Aetna considers dehydration testing with glycerol, urea, or other osmotic diuretics to verify the suspicion of endolymphatic hydrops (Meniere's disease) medically necessary only in members with atypical presentations of this disease.

Aetna considers dehydration testing experimental and investigational for other indications because its effectiveness has not been established.

Aetna considers the following experimental and investigational because their effectiveness for these indications has not been established:

- Endolymphatic sac immunohistochemistry of aquaporin-2, V2R vasopressin receptor, sodium potassium chloride co-transporter 2 (NKCC2), and transient receptor potential cation channel V4 (TRPV4)
- Genetic testing of KCNE1, KCNE3, SIK1, SLC8A1, and SLC26A4 gene mutation for the diagnosis of endolymphatic hydrops (Meniere's disease)
- Intravenous gadolinium inner ear magnetic resonance imaging for the diagnosis of Meniere's disease
- Testing for antibodies against inner ear antigens for the diagnosis of Meniere's disease
- Vestibular evoked myogenic potential (VEMP) for the diagnosis of Meniere disease and monitoring of disease progression
- Video head impulse test.

For electrocochleography for Meniere's disease, see CPB 0564 - Electrocochleogram and Perilymphatic Pressure Measurement (0564.html).

See also CPB 0238 - Chronic Vertigo (../200_299/0238.html), CPB 0467 - Vestibular Autorotation Test (VAT) (../400_499/0467.html), and CPB 0514 - Meniere's Disease and Related Disorders: Surgery (0514.html).

BACKGROUND

Dehydration Testing

Osmotic diuretics are able to reduce endolymphatic pressure and volume, and hence improve peripheral auditory and vestibular function. After baseline audiometric testing, a glycerol, urea or other osmotic diuretic is administered. Repeat audiometric testing is performed at 3 hours (and sometimes at 1 and 2 hours) post-ingestion. The test is considered positive if: (i) there is a 10 dB or more improvement at 2 or more frequencies (250 to 2,000 Hz), or (ii) there is a 12 % or greater improvement in speech discrimination scores. The test is associated with a number of unpleasant side effects, including headache, nausea, thirst, diarrhea, emesis, diuresis, and dizziness.

Because dehydration tests are relatively specific for endolymphatic hydrops, they may be useful in confirming the presence of disease in patients with atypical presentations. However, because the tests are relatively insensitive, they are not useful to rule out endolymphatic hydrops or as screening tests for the disease.
Although the tests appear relatively specific for endolymphatic hydrops, they are relatively insensitive. Snyder (1974) reported the experience using the glycerol test in 122 patients with a combination of sensorineural hearing loss and tinnitus or vestibular symptoms, in whom endolymphatic hydrops was considered a diagnostic possibility. Fifty percent of patients ultimately found to have endolymphatic hydrops had positive tests. One false-positive was found among the positive tests. In a series of 95 patients with Meniere's disease, Akioka et al (1990) found 47% to have a positive glycerol dehydration test. Stahle and Klockhoff (1986) reported 60% of patients with Meniere's disease were found to have positive tests, and that positive tests were only found in ears with Meniere's disease.

Dehydration tests have not been proven to be useful in selecting patients with endolymphatic hydrops who are most likely to respond to surgery. Some authors have suggested that patients with positive glycerol tests are more likely to have beneficial responses to endolymphatic sac decompression, but statistical proof of such a relationship is lacking.

Whether a Meniere's disease patient will have a positive test or not seems to depend in part on the phase of the disease. Tests are more likely negative very early and very late in the course of disease, although the stage of the disease is not predictable from the results of the dehydration testing.

Critics of dehydration testing note that the test is unpleasant, not adequately sensitive, impractical, and subject to significant placebo effects. According to Fagan (1999), dehydration studies are little used these days because they are unpleasant and time consuming. There is only anecdotal evidence that positive responders to dehydration tests may be more likely to respond to endolymphatic sac decompression. Some investigators have found that the results of dehydration testing are highly affected by suggestion to the patients as to what they should expect. These investigators suggest that the use of the dehydration test to select patients for surgery risks induces a bias toward more placebo responders.

In a critical review of diagnostic testing in endolymphatic hydrops, Arts et al (1997) concluded: “At this point, the clinical use of dehydration testing is unclear at best. Despite many legitimate questions with regard to its
practicality and sensitivity, there is considerable evidence that a real phenomenon, specific for endolymphatic hydrops, underlies this test. Given this, the test may be helpful in verifying the suspicion of endolymphatic hydrops in patients with atypical presentations. It is unlikely, however, that the choice of therapy will be altered by the results of this test in many instances”.

