear PE and vestibular EH which combined gave a sensitivity and specificity of 79.5 and 93.6%. By addition of a lower grade vestibular EH, the sensitivity improved to 84.6% without losing specificity (92.3%). Cochlear EH nor vestibular PE showed added-value. CONCLUSIONS: MRI using vestibular-cochlear EH and PE grading system is a reliable technique. A four-stage vestibular EH grading system in combination with cochlear PE assessment gives the best diagnostic accuracy to detect MD.

G. Bier, et al., **In vivo Assessment of an Endolymphatic Hydrops Gradient Along the Cochlea in Patients With Meniere's Disease by Magnetic Resonance Imaging-A Pilot Study**. Otol Neurotol, 2018. 39(10): p. e1091-e1099. OBJECTIVE: To assess three strategies for evaluation and description of potential endolymphatic hydrops (EH) gradients along the cochlea in patients with Meniere's disease. STUDY DESIGN: Prospective observational study. METHODS: Ten patients with definite Meniere's disease revealed by magnetic resonance imaging were included in this prospectively conducted pilot study. The presence of cochlear endolymphatic hydrops as well as a potential hydrops gradient along the cochlea were subjectively evaluated by two readers. Furthermore, both readers performed planimetric measurements of the relative extent of endolymphatic hydrops in the cochlear turns for calculation of an apico-basal-index (ABI) and an average gradient slope of the endolymphatic hydrops. These models were correlated with the available pure tone audiometry (PTA). RESULTS: Qualitatively, 13 of 16 inner ears presented an apical EH distribution. The median

ABI was 1.69 for patients with low-tone hearing loss and 1.17 for patients with a flat PTA curve (p = 0.03). The median EH slope was 7.44 and correlated with the steepness of the PTA (rho = 0.583; p = 0.018). The subjective analysis and the slope model were best fit for prediction of a low-tone hearing loss type with sensitivities of 100% (specificity, 42.86%) and 88.9% (specificity, 71.4%), respectively. The inter-reader agreement in all three approaches was considered substantial to perfect. CONCLUSION: The presented qualitative approach and the slope model represent reliable methods for the description of a potential EH gradient along the cochlea. Furthermore, the average EH steepness along the cochlea correlates with the type of hearing loss.

D. J. Brown, et al., **Response of the inner ear to lipopolysaccharide introduced directly into scala media**. Hear Res, 2018. 370: p. 105-112. In an attempt to develop an animal model of immune mediated Meniere's disease, we have injected lipopolysaccharide (LPS) directly into scala media of guinea pigs and monitored functional and morphological changes over a period of 6 weeks. Depending on the concentration of LPS, changes ranged from moderate-to-severe hearing loss and endolymphatic hydrops with minimal cellular infiltrate or fibrosis, to dense cellular infiltration that filled the scalae. Interestingly, higher concentrations of LPS not only induced severe cellular infiltration, hydrops, and hearing loss, but also a substantial enlargement of the endolymphatic duct and sac. Moreover, LPS injections into perilymph failed to induce hydrops, yet still resulted in cellular infiltration and fibrosis in the cochlea. This suggests that chronic hydrops resulting from an immune challenge of the cochlea may not be due to blockage of the endolymphatic duct and sac, restricting fluid absorption. Furthermore, injecting antigen into endolymph may produce chronic immune-mediated hydrops, and provide a more promising animal model of Meniere's, although animals did not display signs of vestibular dysfunction, and the hearing loss was relatively severe.

A. Canale, et al., **Comparison of VEMPs, VHIT and caloric test outcomes after vestibular neurectomy in Meniere's disease**. Auris Nasus Larynx, 2018. 45(6): p. 1159-1165. OBJECTIVE: Selective unilateral vestibular neurectomy (VN) is considered a reliable surgical treatment in case of recurrent vertigo in Meniere's disease (MD) because of hearing preservation and a minimally invasive posterior fossa retrosigmoid approach. The present study aimed to assess the quality of life and the long-term vestibular function in patients submitted to yearly follow-up after VN because of intractable MD. METHODS: Retrospective series of 15 MD patients undergoing retrosigmoid VN for recurrent vertigo. Outcome measures included cVEMPs and oVEMPs (cervical and ocular vestibular evoked myogenic potentials), VHIT (Video Head Impulse Test) and caloric test, besides to DHI (Dizziness Handicap Inventory) and PTA (Pure Tone Audiometry). RESULTS: Mean DHI score resulted within normal values in 74% of patients, significantly correlated to the duration of the follow-up. In the operated side, cVEMPs and oVEMPs have not been elicited respectively in 11 patients (73%) and 13 patients (87%), whereas it was not possible to evoke any response at bithermal caloric test in 4 cases. The gain of VOR from VHIT resulted always below normal values after VN except in one patient, who has also undergone an episode of posterior BBPV. The difference between average PTA threshold before and after VN resulted not significant. CONCLUSION: The vestibular outcomes prove VN to be an effective and safe surgery in MD; furthermore, the unexpected occurrence of BPPV after VN can justify the presence of neural anastomosis between the inferior vestibular nerve and the cochlear nerve, allowing to still perceive vestibular symptomatology despite of a proper neurectomy.

A. P. Casani, et al., **Report from a Consensus Conference on the treatment of Meniere's disease with betahistine: rationale, methodology and results**. Acta Otorhinolaryngol Ital, 2018. 38(5): p. 460-467. Meniere's disease is a disorder of the inner ear that causes vertigo, tinnitus, fullness and hearing loss. Although several treatments are available, the success rate is reported to be around 70%, similar to placebo. Betahistine, a weak H1 receptor agonist and an effective H3 receptor antagonist, is frequently prescribed for Meniere's disease, especially to reduce recurrent vertigo attacks. The effects of this drug on hearing and other audiological symptoms remains unclear. Given the inconclusive reports in the literature, we proposed a consensus conference on the use of betahistine in Meniere's disease. The aim was to define best practice criteria for therapy for Meniere's disease, improve clinical suitability and reduce heterogeneity of the therapeutic approach.

The consensus conference on betahistine for Meniere's disease involved a group of Italian experts in vestibular disorders who were asked a series of questions prepared by opinion leaders. The Delphi method, an iterative investigation method, was used to increase consensus. Via a tele-voting system, each participant anonymously evaluated all statements using a Likert 5-point scale. Betahistine was considered useful for the treatment of dizziness and vertigo during the intercritical phase of the disease (87% agreeing answers). However, during the acute phase of the disease betahistine was considered less effective and useful only when associated with other drugs (71% agreement). Similarly, the efficacy of the drug was considered low when used to reduce progressive hearing loss, tinnitus, and ear fullness. The experts advocated the use of betahistine during the intercritical phase of Meniere's disease to reduce the number and severity of vertigo attacks. Its use seems to be at low risk of major side effects.

A. P. Casani, et al., **Good Clinical Approach: Delphi Consensus for the Use of Betahistine in Meniere's Disease**. Int J Otolaryngol, 2018. 2018: p. 5359208. Meniere's disease is a disorder of the inner ear that causes vertigo, tinnitus, fullness, and hearing loss. Several pharmacological treatments are available, but none of them has shown significant results. Betahistine has been largely used but its effect on the main symptoms of Meniere's disease remains unclear. In order to improve clinical appropriateness and to reduce the heterogeneity of the therapeutic approaches for Meniere's disease, we proposed a European Consensus Conference on Betahistine's prescription. A group of European experts in vestibular disorders completed a questionnaire, prepared by opinion leaders, on the use of betahistine in Meniere's disease. The Delphi method was used as an iterative investigation method in order to increase and establish the consensus. While betahistine was considered useful to reduce the number of the vertigo attacks during the intercritical phase of the disease, its use during attacks was considered helpful only when associated with other drugs. Betahistine was not considered useful for preventing hearing loss. The experts support the use of betahistine during the intercritical phase of the disease to reduce the number and severity of vertigo episodes. They also defined the parameters for a good clinical approach to evaluate the efficacy of betahistine treatment for Meniere's disease.

Y. S. Cho, et al., **Usefulness of Intravenous Gadolinium Inner Ear MR Imaging in Diagnosis of Meniere's Disease**. Sci Rep, 2018. 8(1): p. 17562. This study aimed to investigate the usefulness of the intravenous gadolinium enhanced inner ear magnetic resonance imaging (IV-Gd inner ear MRI) in diagnosing Meniere's disease(MD) and find a correlation between the degree of endolymphatic hydrops(EH) and the audiovestibular tests. Total 29 patients diagnosed with unilateral definite MD were enrolled. All patients underwent IV-Gd inner ear MRI and auditory and vestibular function tests such as pure tone audiometry (PTA), electrocochleography (ECoG), cervical vestibular evoked myogenic potential (cVEMP) and caloric test. The hydrops ratio in the cochlea and vestibule were significantly higher in the affected side than the unaffected side ($p < 0.001$). Average pure-tone thresholds for 0.5, 1 k, 2 k, and 4 k Hz correlated significantly with cochlear and vestibular hydrops ($p < 0.01$) in the affected side. When comparing the SP/AP ratio of ECoG with hydrops ratio in the vestibule, the affected and unaffected ears showed a significant difference ($p < 0.05$). Similarly, the results of the caloric test also showed a significant correlation ($p < 0.05$) with relative vestibular hydrops. However, the cVEMP response was not related to the hydrops ratio in the cochlea or vestibule. This study presents pertinent data with appropriate correlations with auditory vestibular functional testing which demonstrates the usefulness of IV-Gd inner ear MRI as a diagnostic method for visualizing the endolymphatic hydrops in MD.

G. Conte, et al., **Three-Tesla magnetic resonance imaging of the vestibular endolymphatic space: A systematic qualitative description in healthy ears**. Eur J Radiol, 2018. 109: p. 77-82. BACKGROUND AND PURPOSE: A detailed knowledge of the normal Magnetic Resonance (MR) anatomy of the vestibular endolymphatic space (ES) could be useful to understand the linkage between endolymphatic hydrops (EH) and Meniere's disease (MD). Our aim was to describe the MR anatomy of the vestibular ES as depicted by MR imaging in healthy ears. METHODS: This report describes a single-center retrospective study. Three readers analyzed the healthy ears of 22

consecutive patients who had undergone MRI for unilateral sudden hearing loss. The readers described the vestibular ES based on a delayed post-contrast 3D-FLAIR sequence according to six well-defined planes, three oblique sagittal (lateral, intermediate and medial) planes and three axial (superior, intermediate and inferior) planes. RESULTS: On sagittal lateral and intermediate planes, we identified the SSC ampulla combined with the utricle in 22/22 ears. On the sagittal medial plane, the saccule was detectable in 15/22 (68%) ears, having a club shape with the long axis oriented cranio-caudally; in 7/22 (32%) ears, the saccule presented an oval/round shape that appeared more conspicuously on the axial intermediate plane. The ES occupied the half superior portion of the vestibule in 22/22 ears, never contacting the round and oval windows. On the axial plane, in 17/22 cases, the ES showed a Y-shaped arrangement, while in 5/22 ears (23%), the ES presented a more globular shape. CONCLUSION: MR imaging represents a valid tool to explore the in vivo anatomy of the vestibular ES and to highlight its variability in normal ears.

N. A. G. de Franca, et al., **High parathyroid hormone levels are associated with poor balance in older persons: A cross-sectional study**. Maturitas, 2019. 121: p. 57-62. OBJECTIVES: A high level of parathyroid hormone (PTH) was recently identified as a risk factor for falling. As balance instability is one of the major risk factors for falls, we aimed to investigate whether high PTH concentrations are associated with poor balance in older persons. STUDY DESIGN: Cross-sectional study with 127 community-dwelling older adults (75% female), aged 65-96 years, at the Falls and Fracture Clinic, Western Health-Sunshine Hospital, Melbourne, Australia. Patients with clinical conditions that could affect balance (e.g. Meniere's disease), denosumab users, and those with advanced kidney failure were excluded. MAIN OUTCOME MEASURES: We assessed dynamic balance by timed "up and go" (TUG)and four-square step tests, and by gait parameters; and static balance by posturography on a force platform. Blood tests provided values of PTH, vitamin D, calcium, albumin, and creatinine. Standard questionnaires were applied to assess clinical condition, medications and nutritional status, and to screen for depression. RESULTS: For dynamic balance, elevated PTH concentrations resulted in increased time to complete the TUG test (beta = 0.13; 95%CI: 0.01-0.26), indicating worse performance. For static balance, increased PTH was associated with increased instability in the center of pressure while standing with eyes closed on a hard surface (beta = 0.38; 95%CI: 0.03-0.73). Both models were controlled for vitamin D, renal function, nutritional and depressive status, age, sex, and number of medications. CONCLUSION: Increasing concentrations of PTH in this population of older persons had an independent negative association with both static and dynamic balance, which could place them at risk of falls. However, longitudinal studies are still required.

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.

A. H. Eckhard, et al., **Inner ear pathologies impair sodium-regulated ion transport in Meniere's disease**. Acta Neuropathol, 2019. 137(2): p. 343-357. Meniere's disease (MD), a syndromal inner ear disease, is commonly associated with a pathological accumulation of endolymphatic fluid in the inner ear, termed "idiopathic" endolymphatic hydrops (iEH). Although numerous precipitating/exacerbating factors have been proposed for MD, its etiology remains elusive. Here, using immunohistochemistry and in situ protein-protein interaction detection assays, we demonstrate mineralocorticoid-controlled sodium transport mechanisms in the epithelium of the extraosseous portion of the endolymphatic sac (eES) in the murine and human inner ears. Histological analysis of the eES in an extensive series of human temporal bones consistently revealed pathological changes in the eES in cases with iEH and a clinical history of MD, but no such changes were found in cases with "secondary" EH due to other otological diseases or in healthy controls. Notably, two etiologically different pathologies-degeneration and developmental hypoplasia-that selectively affect the eES in MD were distinguished. Clinical records from MD cases with degenerative and hypoplastic eES pathology revealed distinct intergroup differences in clinical disease presentation. Overall, we have identified for the first time two inner ear pathologies that are consistently present in MD and can be directly linked to the pathogenesis of EH, and which potentially affect the phenotypical presentation of MD.

M. Fukushima, et al., **Vertical head impulse and caloric are complementary but react opposite to Meniere's disease hydrops**. Laryngoscope, 2018. 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, 2018.

A. Gallego-Martinez, et al., **Excess of Rare Missense Variants in Hearing Loss Genes in Sporadic Meniere Disease**. Front Genet, 2019. 10: p. 76. Meniere's disease (MD) is a clinical spectrum of rare disorders characterized by vertigo attacks, associated with sensorineural hearing loss (SNHL) and tinnitus involving low to medium frequencies. Although it shows familial aggregation with incomplete phenotypic forms and variable expressivity, most cases are considered sporadic. The aim of this study was to investigate the burden for rare variation in SNHL genes in patients with sporadic MD. We conducted a targeted-sequencing study including SNHL and familial MD genes in 890 MD patients to compare the frequency of rare variants in cases using three independent public datasets as controls. Patients with sporadic MD showed a significant enrichment of missense variants in SNHL genes that was not found in the controls. The list of genes includes GJB2, USH1G, SLC26A4, ESRRB, and CLDN14. A rare synonymous variant with unknown significance was found in the MARVELD2 gene in several unrelated patients with MD. There is a burden of rare variation in certain SNHL genes in sporadic MD. Furthermore, the interaction of common and rare variants in SNHL genes may have an additive effect on MD phenotype. This study will contribute to design a gene panel for the genetic diagnosis of MD.

Y. Ghavami, et al., **Evaluating Quality of Life in Patients With Meniere's Disease Treated as Migraine**. Ann Otol Rhinol Laryngol, 2018. 127(12): p. 877-887. OBJECTIVE:: To evaluate the change in quality of life (QOL) of patients with Meniere's disease (MD) after treatment with migraine prophylaxis therapy. METHODS:: Patients with definite MD were given the Meniere's Disease Outcomes Questionnaire-Retrospective (MDOQ-R) after migraine prophylactic therapy to assess QOL. Changes in physical, emotional, and social parameters affected by MD were calculated, along with a global pre- and posttreatment QOL scores. RESULTS:: The MDOQ-R was given to 27 consecutive patients with definite MD. Patients who had at least an 18-month follow-up were included, resulting in 25 questionnaires. The mean change in QOL score was 25 +/- 16 (range, -3 to 55), P = .02. Quality of life was improved in 23 (92%) of the respondents in every metric measured, unchanged in 1 (4%), and poorer in 1 (4%) of patients after migraine prophylaxis treatment. CONCLUSIONS:: Majority of MD patients who had all failed diuretic therapy responded positively to medications used for migraine prophylaxis, as indicated by a significant improvement in QOL. This study may further suggest a correlation between the pathophysiologic basis of disease in MD and vestibular migraine. Patients with MD may be successfully managed with medications intended to treat migraine.

