Chapter 12

The Definition Menière Groningen
in future perspective
**Introduction**

The definition of Menière’s disease is subject of continuous evolution as increasing information and knowledge is acquired regarding etiology, diagnosis and treatment. As many diseases can almost duplicate the symptoms of Menière’s disease an accurate assessment of the definition including the exclusion of other diseases is obligatory. The 1995 revised criteria for the diagnosis of Menière’s disease of the American Academy of Ophthalmology and Otolaryngology Committee on Hearing and Equilibrium provide uniformity and allow a more adequate comparison of clinical studies [1]. However, the subdivision in four different categories and the absence of a diagnostic protocol to establish the diagnosis and to exclude other causes for the symptomatology make the application in clinical and scientific practice still unsatisfactory.

The Definition Menière Groningen as used in this scientific project provided a fairly well-defined patient cohort allowing reliable and systematic analysis [1-6]. Nevertheless, a more detailed characterisation of the specific symptoms of Menière’s disease and a revised diagnostic protocol based on the results of the thesis could further contribute to a uniform diagnosis. The Definition Menière Groningen 2001 including a diagnostic protocol is introduced for clinical purposes. The Definition Menière Groningen 2001 including an extended diagnostic protocol is proposed for scientific analysis.

**Definition Menière Groningen 2001 for clinical purposes**

A renewed Definition Menière Groningen including a revised diagnostic protocol for the clinical practice is proposed and summarized in table 1. The Definition Menière Groningen 2001 for clinical purposes (diagnosis, treatment and reporting) includes a well-defined description of the correlating symptoms and a diagnostic protocol, which does not require a specialized test equipment.

Vertigo

In the Definition Menière Groningen 2001 vertigo is defined as a recurrent, spontaneous episodic vertigo. A spell is defined as a spontaneous rotational vertigo lasting at least 20 minutes (commonly several hours), often prostrating, accompanied by disequilibrium that may last several days, usually nausea, commonly vomiting or retching, and with no loss of consciousness. Horizontal or rotatory nystagmus is always present (table 1).

One of the shortcomings in the Definition Menière Groningen was the fact that the duration of a vertigo episode itself had not been defined so far (chapter 3). Defining...
the duration seems to be neccessary to exclude other pathology with a duration of vertigo lasting shorter than 20 minutes like benign paroxysmal positional vertigo (BPPV) or alternobaric vertigo. The vertigo has got to be spontaneous and not provoked by rapid eye movements or postural changes. At least two vertigo episodes in the patient’s history are required to distinguish Menière’s disease from diseases like vestibular neuronitis, labyrinthitis or vascular lesions.

Hearing loss
In this thesis hearing loss is defined as a sensorineural (cochlear) hearing loss with a minimum threshold of 20 dB Hearing Level (HL) or worse at at least one of the six measured thresholds (0.25 kHz, 0.5 kHz, 1 kHz, 2 kHz, 4 kHz or 8 kHz) on the pure-tone audiogram (chapter 3). A conductive component must be absent, excluded by pure-tone audiometry and tympanometry. This 20 dB HL threshold was chosen because the error of measurement in pure-tone audiometry is 10 dB HL. Using these criteria patients with a moderate high-frequency sensorineural hearing loss as the result of a beginning presbyacusis are also included. To overcome this major drawback, in the new Definition Menière Groningen 2001 the cochlear hearing los is defined as the total hearing loss of at least 60 dB over the three worst octaves in the standard pure-tone audiogram. Using this criterion it will still be possible to include patients with different shapes in pure-tone audiogram (table 1).

Tinnitus
Tinnitus is characterized by a spontaneous sensation of noise, buzz or constant tone in the ear. Mostly this sensation will not be synchronous with the pulse rate. Tinnitus can occur continuously or in attacks and can be experienced uni- or bilaterally. In the 1995 definition of the AAOO-HNS tinnitus is not required if aural fullness is present [7]. In our opinion the presence or history of tinnitus is compulsory in the definition (table 1).