An UpToDate review on "Meniere disease" (Dinces and Rauch, 2014) does not mention the use of dehydration testing as a diagnostic tool.

**Note:** Osmotic diuretics such as urea and isosorbide that can be taken orally have also been used as treatment for endolymphatic hydrops.

**Genetic Testing**

In a case-report, Yoshida et al (2015) reported magnetic resonance imaging (MRI) findings in a 13-year old girl with an SLC26A4 gene mutation who had low-frequency sensori-neural hearing loss (SNHL). The patient exhibited bilateral and symmetric low-frequency SNHL. Upon genetic testing, a heterozygous c.1105A > G (p.K369E) mutation of the SLC26A4 gene was detected. Mild endolymphatic hydrops in the right cochlea and marked endolymphatic hydrops in the left vestibulum were seen by MRI 4 hours after an intravenous gadolinium injection. The authors concluded that this was the first reported case of a patient with the SLC26A4 gene mutation c.1105A > G (p.K369E) who had low-frequency SNHL. They stated that co-occurrence of cochlear and vestibular endolymphatic hydrops suggested an association with that pathology. These preliminary findings need to be validated by well-designed studies.

Lee and co-workers (2015) examined the prevalence, inheritance patterns, and clinical characteristics of familial Meniere's disease (MD) in a South Korean population. Direct and telephone interviews were performed for 286 definite MD patients and their family members who were suspected of having MD. The diagnosis of MD in family members was made by obtaining a detailed history, performing basic neurootological examinations and reviewing hearing test results. The clinical characteristics as well as the prevalence and inheritance patterns of familial MD were analyzed. The prevalence of familial Meniere-like
syndrome (at least 1 family member with definite MD and other members with probable MD) and definite familial MD (2 or more family members with definite Meniere’s disease) were 9.8 % and 6.3 %, respectively, and the most common inheritance pattern was autosomal dominant with incomplete penetrance. The significant clinical characteristics of familial cases were an early disease onset and a higher prevalence of migraines. The authors concluded that this was the first report describing the genetic aspects of MD in a single large Asian population. The prevalence of definite familial MD was 6.3 % with an incomplete autosomal dominant inheritance pattern in most cases. Early-onset age and a high prevalence of migraines were significant clinical features of familial MD in this South Korean population. They stated that these data could provide a basis for the analysis of the genetic mechanism of familial MD in Asian populations.

Li and colleagues (2016) noted that MD is defined as an idiopathic disorder of the inner ear characterized by the triad of tinnitus, vertigo, and sensorineural hearing loss. Although many studies have evaluated the association between variants in the KCNE1 or KCNE3 gene and MD risk, debates still exist. These researchers evaluated the association between KCNE gene variants, including KCNE1 rs1805127 and KCNE3 rs2270676, and the risk of MD by a systematic review. They searched the literature in PubMed, SCOPUS and Embase through May 2015, and calculated pooled OR and 95 % CIs using a fixed-effects model or a random-effects model for the risk to MD associated with different KCNE gene variants. The heterogeneity assumption decided the effect model. A total of 3 relevant studies, with 302 MD cases and 515 controls, were included in this meta-analysis. The results indicated that neither the KCNE1 rs1805127 variant (for G versus A: OR = 0.724, 95 % CI: 0.320 to 1.638, p = 0.438), nor the KCNE3 rs2270676 variant (for T versus C: OR = 0.714, 95 % CI: 0.327 to 1.559, p = 0.398) was associated with MD risk. The authors concluded that based on current evidence from published studies, neither of the 2 variants from KCNE was significantly associated with the risk of MD. They stated that larger studies with mixed ethnicity subjects and stratified by clinical and sub-clinical characteristics are needed to validate these findings.
Teggi and associates (2017) examined the role of polymorphisms belonging to genes involved in the regulation of ionic homeostasis in Caucasian patients with MD. These investigators recruited 155 patients with definite MD and 186 controls (Control Group 1) without a lifetime history of vertigo, overlapping with patients for age and rate of hypertension. These researchers validated the positive results on 413 Caucasian subjects selected from a European general population (Control Group 2). The clinical history for migraine and hypertension was collected; genomic DNA was characterized for a panel of 33 SNPs encoding proteins involved in ionic transport. They found a higher rate of migraineurs in MD subjects compared to Group 1 (46.8 versus 15.5 %, p = 0.00005); 4 SNPs displayed differences in MD patients compared to Group 1 controls: rs3746951 and rs2838301 in SIK1 gene, rs434082 and rs487119 in SLC8A1; the p values of Chi-squared test for genotype frequencies are 0.009, 0.023, 0.009 and 0.048, respectively. SLC8A1 gene encodes for Na+-Ca++ exchanger, while SIK1 gene encodes for Salt Inducible Kinase 1, an enzyme associated with Na+-K+ ATPase function. The validation with Control Group 2 displayed that only rs3746951 and rs487119 are strongly associated to MD (p = 0.001 and p = 0.0004, respectively). The authors concluded that these findings support the hypothesis that a genetically induced dysfunction of ionic transport may act as a predisposing factors to develop MD.