W. P. R. Gibson, **Meniere's Disease**. Adv Otorhinolaryngol, 2019. 82: p. 77-86. This article reviews 3 aspects of Meniere's disease (MD), which have been recently revisited: namely, the pathologic mechanism causing the attacks of vertigo, the clinical diagnosis, and the medical and surgical treatments. The characteristic attacks of vertigo are unlikely to be due to membrane ruptures, so a hypothesis that the vertigo is caused by a volume of endolymph shifting suddenly from the cochlea into the pars superior is suggested. The definite diagnosis according to the American Academy of Otolaryngology HNS 1995 criteria [<citeref rid="ref13">13</citeref>] failed to exclude vestibular migraine sufficiently and a revision in 2015 [<citeref rid="ref14">14</citeref>] has partly addressed this problem but another method which stresses the interaction of the cochlear and vestibular symptoms is described. The treatment of MD has been updated, providing evidence for each popular therapy. Newer treatments using intratympanic medications including steroid solutions and gentamicin are discussed. Finally, the role of cochlear implants is mentioned.

L. Girasoli, et al., **Update on Vertigo in Autoimmune Disorders, from Diagnosis to Treatment**. J Immunol Res, 2018. 2018: p. 5072582. The prevalence of autoimmune diseases has been increasing over the last 20 years. The clinical presentation of this large and heterogeneous group of disorders depends on whether the involvement is organ-specific or non-organ-specific. Dizziness, vertigo, and disequilibrium are common symptoms reported by patients with vestibulocochlear involvement. The association of vertigo and autoimmune diseases has been largely documented, suggesting that autoimmune disorders could be overrepresented in patients with vertigo in comparison to the general population. The aim of this review is to present the recent literature findings in the field of autoimmune-mediated diseases with cochleovestibular involvement, focusing on the clinical presentation, diagnosis, and treatment of immune-mediated inner ear diseases including autoimmune inner ear disease (AIED), Meniere's disease, and bilateral vestibulopathy, as well as of systemic autoimmune diseases with audiovestibular disorders, namely, Behcet's disease, Cogan's syndrome, sarcoidosis, autoimmune thyroid disease, Vogt-Koyanagi-Harada syndrome, relapsing polychondritis, systemic lupus erythematosus, antiphospholipid syndrome, IgG4-related disease, and ANCA-associated vasculitides.

T. Grigol, et al., **Cervical vestibular evoked myogenic potentials and video head impulse test in Meniere disease**. Braz J Otorhinolaryngol, 2019. INTRODUCTION: Meniere's disease is among the most frequent causes of vestibular disorders. Although it is a clinical diagnosis, a better understanding of the pathophysiology and clinical course of the disease through tests would allow improvement in the prognosis and more effective treatments. OBJECTIVES: To describe the results of the cervical vestibular evoked myogenic and video-head impulse test in patients with a defined diagnosis of Meniere's disease and to correlate them with disease duration. METHODS: The sample consisted of 50 participants, of whom 29 comprised the study group and 21 the control group. The

individuals were submitted to a questionnaire, otoscopy, audiometry and vestibular function assessment through the cervical vestibular evoked myogenic potential and video head impulse test. RESULTS: For the video head impulse test, lateral canal gain values below 0.77 were considered abnormal and for the vertical channels, below 0.61. The percentages of normality were 82.76% for lateral, 89.65% for posterior and 91.37% for anterior canals. For the cervical vestibular evoked myogenic potential, the upper limits of normal for latencies were defined as 18.07ms for p13 and 28.47ms for n23; and in the SG, 19.57% showed prolongation of latency of p13 and 4.35% of wave n23, whereas 18.96% did not show biphasic potential. CONCLUSION: For the video head impulse test, a decreased gain of the vestibulo-ocular reflex for the lateral canal was observed, with a higher incidence of overt type corrective saccades compared to the control group. For the cervical vestibular evoked myogenic potential, there was a significant difference between the groups for the inter-amplitude parameter, including for asymptomatic ears. There was no correlation between the results of the tests and disease duration.

E. Grill, et al., **Multicenter data banking in management of dizzy patients: first results from the DizzyNet registry project**. J Neurol, 2018. 265(Suppl 1): p. 3-8. PURPOSE: Comprehensive phenotypical data across countries is needed to understand the determinants, prognosis and consequences of vestibular disease. The registry is a data repository for the members of the European DizzyNet. We report results from a pilot study using data from Turkey and Germany. METHODS: The pilot study included a convenience sample of patients aged 18 or above referred to Ege University Medical School Hospital, Dokuz Eylul University Hospital, Izmir, Turkey, and the German Center for German Center for Vertigo and Balance Disorders, University on Munich, Germany, with symptoms of vertigo or dizziness. Health-related quality of life was assessed with the EQ5-D and the Dizziness Handicap Inventory (DHI). To obtain comparable groups we matched data from the two countries for age, sex and diagnosis by propensity score. RESULTS: We included 80 adult patients, 40 from each country (60% female, mean age 54.1, SD 12.4). Matching was successful. Vestibular migraine (34%) was the most frequent diagnosis, followed by benign paroxysmal positional vertigo (29%) and Meniere's disease (12%). Clinical signs and symptoms were comparable in both countries. Patients from Turkey were more likely to report headaches (65 vs. 32%) and to show gait unsteadiness (51 vs. 5%). Patients from Germany reported significantly higher quality of life and lower values of the DHI score. CONCLUSIONS: Sharing data facilitates research, enhances translation from basic science into clinical applications, and increases transparency. The DizzyNet registry is a first step to data sharing in vestibular research across Europe.

P. Guo, et al., **Quantitative evaluation of endolymphatic hydrops with MRI through intravenous gadolinium administration and VEMP in unilateral definite Meniere's disease**. Eur Arch Otorhinolaryngol, 2019. 276(4): p. 993-1000. PURPOSE: To help clinicians to further understand the significance of vestibular-evoked myogenic potential (VEMP) examinations to diagnose MD and the quantitative relationship between VEMP and MRI in assessing the location and degree of endolymphatic hydrops (EH) in definite Meniere's disease (MD) patients. METHODS: Fifty-six patients with unilateral definite MD participated in this study, which used MRIs through intravenous gadolinium administration (IV-Gd), audiometry, caloric tests and VEMP tests. The VEMP results of 26 healthy volunteers were used as a normal reference value. RESULTS: The participants were found through MRI to have differing degrees of vestibular and cochlear EH. Quantitative comparison of MRI and VEMP results found that the response rates of oVEMP decreased with cochlear EH increasing; the asymmetry ratio (AR) of oVEMP can be used to find whether cochlear EH or not, and the P1-N1 amplitude was lower in the extreme cochlear EH group ($P < 0.01$). The AR of cVEMP was larger in severe vestibular EH group than that of the mild or no vestibular EH group ($P < 0.01$). The correlation between the degree of cochlear EH and the mean PTA threshold was statistically significant ($P < 0.05$). The duration of MD correlated positively with vestibular EH ($P < 0.05$). The abnormal rate of caloric tests was higher in severe vestibular EH group than that of the mild or no vestibular EH group ($P < 0.05$). CONCLUSIONS: The advantages of MRIs by IV-Gd administration were obvious in assessing the location and degree of EH. oVEMP and PTA can be indirectly used to

evaluate the extent of cochlear EH, cVEMP and caloric tests can be used to assess the extent of vestibular EH on the condition of absent MRIs.

R. Gurkov, **Drop attacks, hydrops severity, and disease duration in hydropic ear disease (Meniere's)**. Eur Arch Otorhinolaryngol, 2019. 276(5): p. 1553.

R. Gurkov, et al., **Correction to: Clinical manifestations of hydropic ear disease (Meniere's)**. Eur Arch Otorhinolaryngol, 2019. 276(2): p. 619-620. In the original publication, Fig. 1 was incorrectly published with incomplete legends.

R. Gurkov, et al., **Clinical manifestations of hydropic ear disease (Meniere's)**. Eur Arch Otorhinolaryngol, 2019. 276(1): p. 27-40. INTRODUCTION: Hydropic ear disease, initially described by and named after Prosper Meniere, is one of the most frequent vertigo disorders and one of the most frequent inner ear disorders. It is the syndrome of endolymphatic hydrops which until 2007 could be diagnostically confirmed only by post-mortem histology. In the past, various attempts to formulate clinical diagnostic criteria have been undertaken but were hampered by the inability to ascertain the diagnosis in living patients. With the milestone achievement of endolymphatic hydrops imaging, today the pathology can be ascertained. In this study, we have performed a detailed analysis of the clinical features of hydropic ear disease for the first time by examining a large cohort of patients with morphologically confirmed endolymphatic hydrops using a detailed physician-administered neurotologic face-to-face interview. RESULTS: During a hydropic vertigo attack, the patients report nausea, vomiting, sweating, urge to defecate, urge to urinate, phosphenes, headache, photophobia, phonophobia and even transient loss of consciousness. A third of the patients does not experience auditory symptoms during the vertigo attacks. Vertigo attacks last less than 20 min in more than one-fourth of the patients. Audiometric hearing loss has its greatest diagnostic value at the frequencies of 1 kHz and below. Cochleovestibular symptom onset simultaneity is associated with a high frequency of drop-attacks. Migraine and autoimmune disorders are not associated with hydropic ear disease. CONCLUSION: This study marks the beginning of the clinical characterization of hydropic ear disease. The findings have important implications for the future formulation of clinical diagnostic criteria.

J. P. Harcourt, et al., **Long-Term Follow-Up of Intratympanic Methylprednisolone Versus Gentamicin in Patients With Unilateral Meniere's Disease**. Otol Neurotol, 2019. OBJECTIVES: To determine whether long term (>48 months) symptomatic vertigo control is sustained in patients with Meniere's disease from a previous comparative trial of intratympanic methylprednisolone versus gentamicin, and if the two treatments remain nonsignificantly different at long-term follow-up. STUDY DESIGN: Mail survey recording vertigo frequency in the previous one and six months, further intratympanic treatment received, and validated symptom questionnaires. SETTING: Outpatient hospital clinic setting. PATIENTS: Adult patients with definite unilateral refractory Meniere's disease, who previously received intratympanic treatment in a comparative trial. INTERVENTION: A survey of trial participants who received intratympanic gentamicin (40 mg/mL) or methylprednisolone (62.5 mg/mL). OUTCOME MEASURES: Primary: number of vertigo attacks in the 6 months prior to receiving this survey compared with the 6 months before the first trial injection. Secondary number of vertigo attacks over the previous 1 month; validated symptom questionnaire scores of tinnitus, dizziness, vertigo, aural fullness, and functional disability. RESULTS: Forty six of the 60 original trial patients (77%) completed the survey, 24 from the gentamicin and 22 from the methylprednisolone group. Average follow-up was 70.8 months (standard deviation 17.0) from the first treatment injection. Vertigo attacks in the 6 months prior to receiving the current survey reduced by 95% compared to baseline in both drug groups (intention-to-treat analysis, both $p < 0.001$). No significant difference between drugs was found for the primary and secondary outcomes. Eight participants (methylprednisolone = 5 and gentamicin = 3) required further injections for relapse after completing the original trial. CONCLUSION: Intratympanic methylprednisolone treatment provides effective long-lasting relief of vertigo, without the known inner-ear toxicity associated with gentamicin. There are no significant differences between the two treatments at long term follow-up.

T. Heinemeyer, et al., **Underappreciated Roles of the Translocase of the Outer and Inner Mitochondrial Membrane Protein Complexes in Human Disease**. DNA Cell Biol, 2019. 38(1): p. 23-40. Mitochondria are critical for cellular survival, and for their proper functioning, translocation of approximately 1500 proteins across the mitochondrial membranes is required. The translocase of the outer (TOMM) and inner mitochondrial membrane (TIMM) complexes are major components of this translocation machinery. Through specific processes, preproteins and other molecules are imported, translocated, and directed to specific mitochondrial compartments for their function. In this study, we review the association of subunits of these complexes with human disease. Pathogenic mutations have been identified in the TIMM8A (DDP) and DNAJC19 (TIMM14) genes and are linked to Mohr-Tranebjaerg syndrome and dilated cardiomyopathy syndrome (with and without ataxia), respectively. Polymorphisms in TOMM40 have been associated with Alzheimer's disease, frontotemporal lobar degeneration, Parkinson's disease with dementia, dementia with Lewy bodies, nonpathological cognitive aging, and various cardiovascular-related traits. Furthermore, reduced protein expression levels of several complex subunits have been associated with Parkinson's disease, Meniere's disease, and cardiovascular disorders. However, increased mRNA and protein levels of complex subunits are found in cancers. This review highlights the importance of the mitochondrial import machinery in human disease and stresses the need for further studies. Ultimately, this knowledge may prove to be critical for the development of therapeutic modalities for these conditions.

K. Higashi-Shingai, et al., **Change in endolymphatic hydrops 2 years after endolymphatic sac surgery evaluated by MRI**. Auris Nasus Larynx, 2018. 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.

C. J. Huang, et al., **CASP9 genotype confers gentamicin susceptibility in intratympanic treatment of intractable vertigo caused by Meniere's disease**. Acta Otolaryngol, 2019: p. 1-4. BACKGROUND: Meniere's disease (MD) is a disorder of the inner ear, causing episodes of vertigo. Although surgery is reserved for intractable MD, intratympanic gentamicin (ITG) injection has become an alternative for controlling vertigo. AIMS/OBJECTIVES: To investigate the genetic basis of ITG efficacy. MATERIAL AND METHODS: We hypothesized that single nucleotide polymorphisms (SNPs) affect outcomes in patients with MD who receive ITG injections. Whole-exome sequencing was used to determine variations in coding regions. RESULTS: Multivariate analysis revealed two SNPs, rs1052571 in caspase 9 (CASP9; p = .017) and rs3745274 in cytochrome P450 2B6 (p = .053), which were associated with susceptibility to ITG injections. Only the C-allele in the rs1052571 SNP was significantly associated with susceptibility (p = .027; odds ratio: 5.95; 95% confidence interval: 1.26-28.57, by Fisher's exact test). CONCLUSIONS AND SIGNIFICANCE: Our results elucidated the role of the rs1052571 SNP and provide a genetic perspective on gentamicin efficacy (susceptibility) in treating intractable MD.

M. Hulens, et al., **The link between idiopathic intracranial hypertension, fibromyalgia, and chronic fatigue syndrome: exploration of a shared pathophysiology**. J Pain Res, 2018. 11: p. 3129-3140. Purpose: Idiopathic intracranial hypertension (IICH) is a condition characterized by raised intracranial pressure (ICP), and its diagnosis is established when the opening pressure measured during a lumbar puncture is elevated >20 cm H2O in nonobese patients or >25 cm H2O in obese patients. Papilledema is caused by forced filling of the optic nerve sheath with cerebrospinal fluid (CSF). Other common but underappreciated symptoms of IICH are neck pain, back pain, and radicular pain in the arms and legs resulting from associated increased spinal pressure and forced filling of the spinal nerves with CSF. Widespread pain and also several other characteristics of IICH share notable similarities with characteristics of fibromyalgia (FM) and chronic fatigue syndrome (CFS), two overlapping chronic pain conditions. The aim of this review was to compare literature data regarding the characteristics of IICH, FM, and CFS and to link the shared data to an apparent underlying physiopathology, that is, increased ICP. Methods: Data in the literature regarding these three conditions were compared and linked to the hypothesis of the shared underlying physiopathology of increased cerebrospinal pressure. Results: The shared characteristics of IICH, FM, and CFS that can be caused by increased ICP include headaches, fatigue, cognitive impairment, loss of gray matter, involvement of cranial nerves, and overload of the lymphatic olfactory pathway. Increased pressure in the spinal canal and in peripheral nerve root sheaths causes widespread pain, weakness in the arms and legs, walking difficulties (ataxia), and bladder, bowel, and sphincter symptoms. Additionally, IICH, FM, and CFS are frequently associated with sympathetic overactivity symptoms and obesity. These conditions share a strong female predominance and are frequently associated with Ehlers-Danlos syndrome. Conclusion: IICH, FM, and CFS share a large variety of symptoms that might all be explained by the same pathophysiology of increased cerebrospinal pressure.