Aural fullness/pressure
Aural fullness/pressure is not included in the new definition, although 2/3 of all patients in this study suffered from aural fullness/pressure (chapter 4). In this thesis a strong correlation was found between aural fullness/pressure sensation and tinnitus. The presence of aural fullness/pressure has no additional value for the definition of Menière’s disease, because patients with aural fullness/pressure sensation were almost automatically included because of having tinnitus (chapter 4).
Table 1. Definition Menière Groningen 2001 for clinical purposes.

- Vertigo
  - spontaneous, not provoked
  - at least two episodes (> 20 minutes) in the past
- Cochlear hearing loss
  - documented on at least one occasion
  - total hearing loss of at least 60 dB over the three worst octaves in the standard pure-tone audiogram
  - present now or in the past
- Tinnitus
  - ipsi- or bilateral
  - present now or in the past

- Diagnostic Protocol:

I. General and ORL-history
   - otological history
   - emotional stress related factors
   - personality features

II. General and ORL-examination
   - blood pressure measurement

III. Subjective audiometry
   - pure-tone audiometry
   - speech audiometry

IV. Objective audiometry
   - tympanometry
   - stapedial reflex measurements
   - brainstem evoked response audiometry (BERA)

V. Vestibular tests
   - electronystagmography
   - caloric tests
   - rotating chair

VI. Magnetic Resonance Imaging
   - T1, T2, gadolinium
   - petrosal bone, cerebellopontine angle, cerebrum

VII. Laboratory tests
   - full blood count
   - BSE
   - glucose
   - Lues serology
   - Borrelia burgdorferi serology
   - thyroid function test T3, T4, TSH

VIII. Consultation other disciplines on indication
   - internal medicine
   - neurology
   - ophthalmology
   - psychiatry
   - psychology
   - social worker
Diagnostic protocol
The content of the Groningen Diagnostic Protocol as part of the Definition Menière Groningen 2001 for clinical purposes is summarized in table 1. The diagnostic protocol includes the general and otorhinolaryngological history with special attention for the otological history, emotional stress related factors and personality features. The general and ORL-examination is followed by blood pressure measurement in upright and supine position to exclude stress related and essential hypertension, and also alternobaric vertigo (chapter 11).

The basic subjective audiometric tests consist of pure-tone audiometry and speech audiometry (50% speech level and speech discrimination score). Since the outcome of this thesis indicate that the shape of the pure-tone audiogram may contribute to a classification of Menière’s disease, this feature should remain subject of further study (chapter 5).

Tympanometry, stapedial reflex measurements and brainstem evoked response audiometry (BERA) are the required objective audiometric tests. Tympanometry, stapedial reflex measurements are important to exclude conductive hearing disorders and middle ear pathology like otosclerosis or tympanosclerosis. With BERA it is possible to exclude retrocochlear pathology as tumors in the cerebellopontine angle, multiple sclerosis, vascular and immunological disorders. There is no further place for electrocochleography (EcoG), because on an individual basis the EcoG-results as described in this thesis did demonstrate additional specificity and sensitivity regarding the diagnosis of the affected ear and did not provide obvious clues for the classification of Menière’s disease (chapter 6). The measurement is unfortunately invasive and often not reliable enough because of technical problems.

Electronystagmography, the caloric test and the rotating chair test are the standard vestibular tests of the new protocol. In patients with Menière’s disease the labyrinthine preponderance (LP) is the best indicator for the side of the lesion as has been shown in our results (chapter 8). Based on LP, duration of disease, severity of vertigo, shape of the audiogram and asymmetry in time constante T two subgroups of patients could be identified.

Magnetic Resonance Imaging of the inner ear, cerebellopontine angle and centrous nervous system using non-enhanced T1 and T2-weighed images, in combination with gadolinium-enhanced T1-weighed images are neccessary to exclude pathological processes in the labyrinth, cerebellopontine angle or in cerebro.