Vestibular Evoked Myogenic Potentials

An UpToDate review on "Meniere disease" (Dinces, 2015) states that "Laboratory testing – Tests for antibodies against inner ear antigens have been described, but are not considered to be clinically useful and are not part of a routine evaluation for Meniere disease …. Tests for endolymphatic hydrops – The vestibular evoked myogenic potential (VEMP) is a newer test that shows promise for diagnosis and monitoring. Cervical VEMP (cVEMP) is an inhibitory sacculocollic reflex test that shows characteristic changes in symptomatic ears of Meniere patients, and may detect early saccular hydrops before the onset of classic Meniere symptoms. Ocular VEMP (oVEMP) engages both utricular and saccular afferent nerve fibers and may also be useful in assessment of Meniere patients. In addition to diagnosis, VEMP may be useful for
monitoring patients for disease progression, and to identify the active ear in patients with bilateral disease. VEMP is an emerging technology that has not yet been standardized or fully validated clinically".

Zhang and colleagues (2015) evaluated the clinical diagnostic value of VEMPs for endolymphatic hydrops (EH) by systematic review and meta-analysis. The pooled sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio (OR) and area under summary receiver operating characteristic curves (AUC) were calculated. Subgroup analysis and publication bias assessment were also conducted. The pooled sensitivity and the specificity were 49 % (95 % confidence interval [CI]: 46 % to 51 %) and 95 % (95 % CI: 94 % to 96 %), respectively. The pooled positive likelihood ratio was 18.01 (95 % CI: 9.45 to 34.29) and the pooled negative likelihood ratio was 0.54 (95 % CI: 0.47 to 0.61); AUC was 0.78 and the pooled diagnostic OR of VEMPs was 39.89 (95 % CI: 20.13 to 79.03). The authors conclude that the findings of this meta-analysis demonstrated that VEMPs test alone is insufficient for MD or delayed EH diagnosis, but that it might be an important component of a test battery for diagnosing MD or delayed EH. Moreover, VEMPs, due to its high specificity and non-invasive nature, might be used as a screening tool for EH.

Johnson and associates (2016) measured ocular VEMPs (oVEMPs) and cervical VEMPs (cVEMPs) in MD patients with confirmed cochlear hydrops and in the normal ears of volunteers. oVEMPs and cVEMPs were measured in 18 patients with a symptomatic diagnosis of MD and tone burst electrocochleographic confirmation of hydrops, and in the ears of 22 volunteers. Threshold measures: For cVEMP: no significant differences between Meniere's ears and controls; for oVEMP: significantly elevated thresholds in affected ears of Meniere's ears compared with their unaffected ears, but not with controls. Latency measures: cVEMP N1 peaks were significantly prolonged compared with the left and right ears of controls, but not with the non-affected ear. Amplitude measures: cVEMP P1N1 and N1P2 measures were significantly reduced compared with the right ear of controls, but not with the non-affected ear. For oVEMP, N2P2 amplitudes were significantly reduced compared with both ears of controls but not with the non-affected ear. The authors concluded that abnormalities of oVEMPs and cVEMPs were found in 18 MD patients who had an independent confirmation of cochlear hydrops. They noted
that the overlap of the results from MD patients compared with normal controls limited the use of VEMP abnormalities as a sole reliable diagnostic test for MD.