R. Hulse, et al., **Peripheral Vestibular Disorders: An Epidemiologic Survey in 70 Million Individuals**. Otol Neurotol, 2019. 40(1): p. 88-95. BACKGROUND: Dizziness is a common complaint in medicine. Nevertheless, there is a lack of valid data concerning the age and gender distribution of dizziness disorders within a larger population. Therefore, the aim of the present study is to undertake a representative epidemiological survey that examines all age groups of an entire population and describes the age and gender distribution of the most common peripheral vestibular disorders. METHODS: A population-based epidemiological survey based on confirmed ICD-10 codes, of an entire national population was performed. The population-based data of 70,315,919 patients were leveraged, as provided by 123 statutory health insurance companies in Germany. Patients of all age groups were analyzed. Outcome measures were age and gender distribution and the prevalence of unspecific vertigo, Meniere's disease, benign paroxysmal positional vertigo, vestibular neuritis, and other peripheral vestibular disorders. RESULTS: The prevalence among the recorded diagnoses was 6.5% (6,461/100,000 individuals), with women (N = 2,973,323; 65.4%) being significantly more frequently affected by vertigo than men (N = 1,570,240; 34.6%; $p < 0.001$). Vertigo is rare in childhood (i.e., up to 10-14 yr of age). Subsequently, the prevalence of the analyzed diseases increases with age, up to a peak between 74 and 94 years. CONCLUSIONS: The results demonstrate that peripheral vestibular disorders are common in a developed country, across all age groups and a specific distribution of these disorders can be identified for every age group and gender. The impact of these disorders on the German healthcare system is currently underestimated.

D. Huppert, et al., **Dizziness and vertigo syndromes viewed with a historical eye**. J Neurol, 2018. 265(Suppl 1): p. 127-133. Seasickness, fear of heights, and adverse effects of alcohol were the major areas where descriptions of vertigo and dizziness were found in Roman, Greek, and Chinese texts from about 730 BC-600 AD. A few detailed accounts were suggestive of specific vestibular disorders such as Meniere's attacks (Huangdi Neijing, the Yellow Thearch's Classic of Internal Medicine) or vestibular migraine (Aretaeus of Cappadocia). Further, the etymological and metaphorical meanings of the terms and their symptoms provide fascinating historical insights, e.g. Vespasian's feelings of dizzy exultations when becoming Emperor (69 AD) after Nero's suicide or the figurative meaning of

German "Schwindel" (vertigo) derived from English "swindle" to express "financial fraud" in the Eighteenth century. The growth of knowledge of the vestibular system and its functions began primarily in the Nineteenth century. Erasmus Darwin, however, was ahead of his times. His work Zoonomia, or The Laws of Organic Life in 1794 described new dizziness syndromes and concepts of sensorimotor control including the mechanism of fear of heights as well as made early observations on positional alcohol vertigo. The latter is beautifully illustrated by the German poet and cartoonist Wilhelm Busch (1832-1908) who also documented the alleviating effect of the "morning after drink". The mechanism underlying positional alcohol vertigo, i.e., the differential gravities of alcohol and endolymph, was discovered later in the Nineteenth century. The first textbook on neurology (Lehrbuch der Nervenkrankheiten des Menschen, 1840) by Moritz Romberg contained general descriptions of signs and symptoms of various conditions having the key symptom of vertigo, but no definition of vestibular disorders. Our current knowledge of vestibular function and disorders dates back to the seminal work of a group of Nineteenth century scientists, e.g., Jan Evangelista Purkinje, Ernst Mach, Josef Breuer, Hermann Helmholtz, and Alexander Crum-Brown.

D. Huppert, et al., **Risk of traffic accidents after onset of vestibular disease assessed with a surrogate marker**. J Neurol, 2019. 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.

D. Huppert, et al., **Dizziness in Europe: from licensed fitness to drive to licence without fitness to drive**. J Neurol, 2018. 265(Suppl 1): p. 9-17. A common European Community driving licence was established in 1980. However, there are major differences among the countries as regards medical conditions that legally affect driving ability. This article discusses various assessment guidelines for dizzy patients. These range from a total absence of specified binding requirements in Finland or regulations open to clinical interpretation in Switzerland, to inappropriately strict regulations in Germany. We focus on requirements for patients with vestibular disorders in Germany which have been in force since 2014. These guidelines stipulate that for group 1 driving licence (private cars < 3.5 t, motorbikes): (1) patients with Meniere's disease (attacks without prodromes) must have had no attacks for 2 years before it is possible to drive again. (2) Patients with vestibular migraine without prodromes must not have had any attacks for 3 years. For a group 1 and group 2 driving licence ("professional driver"): (3) patients with bilateral vestibulopathy as a rule are considered to have a driving disability. Similarly, strict restrictions have been formulated for ocular motor disorders such as downbeat and upbeat nystagmus and for patients with functional (psychosomatic) forms of dizziness such as phobic postural vertigo. The authors represent a working group of the European Dizzynet focusing on the topic "fitness to drive with vertigo and balance disorders". They agree that European guidelines must be revised and harmonized, for some are too strict and the required

dizziness-free intervals are too long; others must be revised, for they are too lax. A common European standard is needed.

K. Hussain, et al., **Restriction of salt, caffeine and alcohol intake for the treatment of Meniere's disease or syndrome**. Cochrane Database Syst Rev, 2018. 12: p. Cd012173. BACKGROUND: Meniere's disease or syndrome is a chronic inner ear disorder that results in sporadic attacks of vertigo, sensorineural hearing loss, aural fullness and tinnitus.There is no definitive treatment for Meniere's disease and treatment options range from dietary modification through medication to surgery.Modification of diet, including restriction of salt, caffeine and alcohol intake, is a management option that is widely recommended to patients with Meniere's as a first-line treatment. There has not previously been a systematic review of this intervention. OBJECTIVES: To assess the effects of dietary restriction of salt, caffeine and alcohol intake in patients with Meniere's disease or syndrome. SEARCH METHODS: The Cochrane ENT Information Specialist searched the Cochrane ENT Trials Register; Central Register of Controlled Trials (CENTRAL); PubMed; Ovid Embase; CINAHL; Web of Science; ClinicalTrials.gov; ICTRP and additional sources for published and unpublished trials. The date of the search was 28 March 2018. SELECTION CRITERIA: Randomised controlled trials of dietary modification, specifically salt, caffeine and alcohol restriction or substitution (or both), compared to no modification of these agents or a placebo intervention, in adult patients with Meniere's disease or syndrome. DATA COLLECTION AND ANALYSIS: We used the standard methodological procedures expected by Cochrane. Our primary outcomes were control of vertigo or decrease in vertigo attacks, and adverse effects. Secondary outcomes included hearing (change in hearing loss or its progression), tinnitus (severity), perception of aural fullness, well-being and quality of life (overall changes), and other adverse effects. We planned to use GRADE to assess the quality of the evidence for each outcome. MAIN RESULTS: We did not identify any studies that met the inclusion criteria for the review. AUTHORS' CONCLUSIONS: There is no evidence from randomised controlled trials to support or refute the restriction of salt, caffeine or alcohol intake in patients with Meniere's disease or syndrome.High-quality research in this field is warranted. The best evidence may come from a randomised controlled trial comparing dietary interventions (e.g. low salt versus general healthy diet advice), using rigorous methodology for patient selection, randomisation and blinding, and strictly adhering to the Barany Society diagnostic criteria. However, this research question might be more pragmatically addressed by using information from carefully constructed patient registries that include information on dietary intake of substances of interest such as salt, caffeine and alcohol. It will be important to address the question of any possible harms or unwanted effects of dietary modification.

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, 2018. 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. Inui, et al., **Relationship between the results of the head-shaking test and short-term prognosis of hearing impairment in patients with unilateral Meniere's disease: A retrospective analysis of 157 cases**. Clin Otolaryngol, 2019.

T. Ito, et al., **Three-Dimensional Magnetic Resonance Imaging Reveals the Relationship Between the Control of Vertigo and Decreases in Endolymphatic Hydrops After Endolymphatic Sac Drainage With Steroids for Meniere's Disease**. Front Neurol, 2019. 10: p. 46. Meniere's disease is a common disease, that presents with recurrent vertigo and cochlear symptoms. The pathology of Meniere's disease was first reported to involve endolymphatic hydrops in 1938. The endolymphatic sac is thought to have a role to keep the hydrostatic pressure and endolymph homeostasis for the inner ear. As a surgery for intractable Meniere's disease, endolymphatic sac drainage with intraendolymphatic sac application of large doses of steroids is performed to control the endolymphatic hydrops and preserve or improve inner ear function. In the present study, to observe the effect of this surgery, we calculated the endolymphatic space size using 3-Tesla magnetic resonance imaging (MRI) 4 h after intravenous injection of gadolinium enhancement at two time points: just before surgery and 2 years after. To reveal the condition of the endolymphatic space, we constructed three-dimensional MR images semi-automatically and fused the three-dimensional images of the total fluid space of inner ear and the endolymphatic space. After fusing the images, we calculated the volume of the total fluid space and endolymphatic space. Two years after surgery, 16 of 20 patients (80.0%) showed relief from vertigo/dizziness and reductions in the ratio of the volume of the endolymphatic size to the total fluid space of inner ear. Endolymphatic sac drainage with intraendolymphatic sac application of large doses of steroids could control vertigo/dizziness and decrease the endolymphatic hydrops. These results indicate that endolymphatic sac drainage is a good treatment option for patients with intractable Meniere's disease. In addition, volumetric measurement of inner ear volume could be useful for confirming the effect of treatments on Meniere's disease.

C. Jerin, et al., **High-Frequency Horizontal Semicircular Canal Function in Certain Meniere's Disease**. Ear Hear, 2019. 40(1): p. 128-134. OBJECTIVES: To characterize video head impulse testing (vHIT) in definitive Meniere's disease and to investigate the relationship between vHIT results and other audiovestibular function tests. DESIGN: Fifty-four patients with certain Meniere's disease, that is, patients with clinically definite Meniere's disease and endolymphatic hydrops visualized by locally enhanced inner ear MR imaging, were recruited for this study. All patients underwent vHIT. The vestibular-ocular reflex gain at 60 ms and refixation saccades were the outcome parameters measured. Saccades were characterized by determining the saccade frequency, their mean latency, and their mean velocity. RESULTS: Seven of 54 patients had bilateral normal vHITs. Clearly pathologically vHITs with decreased gain and refixation saccades were observed in further seven patients. The majority of patients exhibited vHITs with refixation saccades but normal gain. Saccades mostly occurred bilaterally. There was no correlation between vHIT gain or saccades and caloric irrigation, cervical vestibular evoked myogenic potential or audiometry for Meniere's ears. Furthermore, vHIT gain or saccades correlated neither with age nor with the duration of the disease. CONCLUSIONS: Pathological low vHIT gain values are rarely observed in patients with certain Meniere's disease, while refixation saccades occur very frequently. In the majority of patients, saccades occur bilaterally. In Meniere's disease, in contrast to vestibular neuritis, there is no compensatory decrease of saccade latency over time.

H. Jian, et al., **Correlation between auditory-vestibular functions and estrogen levels in postmenopausal patients with Meniere's disease**. J Clin Lab Anal, 2019. 33(1): p. e22626. BACKGROUND: To investigate auditory and vestibular functions, estrogen levels, and its clinical

correlation in postmenopausal females with Meniere's disease (MD). METHODS: We retrospectively analyzed the serum estradiol (E2) levels and the auditory and vestibular functions measured by auditory brainstem response (ABR) to high click rate, pure-tone audiometry (PTA), and caloric test on postmenopausal women who suffered from MD or not at the Specialist Clinic of Vertigo, Shandong Provincial Hospital, during September 2010 to October 2014. RESULTS: A total of 76 postmenopausal patients with MD and 50 healthy postmenopausal controls were included. The patients with MD had lower estrogen levels (22.50 +/- 16.66 pg/mL vs 30.69 +/- 18.59 pg/mL, P = 0.011), longer I-V interpeak latency of ABR (left 0.22 +/- 0.16 mseconds vs 0.18 +/- 0.10 mseconds, P = 0.118; right 0.24 +/- 0.13 mseconds vs 0.17 +/- 0.09 mseconds, P = 0.001), and higher unilateral weakness (UW) value (P < 0.001) in comparison with the controls. The mean pure-tone thresholds of at the speech frequency (500 Hz, 1 kHz, 2 kHz, and 3 kHz) were significantly elevated in patients with MD than those in the controls (left P < 0.001, right P < 0.01). The estradiol level of patients with MD was correlated with ABR latency (left r = -0.229, P < 0.05; right r = -0.220, P < 0.05) and UW value (r = -0.328, P < 0.05), but not with mean pure-tone threshold. CONCLUSIONS: Estrogen levels correlated with auditory and vestibular function in postmenopausal patients with MD. Low estrogen may be involved in the microcirculatory disturbance of the inner ear, affecting the occurrence and development of MD.

S. Kanzaki, **Gene Delivery into the Inner Ear and Its Clinical Implications for Hearing and Balance**. Molecules, 2018. 23(10). The inner ear contains many types of cell, including sensory hair cells and neurons. If these cells are damaged, they do not regenerate. Inner ear disorders have various etiologies. Some are related to aging or are idiopathic, as in sudden deafness. Others occur due to acoustic trauma, exposure to ototoxic drugs, viral infections, immune responses, or endolymphatic hydrops (Meniere's disease). For these disorders, inner ear regeneration therapy is expected to be a feasible alternative to cochlear implants for hearing recovery. Recently, the mechanisms underlying inner ear regeneration have been gradually clarified. Inner ear cell progenitors or stem cells have been identified. Factors necessary for regeneration have also been elucidated from the mechanism of hair cell generation. Inducing differentiation of endogenous stem cells or inner ear stem cell transplantation is expected. In this paper, we discuss recent approaches to hair cell proliferation and differentiation for inner ear regeneration. We discuss the future road map for clinical application. The therapies mentioned above require topical administration of transgenes or drug onto progenitors of sensory cells. Developing efficient and safe modes of administration is clinically important. In this regard, we also discuss our development of an inner ear endoscope to facilitate topical administration.

S. Y. Kim, et al., **Migraine increases the proportion of sudden sensorineural hearing loss: A longitudinal follow-up study**. Auris Nasus Larynx, 2018. 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.

E. R. Kirsh, et al., **Sequential Imaging in Patient With Suspected Meniere's Disease Identifies Endolymphatic Sac Tumor**. Otol Neurotol, 2018. 39(9): p. e856-e859. OBJECTIVE: The standard evaluation of patients with suspected Meniere's disease (MD) includes initial imaging to rule out tumors of the temporal bone. Few guidelines, however, advocate sequential imaging. We propose that sequential imaging may reveal other etiologies of auditory and vestibular symptoms as demonstrated in a patient with an endolymphatic sac tumor that was originally diagnosed Meniere's after initial imaging. PATIENTS: One patient with MD and initially unremarkable imaging. Repeat imaging several years after diagnosis after additional symptoms demonstrated interval development of an endolymphatic sac tumor (ELST). INTERVENTIONS: Resection of endolymphatic sac tumor. MAIN OUTCOME MEASURES: 1) Audiometry, 2) temporal bone imaging, and 3) otopathology RESULTS:: A 45-year-old man with diagnosis of asymmetric sensorineural hearing loss and intermittent vertigo underwent temporal bone magnetic resonance imaging that did not demonstrate any causative lesions. After an episode of sudden sensorineural hearing loss 4 years after initial presentation, repeat imaging was obtained. Magnetic resonance imaging and surgical resection confirmed diagnosis of ELST. The patient had no history of von Hippel-Lindau disease. CONCLUSIONS: A patient with a longstanding diagnosis of MD demonstrated interval development of an ELST. While ELSTs are rare, the study raises the question regarding whether interval imaging is indicated in patients with MD.