The basic laboratory tests are mentioned in table 1. They are performed to exclude infections, like labyrinthitis (chapter 4). Glucose is determined to exclude diabetes mellitus. Lues and Borrelia burgdorferi serology are established to respectively exclude Lues and Lyme Disease. T3, T4 and TSH is measured to exclude thyreoid pathology.

Consultation of other disciplines (internal medicine, ophthalmology, neurology, psychiatry, psychology) on indication can be required. A social worker is usefull to
study the social environment of the patient and can provide support in this matter if required.

Unilateral and bilateral disease
As described in the separate chapters in this thesis several important differences between uni- and bilateral disease were found. The results support the theory that uni- and bilateral Menière’s disease might be two different entities. Therefore it remains important to distinguish between uni- and bilateral Menière’s disease. Taking the Definition Menière Groningen into account, a patient will receive the diagnosis unilateral Menière’s disease if the vertigo inclusion criterion is positive and the hearing loss criterion is positive in one ear, together with a positive criterion for tinnitus in the same (ipsilateral) ear (figure 1). If the vertigo inclusion criterion is positive, the hearing loss criterion is positive in both ears, together with a positive criterion for a bilaterally perceived tinnitus, this patient suffers from bilateral Menière’s disease. In figure 1 the definition of uni- and bilateral Menière’s disease is given regarding the symptoms.

Figure 1. Definition of uni- and bilateral affection of Menière’s disease in relation to the symptoms.

Definition Menière Groningen 2001 for scientific purposes

Since the discovery of hydrops in the endolymphatic system in the temporal bones of patients with Menière’s disease endolymphatic hydrops has been generally accepted as the basic histopathological substrate of Menière’s disease [8,9]. Although the etiology of Menière’s disease is still unsolved, cumulating evidence suggests that
endolymphatic hydrops may arise as a result of the destabilization of natural regulation through overproduction and/or reduced absorption [10]. The production of endolymph is thought to be regulated mainly by the enzyme Na/K-ATP-ase in the marginal cells of the stria vascularis of the cochlea, as well as in the dark cells of the utricle and the cristae ampullares of the semicircular canals. In earlier experiments a relationship between circulating adrenal steroids and Na/K-ATPase activity in the inner ear was observed. Emotional stress leads to the activation of neuroendocrine effector systems resulting in the increase of endolymph production [11,12]. A borderline capacity of the endolymphatic sac in combination with a periodic increase of endolymph production caused by stressful situations is regarded to be responsible for the development of Menière’s disease. Manifestations of Menière’s disease frequently occur during stressful experiences in patients with physiological systems under challenge due to a neurasthenic psychological profile [13,14,15].

Systematic evaluation of the psychological profile and neuro-imaging studies of CNS structures involved in the neuroendocrine effector systems of Menière’s patients will undoubtly contribute to a further understanding of the etiology of Menière’s disease [16,17]. Menière’s disease is characterized by an unpredictable clinical course sometimes leading to seriously disabling rest-symptomatology. Classification of the various stages of Menière’s disease is essential for an effective application of specific treatment modalities. The additional development of sophisticated diagnostic techniques to classify Menière’s disease should have high priority.

A renewed Definition Menière Groningen including an extended diagnostic protocol for scientific purposes is proposed and summarized in table 2. The Definition Menière Groningen 2001 for scientific purposes includes the identical well-defined description of the correlating symptoms and an extended diagnostic protocol with emphasis on etiology and classification of the disease.