Maxwell and colleagues (2017) examined the effect of increased intracranial pressure on oVEMP amplitudes and frequency tuning in patients with MD to elucidate whether oVEMPS recorded under such conditions could provide a simple and accurate diagnostic test for MD. A total of 10 patients with certain unilateral MD (mean age of 48.2 years, range of 25 to 75, 6 males and 4 females) as confirmed by a locally enhanced inner ear MRI (LEIM) were enrolled in this study. Air-conducted tone-burst oVEMP amplitudes were measured in response to 500-Hz and 1,000-Hz in the horizontal plane (0 degree), a 20-degree head-down position. Tilting the patients from the horizontal position to the 20-degree head-down position led to a large reduction in oVEMP amplitudes to the 500-Hz tone burst (3.02 μV versus 1.17 μV, \( p = 0.005 \)) and to a smaller one in the 1,000-Hz tone burst (2.28 μV versus 1.78 μV, \( p = 0.013 \)) in the Meniere's ear. Accordingly, the 500/1,000-Hz frequency-tuning ratio was significantly decreased in the Meniere's ear as a result of this maneuver (1.36 versus 0.75, \( p = 0.005 \)). The authors concluded that oVEMP amplitudes and frequency tuning in MD patients showed a similar behavior to that found in healthy control subjects. They stated that oVEMP testing of putative MD patients in the tilted position is therefore unlikely to be diagnostically useful.

Yazdani and colleagues (2018) noted that despite some proposed roles for the diagnostic impact of the cervical VEMP test in the patients with MD, the role of this test as an objective instrument in following up patients with MD who underwent intra-tympanic steroid injection is not cleared. In a prospective study, a total of 31 adult patients with definite 1-sided MD with vertigo as main complaint refractory to medical treatments for 3 months, were selected. Patients underwent 3 times of intra-tympanic dexamethasone injection with 1-week intervals. These investigators performed cervical VEMP test at 1st and 4 weeks after the last injection for all participants. They followed the patients for 1 year. The study results were analyzed with the Chi-square test. Cervical VEMP test could not be recorded in 26 patients (83.9 %), and the test results were abnormal in the remaining 5 patients. The results were abnormal in the healthy ear of 32.3 % of the patients. Despite the clinical improvement of
the symptoms after intra-tympanic injection, the test results were not changed. The authors concluded that cervical VEMP test could not be recorded in the majority of the patients with MD; while it is usually recorded in normal ears. On the other hand, results of the cervical VEMP test do not change during the early phase after treatment and could not be a good option for follow-up and evaluating the response in this situation.

Scarpa and colleagues (2019) noted that VEMPs are increasingly used for different pathologies with new clinical insights. Although the study of otolith function selectively in both its saccular (cervical VEMPs; [cVEMPs]) and utricular (ocular VEMPs; [oVEMPs]) parts does not represent a recent achievement, the clinical utility of this tool is still emerging. These researchers described advances in application of VEMPs in diagnosis and clinical study of vestibular neuritis, MD and benign paroxysmal positional vertigo (BPPV). To perform a systematic review of the literature, 3 appropriate strings were run in PubMed to retrieve dedicated articles. A double cross-check was performed on citations and 2 independent investigators independently reviewed all full-text articles and performed a comprehensive quality assessment. Of 140 articles identified, 26 articles were included, comprising a total of 1,181 patients affected by vestibular neuritis (n = 296), MD (n = 378) and BPPV (n = 507). Overall, the use of both cVEMP and oVEMP appeared particularly useful in improving the topographic diagnosis of vestibular neuritis. Most (n = 8) of the studies dedicated to MD and BPPV (10 overall) also reported significantly abnormal VEMP values compared to healthy controls. The authors concluded that although further reports are needed to better define normal threshold levels of VEMPs for each pathology, the findings of this review suggested that VEMPs may represent a useful aid in improving the diagnostic accuracy for these 3 common vestibular pathologies.