T. Kitahara, et al., **Meniere's disease with unremitting floating sensation is associated with canal paresis, gravity-sensitive dysfunction, mental illness, and bilaterality**. Auris Nasus Larynx, 2019. 46(2): p. 186-192. OBJECTIVE: The aim of the present study was to evaluate the association of neuro-otological examination, blood tests, and scoring questionnaire data with treatment-resistant intractability of persistent dizziness in Meniere's disease. METHODS: We managed 1520 successive vertigo/dizziness patients at the Vertigo/Dizziness Center in Nara Medical University from May 2014 to April 2018. Five hundred and twenty-two patients were diagnosed with Meniere's disease (522/1520; 34.3%) according to the 2015 diagnostic guideline of the International Classification of Vestibular Disorders. Among the patients with Meniere's disease there were 102 with intractable rotatory vertigo attacks for more than 3-6 months (102/522; 19.5%), including 20 bilateral cases (20/102; 19.6%), and 88 with intractable unremitting floating sensation rather than rotatory vertigo attacks for more than 3-6 months (88/522; 16.9%), including 28 bilateral cases (28/88; 31.8%). Sixty out of 88 cases with intractable unremitting floating sensation were unilateral and were enrolled for hospitalization to undergo neuro-otological examinations including pure-tone audiometry (PTA), the caloric test (C-test), vestibular evoked cervical myogenic potentials (cVEMP), subjective visual vertical (SVV) test, glycerol test (G-test), electrocochleogram (ECoG), inner ear magnetic resonance imaging (ieMRI), blood tests including anti-diuretic hormone (ADH) and bone alkaline phosphatase (BAP), and self-rating questionnaires of depression score (SDS). Data are presented as positive (+) ratios of the number of patients with examination and questionnaire data outside of the normal range. RESULTS: The ratios (+) were as follows: C-test=33.3% (20/60), cVEMP=25.0% (15/60), SVV=50.0% (30/60), G-test=55.0% (33/60), ECoG=63.3% (38/60), ieMRI=86.7% (52/60), ADH=35.0% (21/60), BAP=11.7% (7/60), and SDS=40.0% (24/60). Multivariate regression analysis revealed that the periods of persistent dizziness were significantly longer in unilateral Meniere's patients with C-test(+), SVV(+), and SDS(+) compared with those with negative findings. Additionally, the periods in bilateral cases were significantly longer than those in unilateral ones. CONCLUSIONS: Although approximately 70% of patients with Meniere's disease are usually treatable through the appropriate conservative medical therapy, the presence of canal paresis, gravity-sensitive dysfunction, neurosis/depression, and bilaterality may make the persistent dizziness intractable and may thus require additional treatments.

L. Koenen, et al., **Meniere Disease**. Journal, 2019(Issue). Meniere disease is a disorder of the inner ear characterized by hearing loss, tinnitus, and vertigo. In most cases, it is slowly progressive

and has a significant impact on the social functioning of the individual affected.[1] The current diagnostic criteria defined by the Barany society by Lopez-Escamez et al. can help differentiate between a probable and a definite Meniere's disease. Patients with a definite Meniere disease according to the Barany Society have: 1. Two or more spontaneous episodes of vertigo with each lasting 20 minutes to 12 hours. 2. Audiometrically documented low- to medium- frequency sensorineural hearing loss in one ear, defining and locating to the affected ear on in at least one instance prior, during or after one of the episodes of vertigo. 3. Fluctuating aural symptoms (fullness, hearing, tinnitus) located in the affected ear. 4. Not better accounted for by any other vestibular diagnosis. Probable Meniere disease can include the following clinical findings: 1. Two or more episodes of dizziness or vertigo, each lasting 20 minutes to 24 hours. 2. Fluctuating aural symptoms (fullness, hearing, or tinnitus) in the affected ear. 3. The condition is better explained by another vestibular diagnosis[2].

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. 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: p. 194599818825458. 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. Y. Lee, et al., **Increased Risk of Benign Paroxysmal Positional Vertigo in Patients With a History of Sudden Sensory Neural Hearing Loss: A Longitudinal Follow-up Study Using a National Sample Cohort**. Otol Neurotol, 2019. 40(2): p. e135-e141. OBJECTIVE: To evaluate the association between benign paroxysmal positional vertigo (BPPV) and sudden sensorineural hearing loss (SSNHL) using a national sample cohort from Korea. METHODS: Data from the years 2002 through 2013 were collected for individuals aged more than or equal to 20 years from the Korean National Health Insurance Service-National Sample Cohort. SSNHL was classified based on the International Classification of Disease-10 (ICD-10) code H91.2. We included only participants who received an audiometry examination and steroid treatment. After exclusion of participants diagnosed with Meniere's disease (H81.0), we extracted data for SSNHL patients (n = 4,109) and 1:4-matched controls (n = 16,436). Matching was performed based on age, sex, income, region of residence, and medical history. BPPV was diagnosed with the ICD-10 code H81.1. Among them, we only included the participants who visit more than or equal to two times for BPPV that does not mean recurrent BPPV. The crude and adjusted hazard ratios (HRs) were calculated using Cox proportional hazard models, and the 95% confidence intervals (CIs) were determined. Subgroup analyses were also performed according to age and sex. RESULTS: The rate of BPPV in the SSNHL group (3.8% [157/4,109]) was higher than that in the control group (1.9% [220/16,436], $p < 0.001$). The adjusted HR of BPPV was 2.90 (95% CI = 2.36-3.56, $p < 0.05$). After experiencing SSNHL, the rate of BPPV in the SSNHL group was significantly higher for patients with two, three to four, and more than or equal to five visits for BPPV. In the subgroup analyses, a significant association between SSNHL and BPPV was observed regardless of age and sex. CONCLUSION: The risk of BPPV is greater in patients with SSNHL.

L. Lemnos, et al., **Postoperative compensation after neurotomy in Meniere's disease: Retrospective study of 15 cases**. Neurochirurgie, 2019. 65(1): p. 20-26. INTRODUCTION: Vestibular neurotomy is a functional surgery for Meniere's disease in the event of medical treatment failure. The aim of the study was to assess the efficacy and complications of vestibular neurotomy, and to address the question of postoperative compensation. MATERIAL AND METHOD: All patients included in this retrospective study underwent a vestibular neurotomy at our center between 2009 and 2016. A preoperative evaluation was performed including MRI, audiometry, and videonystagmography. The functional level of disability was evaluated by the Dizziness Handicap Inventory (DHI) score. In all patients suboccipital retrosigmoid approach was performed. All patients underwent early postoperative vestibular rehabilitation. One month and two years after surgery, we assessed the effectiveness of treatment on dizziness, disability and imbalance. At the time of this study (2 to 8 years), DHI and patients' satisfaction by patient's global impression of change (PGIC) scale were evaluated. RESULTS: Fifteen patients aged between 42 and 74 years of age were included in our study. Postoperative complications occurred in two patients (meningitis and a wound infection). At one month, all patients had a dramatic clinical improvement with decreased vertigo. Two years after surgery, 85% of the patients were cured and had no dizziness or balance disorder. Only one patient experienced bilateralization and only one had a persistent poor compensation. CONCLUSION: Vestibular neurotomy is a very effective treatment in the case of Meniere's disease resistant to medical treatment, with very good functional results and an extremely low failure rate.

X. Li, et al., **Gadolinium-enhanced MRI reveals dynamic development of endolymphatic hydrops in Meniere's disease**. Braz J Otorhinolaryngol, 2018. INTRODUCTION: Meniere's disease is associated with impaired hearing, tinnitus, vertigo, and aural fullness. Many anatomical studies have suggested idiopathic endolymphatic hydrops as the pathological basis of Meniere's disease, which now can be visualized by using gadolinium -enhanced magnetic resonance imaging of the inner ear. OBJECTIVE: To investigate the development of endolymphatic hydrops in Meniere's disease by monitoring the vestibules and cochleae of affected patients. METHODS: Inner ears of 178 patients with definite unilateral Meniere's disease diagnosis were visualized by 3-dimensional fluid-attenuated inversion recovery and three-dimensional real inversion recovery magnetic resonance imaging following

bilateral gadolinium intratympanic injection. The scans were used to evaluate the presence and degree of endolymphatic hydrops in the vestibules and cochlear structures, including the cochlear apical turn, the cochlear middle turn, and the cochlear basal turn. The correlation of endolymphatic hydrops occurrence between the various parts of the inner ear was determined. RESULTS: Symptomatic endolymphatic hydrops was detected on the affected side in all patients, whereas asymptomatic EH was detected on the unaffected contra-lateral side in 32 patients (18.0%). On the affected side, the cochlear apical turn and the cochlear middle turn demonstrated significantly higher rates of endolymphatic hydrops than the cochlear basal turn and the vestibule. The severity of endolymphatic hydrops gradually decreased from the cochlear apical turn to the cochlear basal turn. On the contra lateral side, the incidence and degree of the detected asymptomatic endolymphatic hydrops were significantly greater in the cochleae than in the vestibules ($p<0.05$), with no significant difference detected between the cochlear turns. CONCLUSION: Progression of endolymphatic hydrops appears to be directional, initiated in the cochlea. The order of endolymphatic hydrops severity gradually decreases from the cochlear apical turn to the cochlear basal turn and then to the vestibule. Endolymphatic hydrops in the vestibule is associated with symptomatic Meniere's disease.

Y. Li, et al., **Vincamine exerts protective effect on spiral ganglion neurons in endolymphatic hydrops guinea pig models**. Am J Transl Res, 2018. 10(11): p. 3650-3663. The aim of this study was to investigate the protective effects of vincamine in endolymphatic hydrops (ELH). After ELH guinea pigs treated by vincamine, the concentration of VAP in plasma, and the levels of cAMP, MDA, SOD, GSH-Px in right cochlea were measured using spectrophotometric method. The V2R, NMDAR1, p-NMDAR1, AQP2, p-AQP2, caspase3/9 and c-caspase3/9 expressions in right cochlea were detected using western blot analysis. The cochlear hydrops degree and SGNs density were evaluated by hemotoxylin and eosin staining (HE) test. Normal hearing and vestibular function were warranted by the tests of auditory brainstem response (ABR) and electronystagmography (ENG). After glutamate-injured SGNs treated with vincamine, the MDA, SOD GSH-Px, NGF, BDNF, NT3, NT4 and Trks levels were measured. Meanwhile, the Bcl2, Bax, NMDAR1, p-NMDAR1, PI3K, p-PI3K, Akt, p-Akt, caspase3/9 and cleaved-caspase3/9 expression levels were detected. Furthermore, the viability, apoptosis and necrosis of SGNs were tested by MTT and Hoechst/PI staining methods. The results indicated that vincamine could significantly inhibit the expression levels of cAMP, MDA, V2R, p-NMDAR1, p-AQP2 and c-caspase-3/-9 in cochlea, alleviate the cochlear hydrops degree, regulate the audiological and vestibular dysfunctions. The SGNs density, SOD and GSH-Px levels were also increased by vincamine. In vincamine-treating groups, the MDA, Bax, p-NMDAR1, and c-caspase3/9 levels were observably decreased, while SGNs survival, SOD, GSH, NGF, BDNF, NT3, NT4, Trks, Bcl2, p-PI3K, p-Akt expressions were improved. The present study indicated a novel use of vincamine in suppressing ELH formation by down-regulating the VAP/AQP2 signaling pathway. It also manifested that vincamine exerted protective effects on hearing via improving neurotrophin-dependent PI3K/Akt signaling pathway in SGNs.

A. L. Luryi, et al., **Patient, disease, and outcome characteristics of benign paroxysmal positional vertigo with and without Meniere's disease**. Acta Otolaryngol, 2018. 138(10): p. 893-897. BACKGROUND: Meniere's disease (MD)-associated benign paroxysmal positional vertigo (BPPV) is complex and difficult to diagnose, and reports of its prevalence, pathologic features and outcomes are sparse and conflicting. OBJECTIVE: Report disease characteristics and outcomes associated with the presence of MD in patients with BPPV. MATERIALS/METHODS: A retrospective study of patients with BPPV between 2007 and 2017 at a single, high-volume institution. RESULTS: Of 1581 patients with BPPV identified, 7.1% had MD and 71.9% of those patients had BPPV in the same ear(s) as MD. Patients with MD were more likely to have lateral semicircular canalithiasis (11.6% vs. 5.5%, $p = .009$) and multiple canalithiasis (7.1% vs. 2.5%, $p = .005$). MD was associated with an increased rate of resolution of BPPV ($p = .008$) but also increased time to resolution ($p = .007$). There was no association between MD and recurrence of BPPV. CONCLUSIONS: MD is associated with lateral canalithiasis. Contrary to prior reports, BPPV in MD can affect either ear and was not associated with

poorer outcomes than idiopathic BPPV. SIGNIFICANCE: The largest series to date investigating disease and outcome characteristics for BPPV in MD is presented. These data inform diagnosis and expectations in the management of these complex patients.

P. Marques, et al., **Gentamicin delivery to the inner ear: Does endolymphatic hydrops matter?** PLoS One, 2018. 13(11): p. e0207467. INTRODUCTION: Middle ear application of gentamicin is a common medical treatment for uncontrolled Meniere's disease. The objective of the study was to evaluate the impact of endolymphatic hydrops on inner ear delivery. METHODS: Perilymph gentamicin concentrations and correlation with endolymphatic hydrops in an animal model were assessed. A group of 24 guinea pigs was submitted to surgical obstruction of the endolymphatic sac and duct of the right ear. Gentamicin was applied either to the right ear's round window niche or through a transtympanic injection. Perilymph specimens were collected at different times. Histologic morphometry was used to evaluate both turn-specific and overall hydrops degree. RESULTS: In animals with endolymphatic hydrops, lower concentrations of gentamicin were observed after 20 or 120 minutes of exposure and in both types of administration, when compared to controls. This difference reached statistical significance in the round window niche application group (Mann-Whitney, p = 0,007). A negative correlation between perilymphatic gentamicin concentration and hydrops degree could be observed in both groups, after 120 minutes of exposure (Spearman correlation, round window niche p<0,001; TT p = 0,005). CONCLUSIONS: The study indicates that the endolymphatic hydrops degree has a negative interference on the delivery of gentamicin into the inner ear following middle ear application.

P. S. Marques, et al., **Instrumental head impulse test changes after intratympanic gentamicin for unilateral definite Meniere's disease: A systematic review and meta-analysis***.* Auris Nasus Larynx, 2018. 45(5): p. 943-951. OBJECTIVE: To estimate how much could intratympanic gentamicin (ITG) interfere with the vestibular-ocular reflex (VOR) parameters on instrumental head impulse test (HIT), either with scleral search coil or video head impulse test and, eventually, foresee the control of vertigo crisis in unilateral intractable Meniere's disease (MD). METHODS: A literature search was conducted in PubMed, Scopus, Web of Science and Cochrane search engines. The search terms used were "vestibular ocular reflex", "head impulse test", "gentamicin," and "Meniere's disease". Limitations included text availability to be full text, species to be humans and language to be English. All study types were included. 89 articles were screened identifying four eligible studies were identified. Studies were included after consensus of the authors. Meta-analysis was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Data was analysed using Review Manager software. RESULTS: Instrumental HIT, after ITG for MD, demonstrated, in the treated ear, a decreased gain in the horizontal, posterior and superior semicircular canals (SCC), of 0.36 (0.26; 0.47; 95% CI), 0.35 (0.22; 0.48; 95% CI) and 0.28 (0.21; 0.35; 95% CI), respectively. Gain asymmetry increases between the treated and non-treated ear of 23.78 (7.22; 40.35; 95% CI), 32.01 (12.27; 51.76; 95% CI) and 17.49 (9.99; 24.99; 95% CI), were similarly detected in the horizontal, posterior and superior SCC, respectively. Significantly smaller gain values after the first treatment were observed for a single injection group versus multiple injection group in the horizontal (p=0.002) and superior SCCs (p=0.016). CONCLUSIONS: Instrumental HIT is effective in evaluating the SCC function after ITG for intractable unilateral MD. VOR gain changes in the direction of the treated ear in the three SCC have been clearly registered. An increased reduction of the VOR gain in the horizontal and anterior SCC also seemed to foresee the control of vertigo crisis. Still, after meta-analysis, the small number of patients' data available did not allow to define a treatment end-point value. This review also indicated that further and better-designed studies are warranted.

E. Martin-Sanz, et al., **Delayed Effect and Gain Restoration After Intratympanic Gentamicin for Meniere's Disease***.* Otol Neurotol, 2019. 40(1): p. 79-87. OBJECTIVE: This study aimed to evaluate the changes in the VOR gain after intratympanic gentamicin therapy and to correlate them with the mid-term effects on the control of vertigo, in a population of Meniere's disease patients. STUDY DESIGN: The study design was a prospective "Outcomes research." SETTING: Tertiary referral center. PATIENTS: This study included 20 patients with unilateral Meniere's disease refractory to medical

therapy for at least 1 year, and treated with an on demand intratympanic gentamicin protocol. INTERVENTION: Therapeutic. MAIN OUTCOME MEASURE: Audiometry, caloric testing, and a vHIT before beginning the protocol were performed. Patients underwent weekly vHIT assessments until a significant gain reduction was observed. Subsequently we performed vHIT tests 1 month after the therapy completion, and then every 3 months for at least 1 year. RESULTS: Complete vertigo control (class A) was achieved in 14 patients at the 12-month follow-up assessment. We observed a significant reduction in VOR gain values at the 3-week follow-up assessment. We found a significant correlation between the 1-month posttreatment ipsilateral hVOR gain and the rate of vertigo recurrence after the first IT gentamicin treatment ($p = 0.012$; $r = 0.400$). At the mid-term assessment, 10 patients exhibited a significant partial recovery of the hVOR gain. CONCLUSIONS: The delayed effect of intratympanic gentamicin and the subsequent gain restoration are factors that may influence the patients' outcome. The feasibility of the vHIT system makes it a useful tool to monitorize the VOR changes.