**Endolymphatic Sac Immunohistochemistry of Aquaporin-2, V2R Vasopressin Receptor, NKCC2, and TRPV4**

Asmar and colleagues (2018) stated that endolymphatic sac (ELS) pathophysiology in MD remains poorly understood. These investigators identified from the literature a group of proteins expressed on the ELS and involved in endolymph volume regulation: aquaporin-2 (AQP2),
vasopressin receptor V2R, sodium potassium chloride co-transporter 2 (NKCC2), and transient receptor potential cation channel V4 (TRPV4). In a prospective case-control study, these researchers examined if their ELS expression was altered in MD, to better understand the pathophysiology of endolymphatic hydrops. A total of 24 patients with definite MD undergoing endolymphatic duct blockage surgery were recruited, as well as 23 controls with no history of MD undergoing surgery for vestibular schwannoma (VS). ELS biopsies and blood samples for plasma arginine vasopressin (AVP) were obtained. Immunohistochemistry for AQP2, V2R, NKCC2, and TRPV4 was performed. Slides were scanned digitally for highly sensitive pixel density analysis by specialized software (VIS; Visiopharm). Global scores generated by the software represent total and relative protein expression density of 3 staining intensity levels, exclusively on ELS epithelium. AQP2 expression density was significantly elevated in MD compared to VS (p = 0.003). There was no significant difference in plasma AVP, V2R, NKCC2, and TRPV4 expression. The authors concluded that this original study evaluated simultaneous in-situ expression of AQP2, V2R, NKCC2, and TRPV4 on the human ELS in MD, with a control group. These findings showed only AQP2 up-regulation on the ELS of patients with MD. These researchers suggested a constitutively increased expression of AQP2 in MD, independent of its regulatory axis (AVP-V2R); acquired regulator sequence mutations could support this model. These preliminary findings need to be validated by well-designed studies.

Furthermore, UpToDate reviews on "Meniere disease" (Moskowitz and Dinces, 2018) and "Pathophysiology, etiology, and differential diagnosis of vertigo" (Furman, 2018) do not mention aquaporin-2 (AQP2), vasopressin receptor V2R, sodium potassium chloride co-transporter 2 (NKCC2), and transient receptor potential cation channel V4 (TRPV4) as diagnostic tools for MD.

Video Head Impulse Test

Rubin and colleagues (2018) stated that there have been very few studies of the video head impulse test (VHIT) in patients with MD. Some reported 100 % normal VHIT results, others not. These discrepancies may be due to differences in severity. In a prospective study, these researchers compared VHIT and caloric reflex test results in advanced unilateral
definite MD. This trial included 37 consecutive patients, with a mean age of 56 ± 12 years. Mean hearing loss was 59 ± 18 dB HL; 12 patients were subject to Tumarkin’s otoolithic crises. Abnormal caloric reflex was defined as greater than or equal to 20 % deficit, and abnormal VHIT as presence of saccades or less than 0.64 gain in vertical semicircular canals and less than 0.78 in horizontal canals. All patients had normal VHIT results, and 3 had normal caloric reflex; mean caloric reflex deficit was 45 %. The authors concluded that this study was the only one to use the August 2015 updated definition of MD. The results showed that, outside of episodes of crisis, VHIT was normal during advanced unilateral definite MD, in contrast to abnormal caloric reflex. They noted that this feature could help distinguish MD from other inner ear diseases, and it would be interesting to try to confirm this hypothesis by studying MD patients.

Furthermore, UpToDate reviews on "Meniere disease" (Moskowitz and Dinces, 2018) and "Pathophysiology, etiology, and differential diagnosis of vertigo" (Furman, 2018) do not mention video head impulse test (VHIT) as a diagnostic tool for MD.

**Intravenous Gadolinium Inner Ear Magnetic Resonance Imaging**

Cho and colleagues (2018) examined the usefulness of the intravenous (IV) gadolinium enhanced inner ear MRI (IV-Gd inner ear MRI) in diagnosing MD and found a correlation between the degree of EH and the audio-vestibular tests. A total 29 patients diagnosed with unilateral definite MD were enrolled in this study. All subjects underwent IV-Gd inner ear MRI and auditory and vestibular function tests such as pure tone audiometry (PTA), electrocochleography (ECoG), cervical VEMP (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. The authors concluded that this study
demonstrated that endolymphatic hydrops in the cochlea and vestibule were readily visualized using IV-Gd MRI; and hydrops image by IV-Gd MRI may be a reliable method for diagnosing MD.

The authors stated that this study had several drawbacks. First, it did not have a control group. As these investigators compared the affected and unaffected ear, the hydrops ratio in the unaffected side did not mean the value of completely normal inner ear. As MD could be affected bilaterally, the normal value of hydrops ratio should be searched in the normal control. Second, the duration of the disease was not considered in this trial. Since MD is a long-standing disease, the hydrops level would be changed according to the disease duration. If the hydrops level in MRI is to be utilized for the diagnosis of MD, these researchers should get the data of hydrops level according to the duration of disease. Third, the number of enrolled patients was limited (n = 29). With their quantification method, the authors manually drew the contour of the cochlea and vestibule on the MRC image. The region of interests (ROI) in the vestibule was easily drawn on MR cisternography, and the vestibule in all parts could be occupied by the hydrops to varying degrees. However, the ROI in the cochlea included the areas where the hydrops could not involve such as modiolus and scala tympani. Thus, the hydrops ratio in the vestibule was higher and more reliable than in the cochlea (0.667 versus 0.372), even though these cochlear and vestibular hydrops ratios had a strong correlation. Additionally, these researchers need to increase the number of patients and normal control to have a cut-off value of hydrops ratio in the vestibule and cochlea, especially in the cochlea.

Lopez-Escamez and Attye (2019) stated that the diagnostic criteria for MD are clinical and include 2 categories: definite MD and probable MD, based on clinical examination and without the necessity of advanced vestibular or audiological testing. The condition is a heterogeneous disorder and it is associated with EH, an accumulation of endolymph in the inner ear that causes damage to the ganglion cells. Patients with suspected EH can be examined by MRI, offering new insights into these inner ear disorders. Results of imaging studies using the hydrops protocols show conflicting results in MD patients. These discrepancies can depend either on the MRI sequence parameters or on the method of hydrops grading or the inclusion criteria to select patients. The visualization of EH can be classified based on a semi-quantitative ratio
between endolymph and perilymph liquids, or on the distinction between the saccule and the utricle structures. In addition, MRI can also be used to examine if cochlea-vestibular nerves can present with imaging signs of axonal loss. In a systematic review, these investigators selected case-controlled studies to better characterize the potential added value in the diagnosis and management of patients with MD. Using different techniques, studies have identified the saccule as the most specifically involved structure in MD, and saccular hydrops appeared to be associated with low- to medium-tone SNHL degree. However, early symptoms still appeared too subtle for identification using MRI and the reproducibility of the hydrops protocols with various MRI scan manufacturers is debatable, thus limiting expansion of these techniques into clinical practice for the diagnosis of MD at this time. The authors stated that further research is needed. They stated that the future inclusion of semicircular canal hydrops location in the imaging signs and the application of MRI in patients with atypical presentations hold promise.

Electrocochleography for the Diagnosis of Meniere's Disease / Prediction of Occurrence of Meniere's Disease Among Individuals with Vestibular Migraine

Oh and associates (2014) hypothesized that if endolymphatic hydrops is a cause of MD, electrocochleography (ECoG) results obtained in normal subjects would differ from those obtained during the early symptomatic period of MD. These investigators examined the usefulness of ECoG in the diagnosis of MD during the early symptomatic period. Extra-tympanic ECoG was used to evaluate 60 patients in a MD group (17 men, 43 women; mean age of 43.6 years, range of 19 to 62) and 30 controls (11 men, 19 women; mean age of 43.5 years, range of 21 to 63). The summating potential/action potential (SP/AP) amplitude ratio and SP/AP area ratio were compared between the groups. Statistically significant differences were not demonstrated in the SP/AP amplitude ratio between the definite MD, probable MD, overall MD, or control groups (0.35 ± 0.02, 0.30 ± 0.03, 0.33 ± 0.02, and 0.30 ± 0.01, respectively). Additionally, statistically significant differences were not indicated in the mean SP/AP area ratio between the definite MD, probable MD, overall MD, or control groups (5.18 ± 0.98, 4.78 ± 0.21, 4.01 ± 0.78, and 3.72 ± 0.66,
Eggermont (2017) noted that the less than positive findings by Oh et al (2014) were echoed by a questionnaire on the clinical utility of ECoG in the diagnosis of MD among members of the American Otological Society (AOS) and American Neurotology Society (ANS). It was found that for about 50% of respondents, ECoG has no role in their clinical practice; ECoG was used routinely by only 1 in 6 respondents. This investigator stated that the objective diagnosis of individual cause of deafness, has focused primarily on vestibular schwannoma and MD, which showed comparable broad and long lasting SP-compound action potential (CAP) waveforms. ECoG highlighted the different underlying causes as relatively – compared to the CAP – large SP (MD) and mono-phasic unit contributions (vestibular schwannomas), respectively. The author stated that the specificity and sensitivity of ECoG in these disorders has so far precluded reliable diagnosis in individual cases.