R. Menger, et al., **Rear Admiral (Astronaut) Alan Shepard: Meniere's disease and the race to the moon**. J Neurosurg, 2019: p. 1-7. On May 5, 1961, Alan B. Shepard Jr. piloted the Freedom 7 craft into a suborbital flight to become the first American man in space. His promising astronautical career was soon scuttled by spells of dizziness and tinnitus later diagnosed as Meniere's disease, until William F. House-considered the father of neurotology and a pioneer in surgery for vestibular schwannomas-intervened. In 1968 House implanted an endolymphatic-subarachnoid shunt, which at the time was a virtually experimental procedure. Shepard's debilitating Meniere's disease was cured, but not quite in time for him to pilot the doomed Apollo 13 mission; he was reassigned to Apollo 14 and as a result would step foot on the moon on February 5, 1971. This historical vignette depicts the tale of how the career trajectories of Shepard and House-two notable figures in their respective fields-fatefully intersected.

S. Miuchi, et al., **Volume-rendered computed tomography images of the surgical field for endolymphatic sac surgery**. Eur Arch Otorhinolaryngol, 2019. PURPOSE: Identification of the endolymphatic sac has failed occasionally. Postoperative complications have also rarely been reported. Given a safer and more reliable surgery, preoperative anatomical assessments are valuable, however, the vestibular aqueduct has seldom been seen with multi-planar reconstruction (MPR) computed tomography (CT) images yet. Our study aimed to determine the significance and utility of volume-rendered (VR) CT images of the surgical field for identifying the vestibular aqueduct, compared with MPR CT images. SUBJECTS AND METHODS: 14 patients with Meniere's disease who underwent endolymphatic sac surgery between 2008 and 2011. Location and size of the vestibular aqueduct were assessed using VR and MPR CT images, independently. RESULTS: Accuracy of identifying the location differed significantly between VR and MPR CT images (rate of total correct evaluations: 100% by VR CT images vs 75% by MPR CT images, $p = 0.02$). Size was correctly identified in cases with a small endolymphatic sac using VR CT images (rate of total correct evaluations for size of the vestibular aqueduct: 100% by VR CT vs 57% by MPR CT, $p = 0.046$). VR CT images also demonstrated clearly the relationship between the endolymphatic sac and high jugular bulb. In two cases, the endolymphatic sac was identified by VR images, not by MPR images. CONCLUSION: Accurate information about the location and size of vestibular aqueduct can allow sac surgeons to identify a tiny endolymphatic sac more easily and certainly, and also aids surgical trainees to learn sac surgery safely.

T. Murofushi, et al., **Simultaneous Presentation of Definite Vestibular Migraine and Definite Meniere's Disease: Overlapping Syndrome of Two Diseases**. Front Neurol, 2018. 9: p. 749. Objectives: To review the clinical records of patients that exhibited the clinical features of both vestibular migraine (VM) and Meniere's disease (MD) during each episodic vertigo attack and to discuss the possible pathophysiology of such combination of symptoms. Subjects: Ten patients that were selected according to criteria based on a combination of the diagnostic criteria for definite MD and VM (9 females and one male, age: 22-54 years) were enrolled. They were required to show features of both diseases in each vertigo attack. Methods: The patients' medical histories and pure-

tone audiometry, cervical vestibular evoked myogenic potential (cVEMP), video head-impulse test (vHIT), and caloric test results were examined. cVEMP was recorded using 500 and 1,000 Hz short tone bursts (125dBSPL, air-conducted), 500 Hz-1,000 Hz cVEMP slope, an index of endolymphatic hydrops in the saccule was calculated using normalized amplitudes of p13-n23. For performing vHIT, each subject was seated 1.5 m in front of a target and asked to keep watching it as their head was passively rotated by the examiner. Their eye movements were evaluated using video-oculography while their head movements were recorded using inertial sensors. Results: The patients were predominantly female. On average, the onset of migrainous headaches occurred 9 years earlier than the onset of vertigo attacks. All of the patients but one had migraines with auras. Five of the 10 patients had a family history of vertigo attacks accompanied by both migrainous and auditory symptoms. The patients mainly displayed hearing loss at low frequencies. Nine patients exhibited 500-1,000 Hz cVEMP slope < -19.9, which was suggestive of endolymphatic hydrops. None of the patients who underwent vHIT showed abnormal canal function. One patient showed unilaterally decreased caloric responses. Conclusions: These patients presented with simultaneous MD and VM signs/symptoms might be referred to "VM/MD overlapping syndrome (VM/MD-OS)" as a new clinical syndrome.

S. Nicolas, et al., **Long-term Vertigo Control and Vestibular Function After Low-dose On-demand Transtympanic Gentamicin for Refractory Meniere's Disease***.* Otol Neurotol, 2019. 40(2): p. 218-225. OBJECTIVE: To describe the long-term clinical vertigo control along with measured lateral canal vestibular function in patients with unilateral refractory Meniere's disease (MD) treated with gentamicin transtympanic injections (TTI). STUDY DESIGN: Retrospective analytic study. SETTING: Tertiary referral center. PATIENTS: Thirty-eight patients treated by TTI for medically refractory unilateral MD, defined by the 1995 AAO-HNS criteria, between May 2006 and December 2012. INTERVENTION(S): One-year course of treatment with gentamicin TTI following a low dose on-demand protocol. TTI were repeated in new courses of treatment when MD recurrence occurred. MAIN OUTCOME MEASURE(S): AAO-HNS class of control, caloric tests (CalT), recurrence rate. RESULTS: After an average clinical follow-up of 71 months, all patients entered a class of control A (78%) or B (22%), with an average of 2.3 TTI received. The mean maximal obtained deficit was 88.5%, and the mean long-term deficit was 85.5%. Ten (26%) patients had disease recurrence requiring a new course of treatment. A value of the first CalT in the 3 months following the first TTI strictly higher than 78% was significantly associated with disease control and the absence of symptom recurrence (p</=0.01). In the "recurrence" group, four patients had a significantly lower mean value of all CalT performed after the first TTI when compared with other patients (p</=0.001), indicating gentamicin resistance CONCLUSION:: Achieving a sustainable vestibular deficit on caloric testing is key for MD symptom control after gentamicin TTI. Gentamicin resistance must be diagnosed early to adapt therapeutic strategies.

K. S. Noij, et al., **Cervical Vestibular Evoked Myogenic Potentials in Meniere's Disease: A Comparison of Response Metrics***.* Otol Neurotol, 2019. 40(3): p. e215-e224. OBJECTIVE: The cervical vestibular evoked myogenic potential (cVEMP) has been used to evaluate patients with Meniere's disease (MD). Studied cVEMP metrics include: amplitude, threshold, frequency tuning, and interaural asymmetry ratio (IAR). However, few studies compared these metrics in the same set of MD patients, and methodological differences prevent such a comparison across studies. This study investigates the value of different cVEMP metrics in distinguishing one set of MD patients from age-matched controls. STUDY DESIGN: Prospective study. SETTING: Tertiary care center. PATIENTS: Thirty patients with definite unilateral MD and 23 age-matched controls were prospectively included. All underwent cVEMP testing at 500, 750, 1000, and 2000 Hz on each side. Ears were separated into three groups: affected MD, unaffected MD, and control. MAIN OUTCOME MEASURES: Sound level functions were obtained at each frequency, and normalized peak-to-peak amplitude (VEMPn), VEMP inhibition depth (VEMPid), threshold, frequency-tuning ratio, and IAR were calculated. For all metrics, the differentiation between MD and control ears was compared using receiver operating characteristic (ROC) curves. RESULTS: 500 Hz cVEMP threshold, VEMPn, and VEMPid were similarly

good at distinguishing affected MD ears from healthy ears, with ROC area under the curves (AUCs) of more than 0.828 and optimal sensitivities and specificities of at least 80 and 70%. Combinations of these three metrics yielded slightly larger AUCs (>0.880). Tuning ratios and IAR were less effective in separating healthy from affected ears with AUCs ranging from 0.529 to 0.720. CONCLUSION: The cVEMP metrics most useful in distinguishing MD patients from healthy controls are threshold, VEMPn, and VEMPid, using 500 Hz stimuli.

T. Okayasu, et al., **Focal Degeneration of Vestibular Neuroepithelium in the Cristae Ampullares of Three Human Subjects**. Otol Neurotol, 2018. 39(10): p. e1100-e1110. BACKGROUND: We report a unique pattern of focal degeneration of the neuroepithelium of cristae ampullares, thick subepithelial extracellular deposits, and neural degeneration in three humans. OBJECTIVE: To characterize the pattern of vestibular degeneration and measure the thickness of subepithelial deposits in these three cases and controls. METHODS: The subepithelial deposits of vestibular end organs in three subject cases and controls were studied using hematoxylin and eosin, periotic acid-Schiff, Gomori trichrome staining, and immunostaining for antineurofilament, antimyosin VIIa, and anticollagen 4a1. The thickness of deposit as measured by light microscopy was compared with that of control groups (age-matched controls, patients with unilateral Meniere's disease, vestibular neuritis, cupulolithiasis, severe nonfocal degeneration of the vestibular neuroepithelium, and Alport syndrome). The correlation of thickness of deposits with age from 0 to 100 years was also investigated. RESULTS: Focal loss of hair cells in the neuroepithelium, thick subepithelial deposits, and degeneration of subepithelial dendrites and Scarpa's ganglion were found in all three cristae of three subject cases. Immunostaining demonstrated a decrease of afferent neural fibers in the cristae and focal fragmentation of the basement membrane adjacent to the deposits. The thickness of the subepithelial deposits in three cristae of three subject cases was significantly greater than that of all controls. In the three cristae of normal controls, the thickness of deposits demonstrated a positive correlation with age. CONCLUSION: Although both age and degeneration of the vestibular neuroepithelium may be associated with the thickness of the subepithelial deposits, in this unique pattern of degeneration, the thickness of the subepithelial deposits was significantly greater than that in all controls.

V. A. Parfenov, et al., **Features of the clinical picture in patients of middle age with essential hypertension**. Ter Arkh, 2018. 90(9): p. 15-26. AIM: To evaluate the presence and the severity of the complaints (headache, dizziness, memory loss, concentration of attention, sleep disturbances, decreased mood, increased anxiety), the state of cognitive functions, emotional status and quality of night sleep in treatment-naive middle-aged patients with mild to moderate EAH compared to healthy volunteers of the same age. MATERIALS AND METHODS: 103 treatment-naive patients with EAH aged 40-59 years at the enrollment, who met the inclusion/exclusion criteria and provided written informed consent (46 men, mean age 53.6+/-0.8 years) and 50 healthy volunteers (17 men, mean age 51.5+/-1.0 years) with normal blood pressure (BP) level - control group - were enrolled to the study. Mean EAH duration was 2.9+/-5.7 years. Cognitive assessment included Montreal cognitive assessment, 10-words learning task, verbal fluency test, TMT, Stroop color and word test. Anxiety and depression were evaluated via Hamilton rating scales (HARS and HDRS). 24-hours ambulatory BP monitoring (ABPM) was performed according to European guidelines. RESULTS: 70% of patients with EAH complained of memory disturbance, 68% - lack of attention, 22% - sleep disturbances, 12% - dizziness, 9% - headache. It took statistically significant more time for patients with EAH to perform on TMT B ($p<0.05$), they had significantly higher TMT B - TMT A difference score ($p<0.01$) and lower mean MoCA score ($p<0.05$). Patients with EAH had significantly higher mean score in Hamilton anxiety (2.1+/-3.7) and depression (1.1+/-2.4) rating scales compared to controls (0.3+/-0.9 points, $p<0.01$ and 0.1+/-0.5 points, $p<0.001$, respectively). Patients with EAH who complained of sleep disturbances had low sleep quality (8.7+/-2.8 points). Among patients with EAH who complained about headaches 66.6% had episodic migraine and chronic tension type headache (33.4%). Those patients had a substantial impact of headache on life and daily living according to HIT-6 (mean score - 57.5+/-6.1). Only 2 patients out of 12 with complains about

dizziness had benign paroxysmal positional vertigo and Meniere's disease. CONCLUSION: Complaints about memory dysfunction, lack of attention, sleep disturbances, less common - dizziness and headaches, are most typical in patients with EAH on the early stages of the disease. They differ from healthy volunteers of the same age by having cognitive impairment and higher anxiety and depression scores. Patients with EAH who complained about sleep disturbances had low sleep quality. Headache in patients with EAH was due to episodic migraine and tension type headache which had a negative impact on life and daily living.

I. G. Parker, et al., **A Systematic Review of the Reported Proportions of Diagnoses for Dizziness and Vertigo**. Otol Neurotol, 2019. 40(1): p. 6-15. OBJECTIVES: To determine the typical proportions of diagnoses for patients presenting with dizziness or vertigo based on clinical speciality and to assess the change in proportions of diagnoses over time. DATA SOURCES: Following PRISMA guidelines, systematic searches of PubMed and CINAHL databases and follow-up reference searches were performed for articles published in English up to October 2016. STUDY SELECTION: Analysis of searches yielded 42 studies meeting the criteria of case series of adult patients with dizziness and/or vertigo presenting to general practice, emergency departments or specialist outpatient clinics. DATA EXTRACTION: Data comprising demographics, diagnostic cases, and the total number of cases were recorded and independently tested, followed by a risk of bias analysis. DATA SYNTHESIS: Sample size weighted proportions expressed as percentages with confidence intervals were calculated and compared using chi analysis and a reference proportion formed by the combination of Ear Nose and Throat and Neurotology case series published between 2010 and 2016. Analysis of diagnostic trends over time used Poisson regression with consideration for overdispersion. CONCLUSIONS: This systematic review of case series demonstrated significant differences in the proportions of diagnoses for patients presenting with dizziness or vertigo, depending on the specialty making the diagnosis. ENT proportions were dominated by BPPV, Psychogenic and Meniere's disease diagnostic categories, whereas emergency proportions were dominated by Other, Cardiac, and Neurological categories. Analysis of case series proportions over time revealed increases in diagnoses such as Benign Paroxysmal Positional Vertigo and Vestibular Migraine, and a corresponding decrease in the diagnoses of Meniere's disease.

J. F. Peneda, et al., **Immune-Mediated Inner Ear Disease: Diagnostic and therapeutic approaches**. Acta Otorrinolaringol Esp, 2019. 70(2): p. 97-104. INTRODUCTION: Immune Mediated Inner Ear Disease (IMIED) is a rare form of sensorineural bilateral hearing loss, usually progressing in weeks to months and responsive to immunosuppressive treatment. Despite recent advances, there is no consensus on diagnosis and optimal treatment. METHODS: A review of articles on IMIED from the last 10 years was conducted using PubMed((R)) database. RESULTS: IMIED is a rare disease, mostly affecting middle aged women. It may be a primary ear disease or secondary to autoimmune systemic disease. A dual immune response (both cellular and humoral) seems to be involved. Cochlin may be the inner ear protein targeted in this disease. Distinction from other (core common) forms of neurosensory hearing loss is a challenge. Physical examination is mandatory for exclusion of other causes of hearing loss; audiometry identifies characteristic hearing curves. Laboratory and imaging studies are controversial since no diagnostic marker is available. CONCLUSION: Despite recent research, IMIED diagnosis remains exclusive. Steroids are the mainstay treatment; other therapies need further investigation. For refractory cases, cochlear implantation is an option and with good relative outcome.