In a systematic review and meta-analysis, Ayub and colleagues (2019) examined if combination of ECoG determined SP/AP ratio and other audiological measurements has greater sensitivity and specificity than that achieved with ECoG SP/AP ratio alone in diagnosing definite MD. PubMed, Cochrane Library, and Web of Science were searched using search terms "electrocochleography", "ECochG", "ECoG", "Meniere's Disease", and "Idiopathic Endolymphatic Hydrops". Inclusion criteria were extra-tympanic ECoG methodology, English language publication between January 2002 and December 2017, and the 1995 American Academy of Otolaryngology and Head and Neck Surgery MD diagnostic criteria. A total of 5 articles satisfied inclusion criteria and were sufficiently detailed for aggregate quantitative analysis of SP/AP ratio (315 subjects) and combination audiological measures (113 subjects). The diagnostic sensitivity and specificity of the SP/AP amplitude ratio was 47.6% and 83.8% and of combination diagnostic measures 63.5% and 89.3%, respectively. Point estimates of sensitivity (p = 0.248) and specificity (p = 0.969) and the summary Receiver Operator Characteristic (ROC) Curve (p = 0.407) were not statistically significant. The authors concluded that statistically, combination diagnostic measures did not respectively). The authors concluded that these findings indicated that extra-tympanic ECoG has limited value in diagnosing MD during the early symptomatic period.
result in greater accuracy of definite MD diagnosis compared to the SP/AP amplitude ratio alone. However, given the small sample size further studies are needed to attain a definitive conclusion.

Guidelines on Meniere's disease from the American Academy of Otolaryngology - Head and Neck Surgery (Basura, et al., 2020) state: "Clinicians should not routinely order vestibular function testing or electrocochleography (ECoG) to establish the diagnosis of Ménière’s disease. Recommendation against based on systematic reviews of cross-sectional studies and observational ECoG studies."

Furthermore, an UpToDate review on "Meniere disease: Evaluation, diagnosis, and management" (Moskowitz and Dinces, 2020) states that "Other testing may be used as part of the evaluation of MD, but these tests are not standardized and are not widely available for clinical use … There are tests for endolymphatic hydrops, which include glycerine, urea, or sorbitol "stress" tests and electrocochleography. However, these tests have low sensitivity and specificity, and their role in the diagnosis and management of MD is controversial".

In a preliminary study, Martines and associates (2020) examined electrophysiological findings among patients with vestibular migraine (VM) and compared them with those of patients suffering from definite MD without migraine. A total of 21 consecutive patients suffering from VM were enrolled; all subjects were selected according to the criteria proposed by the Barany Society for Neuro-otology. Each patient underwent a careful otological and neurotological examination. After completing a questionnaire regarding migraine and vertigo complaints, they were evaluated by audiometric testing, video head impulse test (vHIT), and ECoG. Data were compared with those of 21 patients who met the criteria for definite MD; 52.38 % of the patients with VM suffered from at least 2 episodes of migraine per week, with 42.85 % of the subjects complaining of migraines lasting greater than or equal to 24 hours; 57.14 % of the patients reported at least 4 episodes of vertigo per month, whereas 61.9 % suffered from symptoms of chronic unsteadiness. No significant difference (p = 0.76) resulted from the comparison of vHIT gain between patients with VM and MD; 11 out of 21 patients (52.38 %) with definite MD presented at least 1 ear with SP/AP of greater than 0.4, differently from patients with VM who exhibited SP/AP values suggestive
of endolymphatic hydrops (EH) in only 3 cases (14.28%). The authors concluded that this study found a higher proportion of abnormal ECoG in MD than in VM (p = 0.02) without any significant difference in the vHIT gain. On the basis of these findings, the identification of EH in some patients with VM could not be definitely related to the same pathway that triggers MD symptoms. These researchers stated that future longitudinal studies may help in better understanding whether abnormal ECoG findings could predict the occurrence of MD among patients with VM.

The authors stated that this study had several drawbacks. First, all subjects were evaluated in a symptom-free interval; this may have accounted for the lower prevalence of abnormal vestibular testing results compared to other investigators. Second, the study sample was relatively small (n = 21); however, different from other researchers, the authors only selected patients with definite VM without overlapping with definite MD. Third, these researchers did not follow-up on patients with VM; thus, they could not conclude that subjects with pathological SP/AP will not develop MD in the future, nor that patients with normal SP/AP will not show pathological ECoG over time.