N. Perez-Fernandez, et al., **Endolymphatic hydrops severity in magnetic resonance imaging evidences disparate vestibular test results**. Auris Nasus Larynx, 2019. 46(2): p. 210-217. OBJECTIVES: It has been suggested that in Meniere's disease (MD) a dissociated result in the caloric test (abnormal result) and video head-impulse test (normal result) probably indicates that hydrops affects the membranous labyrinth in the horizontal semicircular canal (HSC). The hypothesis in this study is that based on endolymphatic hydrops' cochleocentric progression, hydrops should also be more severe in the vestibule of these patients than in those for whom both tests are normal. METHODS: 22 consecutive patients with unilateral definite MD were included and classified as NN if

both tests were normal or AN if the caloric test was abnormal. MRI evaluation of endolymphatic hydrops was carried out with a T2-FLAIR sequence performed 4h after intravenous gadolinium administration. The laterality and degree of vestibular endolymphatic hydrops and the presence or absence of cochlear endolymphatic hydrops were recorded. Demographic data, audiometric and vestibular evoked myogenic potentials were collected, and video head-impulse and caloric tests were performed. RESULTS: Patients in both groups (NN and AN) were similar in terms of demographic data and hearing loss. The interaural asymmetry ratio was significantly higher for ocular and cervical VEMP in patients in the AN group. There was a significantly higher degree of hydrops in the vestibule of the affected ear of AN patients (chi(2); p=0.028). CONCLUSION: Significant canal paresis in the caloric test is associated with more severe endolymphatic hydrops in the vestibule as detected with gadolinium-enhanced MRI and with a more severe vestibular deficit. LEVEL OF EVIDENCE: 2a.

I. Pyykko, et al., **Imaging of Temporal Bone**. Adv Otorhinolaryngol, 2019. 82: p. 12-31. Multidetector computed tomography has been the benchmark for visualizing bony changes of the ear, but has recently been challenged by cone-beam computed tomography. In both methods, all inner ear bony structures can be visualized satisfactorily with 2D or 3D imaging. Both methods produce ionizing radiation and induce adverse health effects, especially among children. In 3T magnetic resonance imaging, the soft tissue can be imaged accurately. Use of gadolinium chelate (GdC) as a contrast agent allows the partition of fluid spaces to be visualized, such as the bulging of basilar and Reissner's membranes. Both intravenous and intratympanic administration of GdC has been used. The development of positive endolymph imaging method, which visualizes endolymph as a bright signal, and the use of image subtraction seems to allow more easily interpretable images. This long-awaited possibility of diagnosing endolymphatic hydrops in living human subjects has enabled the definition of Hydropic Ear Disease, encompassing typical Meniere's disease as well as its monosymptomatic variants and secondary conditions of endolymphatic hydrops. The next challenge in imaging of the temporal bone is to perform imaging at the cellular and molecular levels. This chapter provides an overview of current temporal bone imaging methods and a review of emerging concepts in temporal bone imaging technology.

N. Quaranta, et al., **Therapeutic strategies in the treatment of Meniere's disease: the Italian experience**. Eur Arch Otorhinolaryngol, 2019. 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.

R. Quatre, et al., **Relationship Between Audio-Vestibular Functional Tests and Inner Ear MRI in Meniere's Disease**. Ear Hear, 2019. 40(1): p. 168-176. OBJECTIVES: Meniere's disease is an inner ear disorder generally attributed to an endolymphatic hydrops. Different electrophysiological tests and imaging techniques have been developed to improve endolymphatic hydrops diagnosis. The goal of our study was to compare the sensitivity and the specificity of delayed inner ear magnetic resonance imaging (MRI) after intravenous injection of gadolinium with extratympanic clicks electrocochleography (EcochG), phase shift of distortion product otoacoustic emissions (shift-DPOAEs), and cervical vestibular-evoked myogenic potentials (cVEMP) for the diagnosis of Meniere's disease. DESIGN: Forty-one patients, with a total of 50 affected ears, were included prospectively from April 2015 to April 2016 in our institution. Patients included had definite or possible Meniere's disease based on the latest American Academy of Otolaryngology-Head and Neck Surgery guidelines revised in 2015. All patients went through delayed inner ear MRI after intravenous injection of gadolinium (three dimension-fluid attenuated inversion recovery sequences), pure-tone audiometry, extratympanic clicks EcochG, shift-DPOAEs, and cVEMP on the same day. Endolymphatic hydrops was graded on MRI using the saccule to utricle ratio inversion defined as when the saccule appeared equal or larger than the utricle. RESULTS: Abnormal EcochG and shift-DPOAEs in patients with definite Meniere's disease (DMD) were found in 68 and 64.5%, respectively. The two methods were significantly associated in DMD group. In DMD group, 25.7% had a positive MRI. The correlation between MRI versus EcochG and MRI versus shift-DPOAEs was not significant. MRI hydrops detection was correlated with hearing loss. Finally, 22.9% of DMD group had positive cVEMP. CONCLUSIONS: EcochG and shift-DPOAEs were both well correlated with clinical criteria of Meniere's disease. Inner ear MRI showed hydrops when hearing loss was higher than 35 dB. The shift-DPOAEs presented the advantage of a rapid and easy measurement if DPOAEs could be recorded (i.e., hearing threshold <60dB). In contrast, EcochG can be performed regardless of hearing loss. In combination with shift-DPOAEs, it enhances the chances to confirm the diagnosis with a better confidence.

R. D. Rabbitt, **Semicircular canal biomechanics in health and disease**. J Neurophysiol, 2019. 121(3): p. 732-755. The semicircular canals are responsible for sensing angular head motion in three-dimensional space and for providing neural inputs to the central nervous system (CNS) essential for agile mobility, stable vision, and autonomic control of the cardiovascular and other gravity-sensitive systems. Sensation relies on fluid mechanics within the labyrinth to selectively convert angular head acceleration into sensory hair bundle displacements in each of three inner ear sensory organs. Canal afferent neurons encode the direction and time course of head movements over a broad range of movement frequencies and amplitudes. Disorders altering canal mechanics result in pathological inputs to the CNS, often leading to debilitating symptoms. Vestibular disorders and conditions with mechanical substrates include benign paroxysmal positional nystagmus, direction-changing positional nystagmus, alcohol positional nystagmus, caloric nystagmus, Tullio phenomena, and others. Here, the mechanics of angular motion transduction and how it contributes to neural encoding by the semicircular canals is reviewed in both health and disease.

C. Reichmayr, et al., **Tenotomy of the middle ear muscles : An unknown surgical approach in Meniere's disease**. Wien Klin Wochenschr, 2019. 131(3-4): p. 87-91. Tenotomy of the tendon of the stapedius and tensor tympani muscles is a relatively unknown therapeutic procedure in Meniere's disease. Widespread approaches include medicinal treatment with betahistine or diuretics as well as interventional procedures, such as intratympanic gentamicin or glucocorticoid injection, vestibular neurectomy, labyrinthectomy or endolymphatic sac surgery. The exact pathomechanism of this approach is not fully known. It is assumed that by cutting the tendons of both middle ear muscles in cases of endolymphatic hydrops the stapes is not additionally actively pushed against the oval window but can deviate laterally and thereby does not augment the inner ear pressure even further. Studies have shown that this method does not only improve vestibular symptoms but also, in contrast to most other strategies, increases the hearing level. The formation of scar tissue and the resulting reduction of ossicular chain mobility, especially due to postoperative infections, may limit

the success of tenotomy and should be considered as a possible factor in cases of limited postoperative vertigo control.

J. Rey-Martinez, et al., **Enhanced Vestibulo-Ocular Reflex Responses on vHIT. Is It a Casual Finding or a Sign of Vestibular Dysfunction?** Front Neurol, 2018. 9: p. 866. In current clinical practice, when in response to vHIT testing the observed slow-phase eye-velocity responses are significantly higher than head velocity, the most probable cause is considered to be an inadequate collection method or a recording artifact. We present two cases with clinical diagnoses of Meniere's Disease: for both cases, enhanced eye velocity responses were measured with a rigorous vHIT testing protocol. In the first case we measured these enhanced responses on each test performed during a 5 year time series; in the second case multiple measurements were obtained from a patient after the radiologic diagnosis of vestibulo-cochlear hydrops. The two cases presented and the new evidence reported by other researchers suggest that owing to the low probability of artifact and the high consistency of the vHIT measurements, we should consider the hypothesis of a physio-pathologic cause for the enhanced eye responses to vHIT testing of some patients with vestibular dysfunction.

P. Reynard, et al., **Delayed endolymphatic hydrops. Special emphasis on nystagmus associated with episodes and contribution of chemical labyrinthectomy**. Eur Ann Otorhinolaryngol Head Neck Dis, 2018. 135(5): p. 321-326. OBJECTIVES: The main objective was to describe spontaneous nystagmus characteristics during an episode of delayed endolymphatic hydrops (DEH), including an initial vertical upbeating nystagmus in one patient. The secondary objective was to highlight the contribution of chemical labyrinthectomy. METHODS: Episodic vertigo after a prolonged period of time of sensorineural hearing loss (profound or total) in one ear characterized ipsilateral DEH and was associated with the development of hearing loss in the opposite ear in contralateral DEH. RESULTS: Ten patients met the criteria for DEH: 7 ipsilateral and 3 contralateral. Three (all ipsilateral DEH) were examined during a vertigo episode. Two patients had a typical horizontal-torsional nystagmus beating contralaterally to the hearing loss. One patient showed atypic initial vertical upbeating nystagmus with a slight torsional component, which secondarily became horizontal-torsional beating contralaterally to the hearing loss. Four patients had disabling vertigo with unilateral total deafness (ipsilateral DEH), successfully treated by 1-3 transtympanic gentamycin (Gentalline((R))) injections. CONCLUSION: Nystagmus direction during vertigo episodes varies, and may initially present as vertical upbeating nystagmus, which, to our knowledge, has not been previously reported in DEH or Meniere's disease. This nystagmus might reflect an inhibition of the superior semicircular canal (on the hearing-impaired side), suggesting incipient hydrops in this canal. Chemical labyrinthectomy is a simple and effective procedure in unilateral DEH, especially as the patient often suffers from total deafness.

H. Rizk, et al., **Quality Improvement in Neurology: Neurotology Quality Measurement Set**. Otolaryngol Head Neck Surg, 2018. 159(4): p. 603-607.

S. M. Rosengren, et al., **Vestibular evoked myogenic potentials in practice: Methods, pitfalls and clinical applications**. Clin Neurophysiol Pract, 2019. 4: p. 47-68. Vestibular evoked myogenic potentials (VEMPs) are a useful and increasingly popular component of the neuro-otology test battery. These otolith-dependent reflexes are produced by stimulating the ears with air-conducted sound or skull vibration and recorded from surface electrodes placed over the neck (cervical VEMPs) and eye muscles (ocular VEMPs). VEMP abnormalities have been reported in various diseases of the ear and vestibular system, and VEMPs have a clear role in the diagnosis of superior semicircular canal dehiscence. However there is significant variability in the methods used to stimulate the otoliths and record the reflexes. This review discusses VEMP methodology and provides a detailed theoretical background for the techniques that are typically used. The review also outlines the common pitfalls in VEMP recording and the clinical applications of VEMPs.

J. Rutka, **Aminoglycoside Vestibulotoxicity**. Adv Otorhinolaryngol, 2019. 82: p. 101-110. Many pharmaceuticals have ototoxicity (both cochlear and/or vestibular) as part of their adverse medication profile. The aminoglycoside class of antimicrobials has been especially well studied in

this regard. Many questions remain unanswered as to how to best monitor and prevent this complication. A bilateral vestibular loss profoundly affects an individual's quality of life, physical activities, and overall independence. Paradoxically, the effects of gentamicin ototoxicity have provided further insight into the workings of the vestibular system, especially the vestibulo-ocular reflex. The microbiological activity, therapeutic use, toxicities, and genetics predisposing a person to aminoglycoside ototoxicity are presented. The clinical importance of recognizing ataxia, disequilibrium, and oscillopsia as presenting symptoms for vestibulotoxicity rather than hearing loss or vertigo is stressed. Documented risk factors and new observations regarding the spectrum of vestibular dysfunction and differences in vestibulotoxicity from multiple daily dosing vs. single daily dosing schedules are presented for the first time. While most vestibulotoxicity arises from systemic aminoglycoside administration, intratympanic application has been used therapeutically for intractable Meniere's disease. Commercially available ototopical aminoglycoside preparations for the treatment of external/middle ear disease in the presence of a tympanic membrane defect have also been documented to cause unintentional ototoxicity.

I. Saliba, et al., **Endolymphatic duct blockage for refractory Meniere's disease: assessment of intraoperative CSF leak on short-term surgical outcomes**. Acta Otolaryngol, 2018. 138(10): p. 886-892. BACKGROUND: Endolymphatic sac decompression has shown limited success for the treatment of Meniere's disease (MD). We have published a novel technique with very promising results for the treatment of refractory MD: the Endolymphatic Duct Blockage (EDB) with two titanium clips. One of the challenges of this technique was an increased incidence of intraoperative Cerebrospinal Fluid (CSF) Leak. OBJECTIVE: To assess the effect of intraoperative CSF Leak on short-term surgical outcomes. METHODS: Retrospective comparative study in a tertiary care center (61 patients). MD patients who underwent EDB were included. Intraoperative CSF Leaks were documented. Surgical outcomes assessed were the presence of postoperative Benign Paroxysmal Positional Vertigo (BPPV), aural fullness, tinnitus, vertigo spells and pure tone average (PTA), speech discrimination scores (SDS) and bone conduction thresholds (BCT). Data were collected for these visits: preoperative, 1 week, 1 and 6 months postoperatively. RESULTS: Outcomes for the CSF Leak group (CSF +) (n = 22) were compared to remaining patient (CSF-) (n = 39). There was no significant difference in the occurrence of postoperative BPPV, aural fullness, tinnitus and vertigo spells. There was no significant difference in PTA, BCT or SDS between our groups at any visit. CONCLUSIONS: Intraoperative CSF Leak may cause a temporary non-significant worsening of hearing in the first-month postoperatively without any difference at 6 months.

I. Sanchez-Sellero, et al., **Caffeine intake and Meniere's disease: Is there relationship?** Nutr Neurosci, 2018. 21(9): p. 624-631. OBJECTIVES: Although it is commonly recognized that dietary restrictions may improve the clinical course of Meniere's disease, their effectiveness has not been definitely demonstrated. The aim of this study was to examine whether caffeine consumption could be involved in Meniere's disease. METHODS: Cross-sectional, observational, case-control study, comparing caffeine consumption (intake of coffee, tea, kola-type beverages, energy drinks, and chocolate-containing beverages or foods) between patients with Meniere's disease (group A) and patients affected by vertigo with other origins (group B) and/or control subjects (group C). PATIENTS: 180 subjects (72 in group A, 72 in group B, and 36 in group C). Caffeine intake was categorized in four levels: very low (0-25 mg/day), low (26-100 mg/day), moderate (101-300 mg/day), and high (>/=301 mg/day). Very low and low intake were considered light consumption, and moderate and high intake, heavy consumption. RESULTS: Mean daily caffeine intake was 175.8 mg. Meniere's disease patients showed a daily caffeine intake (222 mg) greater than those not affected by this disease (145 mg). Excluding in group B migraine patients, differences in caffeine intake are significant among the three groups (P = 0.021). There were significantly more heavy-consumers in group A than in other two groups jointed (P = 0.024; OR = 1.301, IC95% (1.015;1.668)). In group A, the age at onset of symptoms in caffeine consumers (49.7 years) was lower than in non-consumers (55.9 years). DISCUSSION: It should be recommended to reduce caffeine intake in those population

groups with higher risk of Meniere's disease (e.g. subjects with family members suffering from this disease).

K. C. Shen, et al., **Lermoyez syndrome revisited: 100-year mystery**. Acta Otolaryngol, 2018. 138(11): p. 981-986. OBJECTIVE: This study revisited seven patients with Lermoyez syndrome over the past 25 years using an inner ear test battery to elucidate its mechanism. METHODS: From 1992 to 2017, we have experienced 4096 patients with Meniere's disease (MD) and seven patients (5 males and 2 females, 8 ears) with Lermoyez syndrome. Two of the Lermoyez patients were elderly, aged 71 and 85 years. An inner ear test battery comprising audiometry, ocular and cervical vestibular-evoked myogenic potential (oVEMP and cVEMP) tests, and caloric test were performed. RESULTS: Significant improvement of mean hearing levels (MHLs) was identified at low and middle frequencies after vertiginous attack, but not at high frequencies. Inner ear deficits in Lermoyez patients ran from abnormal hearing (100%) to abnormal cVEMP (43%), caloric (38%) and oVEMP (0) tests, exhibiting a significantly declining sequence. This declining sequence differed from that in MD. CONCLUSIONS: Lermoyez syndrome is extremely rare, with prevalence relative to MD of 0.2%. The mechanism is considered as blockage in the ductus reuniens caused by dislodged saccular otoconia. Aging and trauma are two precipitating factors for the dislodged saccular otoconia, which may explain why Lermoyez syndrome occurs most frequently in males and some elderly.