Conway and colleagues (2021) noted that MD is a clinical entity with no definitive objective testing. It has been hypothesized that underlying endolymphatic hydrops stiffens the basilar membrane leading to increased speed of the acoustic stimulus; thus, traveling wave velocity has been proposed as an objective test to aid in the diagnosis. These researchers compared ECoG frequency-specific action potential latency, basilar membrane traveling wave time, and summation to action potential (SP/AP) ratio in MD and non-MD patients. Tympanic electrocochleography was carried out with frequency-specific action potential latency time and SP/AP ratio recorded. Patient demographics, symptoms, audiogram data, AAO-HNS classification of MD, management interventions, and follow-up were recorded. Statistical analysis was carried out to compare outcome measures across patient groups, demographics, and clinical data. A total of 91 patients (182 ears) were included. There was a significant difference between a "definite" Meniere’s diagnosis and an "unlikely" or "probable" diagnosis by an average of 13 dB HL for the pure-tone thresholds at 250 Hz on the affected side (p = 0.006). There was no significant difference in pure-tone thresholds at any other frequency, AP latency at any frequency, or AP/SP
ratio between the different Meniere's classification groups. The authors concluded that this study failed to show the significance of the traveling wave velocity as an objective test for MD. A significant correlation was found with low-frequency hearing loss between AAO-HNS Meniere's classification groups.

**CPT Codes/ HCPCS Codes/ICD-10 Codes**
Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by “+”

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<tbody>
<tr>
<td><strong>CPT codes not covered for indications listed in the CPB:</strong></td>
<td></td>
</tr>
<tr>
<td>81406</td>
<td>Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia)</td>
</tr>
<tr>
<td>92517</td>
<td>Vestibular evoked myogenic potential (VEMP) testing, with interpretation and report; cervical (cVEMP)</td>
</tr>
<tr>
<td>92518</td>
<td>Vestibular evoked myogenic potential (VEMP) testing, with interpretation and report; ocular (oVEMP)</td>
</tr>
<tr>
<td>92519</td>
<td>Vestibular evoked myogenic potential (VEMP) testing, with interpretation and report; cervical (cVEMP) and ocular (oVEMP)</td>
</tr>
<tr>
<td>92584</td>
<td>Electrocochleography</td>
</tr>
<tr>
<td><strong>Other CPT codes related to the CPB:</strong></td>
<td></td>
</tr>
<tr>
<td>69805 - 69806</td>
<td>Endolymphatic sac operation</td>
</tr>
<tr>
<td><strong>HCPCS codes not covered for indications listed in the CPB:</strong></td>
<td></td>
</tr>
<tr>
<td>A9579</td>
<td>Injection, gadolinium-based magnetic resonance contrast agent, not otherwise specified (nos), per ml</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>----------------------------------------------</td>
</tr>
<tr>
<td>H81.01 - H81.09</td>
<td>Meniere's disease</td>
</tr>
<tr>
<td>H81.10 - H81.13</td>
<td>Benign paroxysmal vertigo</td>
</tr>
<tr>
<td>H81.311 - H81.399</td>
<td>Other peripheral vertigo</td>
</tr>
<tr>
<td>H81.41 - H81.49</td>
<td>Vertigo of central origin</td>
</tr>
<tr>
<td>H83.01 - H83.2X9</td>
<td>Labyrinthitis</td>
</tr>
<tr>
<td>R26.0 - R26.9</td>
<td>Abnormalities of gait and mobility</td>
</tr>
<tr>
<td>R42</td>
<td>Dizziness and giddiness</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:


10. Dinces EA. Meniere disease. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed April 2015.


33. Yazdani N, Nejadian F, Rezazadeh N, et al. The follow-up role of
the vestibular evoked myogenic potential test in Meniere's
34. Yoshida T, Sone M, Naganawa S, Nakashima T. Patient with an
SLC26A4 gene mutation who had low-frequency sensorineural
hearing loss and endolymphatic hydrops. J Laryngol Otol.
myogenic potentials in endolymphatic hydrops: A meta-analysis.
AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0571 Endolymphatic Hydrops (Meniere's Disease) Tests

For the Pennsylvania Medical Assistance plan Vestibular evoked myogenic potential (VEMP) would be considered medically necessary when a diagnosis of Meniere’s disease is being considered but the diagnosis is unclear. It is not medically necessary for monitoring of progression of disease.

updated 07/22/2021