S. Shi, et al., **Clinical Features and Endolymphatic Hydrops in Patients With MRI Evidence of Hydrops**. Ann Otol Rhinol Laryngol, 2019. 128(4): p. 286-292. OBJECTIVES:: The purpose of this study was to investigate the correlation between grades of endolymphatic hydrops (ELH) and clinical characteristics and determine the detailed clinical characteristics of Meniere's disease (MD) patients with evidence of hydrops based on magnetic resonance imaging (MRI). METHODS:: One hundred ninety-eight MD patients (396 ears) with MRI evidence of hydrops were included. ELH grades were evaluated using the Nakashima grading standard. Correlations between the extent of ELH and clinical features were evaluated. Detailed clinical characteristics were analyzed to assess the clinical diagnostic criteria. RESULTS:: Of 198 patients, ELH was observed in 100% of cases on the clinically affected side and 8.6% of cases on the asymptomatic side. In addition, 98.5% of ELH was classified as moderate or significant grade. Low-frequency hearing loss was significantly correlated with the extent of both vestibular and cochlear hydrops, whereas the vertigo attack frequency showed no significant correlation with ELH grades. The disease duration of MD with bilateral ELH was longer than that with unilateral ELH. The clinical characteristics were variant and did not completely fit the proposed diagnostic criteria. CONCLUSIONS:: MRI findings have relevance to the clinical severity, to a certain extent, but not vestibular symptoms. The proposed diagnostic criteria based on clinical characteristics may be partially effective; analysis of the detailed clinical characteristics of MD was meaningful. Diagnosis of MD based on both MRI and clinical symptoms could facilitate an early diagnosis.

S. Shi, et al., **Magnetic Resonance Imaging of Meniere's Disease After Intravenous Administration of Gadolinium**. Ann Otol Rhinol Laryngol, 2018. 127(11): p. 777-782. OBJECTIVES: A three-dimensional (3D) inversion-recovery (IR) sequence with real reconstruction (3D-real IR) sequence 4 hours after intravenous (IV) gadolinium injection has been used to visualize the endolymphatic hydrops (ELH) in Meniere's disease (MD). This study was designed to investigate the ELH characteristics in clinically diagnosed definite MD and to explore the pathology of MD with magnetic resonance imaging (MRI). METHODS: One hundred fifty-four patients with definite MD were included in this study. All patients underwent the IV method. The grades of ELH were analyzed on each image, regions of interest of the cochlear perilymph and the cerebellum white matter were determined, and the signal intensity ratio of the former to the latter (CC ratio) on both sides in patients with unilateral MD was subsequently evaluated. RESULTS: Endolymphatic hydrops was observed in 148 patients (96.1%) on the clinically affected side; the remaining 6 patients (3.9%) had no apparent ELH. One hundred fifteen patients (74.7%) had unilateral ELH, and 33 patients (21.4%) had bilateral ELH. Eighteen patients (11.7%) had ELH on the clinically silent side. Patients with moderate and significant grades of ELH in the vestibule and cochlea accounted for 88.3% and 90.3%,

respectively. The CC ratio of the affected side (1.39 +/- 0.37) was higher than that of the unaffected side (1.18 +/- 0.29) (P < .01) in 115 patients with unilateral MD. CONCLUSIONS: Moderate and significant grades of ELH are common in MD; however, the proposed diagnostic criteria are not fully consistent with ELH. The elevated contrast effect in the affected side in patients with unilateral MD may better reflect the pathologic condition of MD.

C. H. Shin, et al., **Management of Meniere's Disease: How Does the Coexistence of Vestibular Migraine Affect Outcomes?** Otol Neurotol, 2019. 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.

J. H. Sin, et al., **Nimodipine for the treatment of otolaryngic indications**. Am J Health Syst Pharm, 2018. 75(18): p. 1369-1377. PURPOSE: The uses of nimodipine for otolaryngic indications are reviewed, and recommendations for its use in clinical practice are provided. SUMMARY: Nimodipine is currently indicated for the improvement of neurologic outcomes in adult patients with aneurysmal subarachnoid hemorrhage (aSAH). However, other oral and i.v. calcium channel blockers have not exhibited the same beneficial effects in patients with aSAH, leading clinicians to believe that nimodipine possesses unique neuroprotective effects in addition to its calcium channel-blocking and vasodilatory properties. Consequently, clinical investigations of nimodipine have been conducted for cochlear and facial nerve preservation after vestibular schwannoma (VS) surgery, symptomatic management of Meniere's disease and peripheral vertigo, and recovery of vocal cord paralysis after laryngeal nerve injury. Three prospective randomized studies have investigated nimodipine for hearing and/or nerve preservation in patients undergoing VS resection, the results of which have suggested a potential benefit of initiating nimodipine during the perioperative period. Several studies of Meniere's disease and/or peripheral vertigo have reported improved symptom control with nimodipine. For vocal fold paralysis associated with recurrent laryngeal nerve (RLN) injury, nimodipine may increase the recovery rate based on the results of 1 nonrandomized prospective study that used nimodipine in a protocolized manner. One small pilot study found that nimodipine improved facial nerve function after maxillofacial surgery. CONCLUSION: Due to its proposed vasoactive and neuroprotective effects, nimodipine may play a role in the treatment of a number of otolaryngic pathologies including VS, Meniere's disease, peripheral vertigo, RLN injury, and facial weakness after maxillofacial surgery. Small studies have shown improved symptom control and recovery after surgery. Since all of the aforementioned indications are still considered off label, clinicians and patients should collaboratively assess the risks and benefits before initiating treatment.

N. K. Singh, et al., **Inter-frequency amplitude ratio of oVEMP for differentiating Meniere's disease from BPPV: clinical validation using a double-blind approach**. Int J Audiol, 2019. 58(1): p. 21-28. OBJECTIVE: The study aimed at examining the usefulness of inter-frequency amplitude ratio (IFAR) of ocular vestibular evoked myogenic potential (oVEMP) in identifying Meniere's disease (MD) and differentiating it from benign paroxysmal positional vertigo (BPPV). DESIGN: A case-control design was used with a double blind approach. Phase 1 included 70 healthy individuals and 36 individuals each with MD and BPPV and Phase 2 included 20 individuals each with MD and BPPV. The age range of the participants in both phases was 15-50 years. All participants underwent oVEMP testing using 500 and 1000 Hz tone bursts and IFAR was obtained. RESULTS: The results in phase 1 revealed significantly higher IFARs in Meniere's disease than BPPV and healthy individuals ($p < 0.001$). An optimum criterion point of IFAR >/=1.11 for diagnosing MD was found which yielded 80% sensitivity and 98% specificity. The results in phase 2 demonstrated 85% correct identification of MD and 95% correct rejection of BPPV as non-MD. CONCLUSIONS: IFAR of oVEMP appears highly sensitive and specific parameter for identifying MD and a clinically valid tool for differentiating MD from BPPV.

M. E. Smith, et al., **The Performance of Patient-reported Outcome Measures as Diagnostic Tools for Eustachian Tube Dysfunction**. Otol Neurotol, 2018. 39(9): p. 1129-1138. OBJECTIVE: To develop and validate a novel patient-reported outcome measure (PROM) to distinguish patulous from obstructive Eustachian Tube Dysfunction (ETD). To determine accuracy of PROMs and ET function tests as diagnostic tools for ETD. STUDY DESIGN: 1) PROM development and validation. 2) Test case-control diagnostic accuracy study. INTERVENTIONS: Cambridge ETD Assessment (CETDA) and ETDQ-7 PROMs, sonotubometry and tubomanometry ET function tests. SETTING: Tertiary referral center. PATIENTS: Cases with patulous (n = 7) or obstructive (n = 60) ETD, controls with either no ear symptoms (n = 33), or symptoms arising from hearing loss or Meniere's disease (n = 24). MAIN OUTCOME MEASURES: PROMs were assessed in terms of internal consistency, ceiling and floor effects, test-retest reliability and content, structural and criterion validity. PROMs and function test sensitivity and specificity was determined as diagnostic tests for ETD. RESULTS: The 10-item CETDA was developed. CETDA validity and performance were good, though five items suffered floor effects. There was no difference in scores for either PROM in the patulous ETD, obstructive ETD, and symptomatic control groups. Both PROMS had excellent diagnostic accuracy using only healthy controls as comparator for ETD, but specificity was very poor when controls with other otological disorders were included. Both objective tests had sensitivity and specificity of 63% and 79% for obstructive ETD. CONCLUSIONS: The CETDA and ETDQ-7 are not disease-specific and cannot distinguish obstructive from patulous ETD subtypes. A relatively weak correlation between sonotubometry and tubomanometry results, PROM scores, and the clinical diagnosis suggests that a varied core set of outcome measures is required to monitor response to treatments for ETD.

K. Stolzel, et al., **Comorbid Symptoms Occurring During Acute Low-Tone Hearing Loss (AHLH) as Potential Predictors of Meniere's Disease**. Front Neurol, 2018. 9: p. 884. Acute low-tone sensorineural hearing loss (ALHL) is a type of idiopathic sudden sensorineural hearing loss. ALHL is rarely a solitary condition but rather co-occurs with vertigo and tinnitus, being an element of contemporary diagnostic criteria for Meniere's disease (MD). The goal of our present study was to determine the value of ALHL for the early diagnosis of MD in patients presenting in the emergency room with ALHL as a main complaint. The files of 106 patients with ALHL who were admitted to the emergency room over the period of 7 years and 104 patients with acute high- tone sensorineural hearing loss (AHHL) from the same period were included in this retrospective study. Forty ALHL patients presented with recurrent episode of hearing loss and 66 remaining patients presented with ALHL for the first time. Of the latter group, 25 patients gave consent for the follow-up. First, we analyzed the difference in the occurrence of tinnitus and vertigo between the ALHL and AHHL groups. In patients with ALHL, the incidence of vertigo with tinnitus and the number of recurrent episodes were statistically higher than in patients with AHHL. Next, we focused on the ALHL follow-up group (25 patients). In that group, two patients had all MD symptoms at presentation, 18 had

ALHL and tinnitus and five ALHL only. Of 18 patients with ALHL and tinnitus at admission, five developed vertigo and thus the triad of Meniere's disease. None of the five patients with AHLH as a sole symptom developed MD during the follow-up time but four of them have developed tinnitus. Patients with recurrent ALHL had significantly higher incidence of MD than the patients with first episode. We conclude that some patients who present with ALHL and concomitant tinnitus or have recurrent episodes of ALHL are more likely to develop Meniere's disease than these patients, who present with ALHL as a sole symptom. Nonetheless, we recommend otological follow-up for all patients presenting with ALHL.

M. Strupp, et al., **Meniere's disease: combined pharmacotherapy with betahistine and the MAO-B inhibitor selegiline-an observational study**. J Neurol, 2018. 265(Suppl 1): p. 80-85. OBJECTIVES: Since oral betahistine has a very high first-pass effect (ca. 99%), metabolized by monoamine oxidases (MAO), the benefits of a high-dosage betahistine monotherapy were compared with those of a lower dosage of betahistine in combination with the MAO-B inhibitor (MAO-B) selegiline on the frequency of acute attacks of vertigo in patients with Meniere's disease (MD). METHODS: Thirteen adults aged 40-75 years (mean 58.9 years; six females) had initially been treated with a high dosage of betahistine dihydrochloride for at least 1 year. Under this therapy, all of them had </= 1 attack for >/= 3 months prior to the combination pharmacotherapy. Subsequently, they received 5 mg/day selegiline and the dosage of betahistine was reduced to about one tenth and then individually adjusted to the dosage needed to achieve the same treatment response (</= 1 per 3 months, observational period of at least 6 months). RESULTS: The initial dosage for the long-term "titration" of the attacks of vertigo was 9-80 24-mg tablets/day (mean 37.3), i.e. 216-1920 mg/day (mean 895.4 mg/day). After the combination with selegiline, the dosage needed to achieve the same benefit for >/= 3 months was 3-36 24-mg tablets (mean 8.5), i.e., 72-864 mg/day [mean 204.9 mg/day, $p < 0.001$ (paired t test)]. One patient transiently stopped the treatment with selegiline, another one reduced the dosage to 2.5 mg/day and the attacks re-occurred after 2-4 weeks. Six out of 13 patients reported transient fullness of the head during the combined treatment; in 2 of them this went away when they switched to 2.5 mg bid. In the longer term (> 9 months), one patient had to increase the selegiline dosage to 5 mg bd, one patient stopped the treatment with selegiline. CONCLUSIONS: The achievement of the same clinical effect with a significantly lower (about 1/5) dosage of betahistine can be explained by the inhibition of the MAO-B by selegiline leading to higher serum concentrations of betahistine. This approach is in line with recent developments to bypass the first-pass effect of betahistine by transbuccal or intranasal application. Despite the substantial methodological limitations of such an observational study, this combined pharmacotherapy could be an alternative to a high-dosage monotherapy with betahistine of MD.

M. Strupp, et al., **Peripheral vestibular disorders: an update**. Curr Opin Neurol, 2019. 32(1): p. 165-173. PURPOSE OF REVIEW: To provide an update on the most frequent peripheral vestibular disorders. RECENT FINDINGS: The on-going classification of vestibular disorders by the Barany Society represents major progress. The diagnosis of bilateral vestibulopathy (BVP) requires quantitative testing of vestibular function. 'Acute unilateral peripheral vestibulopathy' (AUPVP) is now preferred over 'vestibular neuritis.' Meniere's disease is a set of disorders with a significant genetic contribution. The apogeotropic variant of horizontal canal benign paroxysmal positional vertigo (hcBPPV) and anterior canal BPPV (acBPPV) can be distinguished from a central vestibular lesion. Vestibular paroxysmia is now an internationally accepted clinical entity. The diagnosis of SCDS is based on conclusive findings. SUMMARY: Diagnosis of BVP requires significantly reduced vestibular function. The clinical picture of AUPVP depends on how much the vestibular end organs or their innervation are affected. Meniere's disease phenotype is a constellation of symptoms. Although diagnostic and therapeutic criteria for pc and hcBPPV are well defined, a number of less frequent and controversial are increasingly diagnosed and can be treated. Diagnosis of vestibular paroxysmia requires that a patient responds to treatment with a sodium channel blocker. The

diagnosis of SCDS requires conclusive findings with various methods. There is still a great need for state-of-the-art randomized controlled treatment trials in most peripheral vestibular disorders.

M. J. Suh, et al., **Clinical Characteristics of Bilateral Meniere's Disease in a Single Asian Ethnic Group**. Laryngoscope, 2018. 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, 2018.

K. K. Talewar, et al., **Living with Meniere's disease: an interpretative phenomenological analysis**. Disabil Rehabil, 2019: p. 1-13. PURPOSE: To explore the meanings of Meniere's disease from the perspective of people living with this condition and to understand what was considered significant and important in participants' everyday lives. MATERIALS AND METHODS: Four women with Meniere's disease participated in face-to-face semi-structured interviews. Accounts were recorded, transcribed, and analysed using an iterative process integral to Interpretative Phenomenological Analysis. RESULTS: Three interconnected themes were identified. "You have no control whatsoever" conveys participants' perceptions of vertigo as having a disruptive and ongoing impact on physical and psychosocial function in everyday life. "Meniere's takes away your life completely" describes Meniere's as impinging on participants' most meaningful activities and relationships, and as restricting their ability to live their lives on their own terms. "You get on with life" recounts participants' efforts to refashion their lives whilst living with this condition and manage its most harmful effects. The psychosocial impact of living with Meniere's disease and its relevance to rehabilitation is discussed. CONCLUSIONS: Meniere's disease has an enduring physical and psychosocial impact. Clinicians who acknowledge and respond to an individual's subjective experience of their condition may be key to their engagement in therapy. Service users should have a voice in health service design and delivery. Implications for rehabilitation Meniere's disease is a long-term disabling condition that not only impacts on physical and psychosocial functioning but also restricts quality of life through stigmatisation. Fear of triggering an attack of vertigo may prevent people with Meniere's disease from engaging with rehabilitation. Therapists who adopt a biopsychosocial approach and who recognise patients' efforts to control their symptoms as a positive form of resistance may be better equipped to empathetically support patients to engage in new activities that may be vital to improving their lives.

R. L. Taylor, et al., **Otolith Function Testing**. Adv Otorhinolaryngol, 2019. 82: p. 47-55. Two technically simple tests, vestibular evoked myogenic potential (VEMP) and subjective visual vertical/horizontal (SVV/H) test, have the potential to transform otolith function testing from the research laboratory to the outpatient clinic. Cervical- and ocular-VEMPs are short latency surface potentials produced through the activation of saccular and utricular afferents by sound and vibration. They are tests of dynamic otolith function. The SVV/H test in peripheral lesions probes static asymmetries in utricular function and represents a perceptual error in perceived gravitational

vertical/horizontal. VEMPs and SVV/H enable the characterization of patterns and severity of otolith dysfunction in common vestibular disorders. Combined with tests of semicircular canal function, they provide a useful tool for eliciting diagnostic profiles in vestibular neuritis and Meniere's disease. VEMPs are valuable in the pre-surgical confirmation of superior semicircular canal dehiscence and in some cases, may alert the clinician to the presence of a vestibular schwannoma in patients with symmetrical hearing.

A. Thompson-Harvey, et al., **Symptoms in cervical vertigo**. Laryngoscope Investig Otolaryngol, 2019. 4(1): p. 109-115. Objective: To use a unique, 41-question survey to identify patient features distinguishing cervical vertigo from vestibular causes of vertigo and vestibular migraine. Methods: In this study, a unique, 41-question survey was administered to 48 patients diagnosed with cervical vertigo (n = 16), migraine (n = 16), and vestibular vertigo (eg, unilateral vestibular paresis, Meniere's disease) (n = 16) to test the hypothesis that a set of distinct symptoms can characterize cervical vertigo. Responses between the three diagnostic groups were compared to identify questions which differentiated patients based on their symptoms. Results: Eight questions were successful in differentiating vestibular vertigo from migraine and cervical vertigo. Symptoms endorsed by subjects with cervical vertigo overlapped substantially with subjects with well-established vestibular disturbances as well as symptoms of subjects with migraine. Twenty-seven percent of cervical vertigo subjects reported having true vertigo, 50% having headache, and 94% having neck pain. Conclusion: Lacking knowledge of neck disturbance, the symptoms we elicited in our questionnaire suggest that cervical vertigo subjects may resemble migraine subjects who also have evidence of neck injury. Whether or not subjects with "cervical vertigo" also overlap with other diagnoses defined by a combination of symptoms and exclusion of objective findings such as chronic subjective dizziness and other variants of psychogenic dizziness remain to be established. Level of Evidence: IV.

D. Tse, et al., **Novel Use of Portable Audiometry to Track Hearing Fluctuations in Meniere's Disease: A Pilot Study**. Otol Neurotol, 2019. 40(2): p. e130-e134. INTRODUCTION: Meniere's Disease (MD) is a disorder of the inner ear consisting of episodic attacks of vertigo associated with aural fullness, tinnitus, and fluctuating hearing loss. Hearing levels in MD can often fluctuate over time, and may eventually decline permanently in a step-wise fashion. There are no current studies examining daily hearing fluctuations for prolonged periods in patients with MD. Portable audiometry has the potential to allow the patient to monitor their hearing on a daily basis without attending a center for formal audiology. The objective of this pilot study was to assess feasibility of using iPad-based audiometry on a daily basis to capture hearing fluctuations in a small sample of adult patients with active MD. METHODS: We recruited five patients with active MD as defined by current diagnostic criteria (International Classification of Vestibular Disease 2015). "Active" MD was defined as the patient having had at least one typical Meniere's episode within the last 4 weeks. Patients were trained on how to use the portable audiometer and asked to perform at least daily audiograms for 3 months. Patients were asked to manually track vertigo attacks in a diary. Qualitative feedback was obtained from each patient at each monthly visit. For each patient, individual pure tone thresholds at each frequency and pure-tone averages (PTA) were analyzed for maximum and minimum values and interquartile ranges. RESULTS: There were four women and one man, with an average age of 49.8 years. Duration of MD ranged from 4 months to 5 years. None of the patients experienced any technical difficulties performing the testing at home. The average duration of each test was 4.2 minutes, with the longest test taking 19.2 minutes. Patients completed between 45 and 102 tests, with an average of 72. The interquartile range for the PTA ranged from 2.5 to 25 dB for affected ears, and 0 to 6.25 dB for unaffected ears with maximums ranging from 5 to 35 dB in affected ears, and 0 to 10 dB in unaffected ears. CONCLUSIONS: Daily portable audiometry is feasible in patients with MD. Future studies are planned to further analyze hearing fluctuations in MD with respect to frequencies affected, relationship to vertigo attacks, and response to treatments. Understanding hearing fluctuations in MD may aid refinement of diagnostic criteria and improve prognostication for long-term hearing loss, with a goal of informing treatments that might improve final hearing outcome.

B. F. van Esch, et al., **Video-head impulse test results in patients with Meniere's disease related to duration and stage of disease**. J Vestib Res, 2019. BACKGROUND: The video-head impulse test employs the vestibulo-ocular reflex (VOR) to assess vestibular function. To this day, no consensus has been reached among scientists in terms of whether or not vHIT results change in MD patients as the disease progresses. OBJECTIVE: To assess whether the vHIT is more often abnormal in later stages of MD compared to earlier stages. METHODS: We retrospectively analyzed patients with 'definite' MD who had undergone a vHIT and caloric test between 2012 and 2015. Patients were evaluated based on duration of disease in years (</=1, >1</=5, >5</=10, >10) and stage of disease (stage I and II versus III and IV). For the vHIT, an abnormal vestibulo-ocular reflex was defined as a gain cut-off value of</=0.8 and presence of correction saccades including subanalyses using a cut-off value of</=0.9. RESULTS: In 89 definite MD patients (42 (47%) male, mean age 55+/-5 (SD)), data on both the caloric test and the vHIT were available. The risk of an abnormal vHIT was 25% in patients with a duration of disease over 10 years compared to 22% in the patients with a disease duration of 10 years or less (risk difference 3%, 95% CI:- 28% to 35%), p = 0.82). The risk for an abnormal vHIT in the Stage I and Stage II was 17% compared to 26% in Stage III and IV (risk difference 9%, 95% CI:- 30% to 11%). When using a cut-off value of 0.9 we also did not demonstrate a relationship between the duration of disease and the proportion of abnormal vHIT test results. CONCLUSIONS: There is no relationship between the proportion of abnormal vHIT test results in patients with MD and either duration or stage of disease.

Y. Wang, et al., **Association of Meniere's disease and retinal vascular calibre: a prospective observational study in China**. BMJ Open, 2018. 8(10): p. e022069. OBJECTIVE: It is believed that Meniere's disease (MD) is associated with vascular disorders, but few studies have reported the relationship between retinal vascular disorders and MD. We evaluated and compared the retinal vascular calibres in patients with MD with healthy subjects matched for age, sex and vascular risk factors using retinal photographs to explore the association between MD and retinal vascular calibre. STUDY DESIGN: A prospective study. SETTING: Tertiary referral centre. PARTICIPANTS: Sixty patients with MD and 62 healthy subjects matched for age, sex and vascular risk factors were enrolled in this study. Twenty-four patients with MD had migraines, and 36 patients with MD did not have migraines. MAIN OUTCOME MEASURE: Retinal vascular calibres were calculated and compared not only between patients with MD and healthy subjects but also between subgroups of patients with MD. RESULTS: Compared with healthy subjects, patients with MD had a slightly larger retinal artery calibre (126.30+/-10.45vs 119.61+/-15.86, p=0.006) and a higher retinal artery/vein ratio (0.79+/-0.09vs 0.75+/-0.10, p=0.005). Among patients with MD, those with migraines had a larger retinal artery calibre (130.73+/-11.55vs 123.35+/-8.61, p=0.006) than those without migraines. Moreover, the presence of migraines and the high frequency of vertigo attacks appeared to increase the retinal artery calibre. CONCLUSIONS: Our study suggests that a relationship exists between retinal vascular calibre and MD. Although the pathophysiological relationship between migraine and MD remains unclear, the presence of migraine attacks may aggravate endolymphatic hydrops (EH) and accelerate the outflow of EH in patients with MD. More extensive studies are required to explore the association between retinal vascular calibre and MD.

A. Wesseler, et al., **Diagnostic Value of the Magnetic Resonance Imaging With Intratympanic Gadolinium Administration (IT-Gd MRI) Versus Audio-Vestibular Tests in Meniere's Disease: IT-Gd MRI Makes the Difference**. Otol Neurotol, 2019. 40(3): p. e225-e232. OBJECTIVE: Our aim was to evaluate the validity and reliability of clinically relevant tests in the diagnosis of Meniere's disease (MD) according to the criteria formulated during 2015 as well as their efficacy in detecting endolymphatic hydrops (EH). The focus was on: three-dimensional fluid-attenuated inversion recovery-SPectral Attenuated Inversion Recovery (3D-FLAIR-SPAIR) sequences using 3 Tesla magnetic resonance imaging (3T MRI) performed 24 hours after intratympanic Gadolinium injection (IT-Gd) in comparison with the functional tests pure tone audiometry (PTA), caloric test, video head impulse test (vHIT), and cervical-vestibular-evoked-myogenic-potentials (cVEMP). STUDY DESIGN: Retrospective study. SETTING: Tertiary care center. PATIENTS: Primary eligibility criteria were given

clinical suspicion of MD and the performance of an IT-Gd MRI leading to a group of 31 patients and 52 ears to be analyzed separately. MAIN OUTCOME MEASURE (S): Reanalysis of the raw diagnostic data leading to comparability of IT-Gd MRI, PTA, caloric test, vHIT, and cVEMP concerning their valency for clinically diagnosed MD and quantifiability of EH. RESULTS: Considering sensitivity, specificity, and the likelihood-ratio only the IT-Gd MRI displayed results qualifying it as a viable device for MD-diagnostics in regards to the criteria of 2015 ($p = 0.01$), it even provides direct imaging evidence for the underlying pathology of the disease. Furthermore, the comparison between MRI images and test results of caloric test, vHIT and cVEMP revealed that neither of these diagnostic functional tests serves as a reliable indicator for EH. CONCLUSIONS: It appears that the diagnosing process of MD would benefit from turning IT-Gd MRI into a standard diagnostic procedure in cases of suspected MD, displaying better results than caloric test, vHIT, and cVEMP.

A. Wolfovitz, et al., **The pattern of hearing outcome following surgery of the semicircular canals**. Laryngoscope Investig Otolaryngol, 2019. 4(1): p. 132-137. Objective: To analyze demographic, clinical, surgical, and audiometric factors that may affect hearing outcome following surgery for the semicircular canals (SCC). Method: This is a retrospective case review of adults who underwent surgeries for superior SCC (SSCC), lateral SCC (LSCC), or posterior SCC (PSCC) and whose data were extracted and analyzed for factors affecting the hearing outcome in these procedures. Results: Thirteen patients underwent surgery for SSCC, seven cases for the LSCC, one for the PSCC, and one case of combined PSCC/SSCC surgery. The mean age was 49.8 +/- 12 years (21-66). There was no difference between the preoperative and postoperative pure tone average (PTA) thresholds at 0.5-3 kHz. Higher thresholds were noted at 4, 6, and 8 kHz postoperatively. Deterioration (>10 dB) in the bone-conduction (BC) PTA was demonstrated in 3 of 22 (13.6%) cases with no significant difference in the demographic, clinical, surgical, and preoperative audiometric parameters relative to the cases without PTA BC change. A significantly larger difference in PTA BC (pre- vs. postoperative) was seen for males. Small effect size was noted for Air conduction (AC) PTA in males, and moderate effect size for Word Recognition Score (WRS) in surgery for the LSCC compare to SSCC. Conclusions: SCC surgeries carry a relatively low risk of deterioration in PTA BC. High frequency thresholds should also be included in postoperative hearing outcome assessment. Cases of LSCC for intractable Meniere's disease and surgery in males carry higher risk of poor postoperative hearing outcomes. Level of Evidence: 4.

Q. Wu, et al., **Response to "Drop attacks, hydrops severity and disease duration in hydropic ear disease (Meniere's)"**. Eur Arch Otorhinolaryngol, 2019.

Q. Wu, et al., **Clinical features and management of Meniere's disease patients with drop attacks**. Eur Arch Otorhinolaryngol, 2019. 276(3): p. 665-672. PURPOSE: The aims of the present study are to investigate the variations in clinical features, including medical history, hearing function, vestibular function, and degree of endolymphatic hydrops (EH), in Meniere's disease (MD) patients with and without drop attacks (DAs), and to examine the efficacy of intratympanic gentamicin (ITG) treatment in alleviating DAs. METHODS: In total, 177 unilateral definite MD patients, including 16 patients with DAs and 161 patients without DAs, were enrolled. The results of hearing test, vestibular-evoked myogenic potentials (VEMPs), and magnetic resonance imaging (MRI) were analyzed. Thirteen patients with DAs received a single ITG treatment and were followed up. RESULTS: The disease course of MD in the DA group was significantly longer than that in the control group ($p = 0.007$). MD patients with DAs had significantly greater hearing loss and worse EH than MD patients without DAs ($p < 0.05$). However, there was no between-group difference in vestibular function. In the study, 92.31% of refractory definite MD patients with DAs achieved satisfactory control of DAs after ITG treatment. CONCLUSIONS: MD patients with DAs tend to suffer from severe hearing loss and a significant degree of EH in the inner ear. However, the vestibular function of MD patients with DAs may not be completely abolished, but be sensitive to stimulating signals. ITG treatment, which helps to decrease vestibular sensitivity, was an effective treatment to control DAs.

Q. Wu, et al., **The Degeneration of the Vestibular Efferent Neurons After Intratympanic Gentamicin Administration**. J Histochem Cytochem, 2018. 66(11): p. 801-812. Intratympanic

gentamicin (ITG) has been used to treat refractory Meniere's disease. Disequilibrium after ITG was still a challenge for some patients, and the underlying mechanism is poorly understood. Our previous study demonstrated that gentamicin distributed in the bilateral vestibular efferent neurons (VEN) after ITG; however, does it lead to VEN damage and cause further disequilibrium in patients following ITG? In this study, we observed severe damaged gentamicin-positive neurons of VEN and severe fractured myelin layer plates around neural fibers when viewed under transmission electron microscopy at day 3 after ITG. At day 30, neurons of VEN presented with relatively normal structures. Compared with the control group, the total number of choline acetyltransferase (CHAT) immunolabeling neurons in bilateral VEN showed a significant decrease both at day 3 and day 30. However, there was no significant difference in the total number of CHAT immunolabeling neurons between day 3 and day 30. It indicates that gentamicin is not only retrogradely transported into bilateral VEN, but also results in the degeneration of VEN after ITG. These findings may be related to patients' disequilibrium symptom after ITG. Furthermore, we speculate that VEN may play a role in vestibular compensation.

J. Zhang, et al., **Molecular genetic studies of familial Meniere's disease**. Sci China Life Sci, 2019.

Y. Zhang, et al., **The Clinical Outcomes After Intratympanic Gentamicin Injection to Treat Meniere's Disease: A Meta-analysis**. Otol Neurotol, 2019. 40(4): p. 419-429. OBJECTIVES: In recent decades, intratympanic gentamicin (ITG) has increasingly been used to treat intractable Meniere's disease (MD). We performed a meta-analysis of pooled clinical outcomes, exploring whether ITG was effective and safe. DATA SOURCES: Cochrane Library database, Embase, and Medline. STUDY SELECTION: We searched scientific and medical databases to March 2018 for articles evaluating clinical outcomes after ITG treatment of intractable MD according to the American Academy of Otolaryngology Head and Neck Surgery (AAO-HNS) guidelines. DATA EXTRACTION: We performed a meta-analysis to evaluate treatment efficacy and safety. Quantitative and descriptive information of included RCTs was obtained. DATA SYNTHESIS: We ultimately evaluated 49 of the initially retrieved 1,062 citations (the 49 articles included data from a total of 2,344 MD patients). In almost all studies, patients served as their own controls; "before-and-after" clinical outcomes were reported. The I metric was used to explore heterogeneity. CONCLUSION: Overall, our results seem to provide the limited evidence about efficacy and toxicity effects of ITG. However, clinical outcomes require further confirmation; many included studies were poorly designed, less than 2 years for reporting results in MD are in the majority of patients. More long-term prospective follow-up, high-quality, large-scale, randomized controlled trials are needed to confirm that ITG is safe and effective when used to treat intractable MD.