*Table 2. Definition Menière Groningen 2001 for scientific purposes.*

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertigo</td>
<td>spontaneous, not provoked</td>
</tr>
<tr>
<td>Cochlear hearing loss</td>
<td>at least two episodes (&gt; 20 minutes) in the past</td>
</tr>
<tr>
<td></td>
<td>documented on at least one occasion</td>
</tr>
<tr>
<td></td>
<td>total hearing loss of at least 60 dB over the three worst octaves in the standard pure-tone audiogram</td>
</tr>
<tr>
<td></td>
<td>present now or in the past</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>ipsi- or bilateral</td>
</tr>
<tr>
<td></td>
<td>present now or in the past</td>
</tr>
<tr>
<td>Extended Diagnostic Protocol:</td>
<td></td>
</tr>
</tbody>
</table>

149
I. General and ORL-history
   - otological history
   - emotional stress related factors
   - personality features

II. General and ORL-examination
   - blood pressure measurement

III. Subjective audiometry
   - pure-tone audiometry
   - speech audiometry
   - fine structure audiometry
   - low-frequency masking

IV. Objective audiometry
   - tympanometry
   - stapedial reflex measurements
   - brainstem evoked response audiometry (BERA)
     including threshold and latency measurement
   - otoacoustic emissions (OAEs)
     including postural changes

V. Vestibular tests
   - electronystagmography
   - caloric tests
   - rotating chair

VI. Magnetic Resonance Imaging
   - T1, T2, gadolinium, 3DFT-CISS, 0.7mm slices
   - petrosal bone, cerebellopontine angle, cerebrum
   - distance between vertical part of posterior semicircular canal and
     posterior fossa
   - hippocampus

VII. Laboratory tests
   - full blood count
   - BSE
   - glucose
   - Lues serology
   - Borrelia burgdorferi serology
   - thyroid function test T3, T4, TSH
   - cortisol assessment
   - dexamethasone suppression test

VIII. Psychometric analysis
   - personality characteristics
   - coping
   - quality of life

IX. Symptomatology profile questionnaire (intake+follow-up)

X. Consultation other disciplines on indication
   - internal medicine
   - neurology
   - ophthalmology
   - psychiatry
   - psychology
   - social worker

XI. Donor codicil for post-mortem studies
Routine subjective audiometry is extended with fine structure audiometry. Based on von Békésy audiometry a more subtile description of the pure-tone audiogram can be measured to study the predictive value of the method with regard to the unaffected ear. In addition, this method can investigate the physiological state of the cochlea and may indicate the imminence of the attacks [18]. Low-frequency masking is a promising method for the early diagnosis of endolymphatic hydrops in Menière’s disease. A short acoustic stimulus and a low-frequency masker tone are applied to the same ear in an adjustable phase relationship. Phase-dependent masked thresholds are recorded. In Menière patients the phase-dependence may be totally absent and varies as the disease progresses. This low-frequency masking test might be a new diagnostic tool to non-invasively and quickly indicate endolymphatic hydrops. [19].

Brainstem evoked response audiometry is extended with threshold and latency measurements to obtain more information regarding central auditory processes involved in Menière’s disease.

Click-evoked as well as distorsion product otoacoustic emissions (OAEs) in patients with Menière’s disease are strongly associated with OAEs in normal or near-normal hearing (chapter 7). To provide more information with regard to the classification of Menière’s disease click-evoked OAEs in upright and supine position will be measured as part of the extended protocol and subsequently in periods of instability of the disease [20,21].

Magnetic Resonance Imaging of the inner ear, cerebello pontine angle and centrous nervous system using non-enhanced T1 and T2-weighed images, in combination with gadolinium-enhanced T1-weighed images are necessary to exclude pathological processes in the labyrinth, cerebellopontine angle or in cerebro. The three-dimensional Fourier transformation-constructive interference in steady state (3DFT-CISS) sequence provides excellent visualization of small anatomic structures of the inner ear and cerebello pontine angle. Significant differences in distance between the vertical part of the posterior semicircular canal and the posterior fossa were observed between Menière’s patients and the control group, indicating a higher incidence of hypoplasia of the endolymphatic sac and duct in Menière’s disease (chapter 9). Differences in the distance between the posterior semicircular canal and the posterior fossa were also found between uni- and bilaterally affected patients, suggesting separate entities. More detailed imaging using increasingly thin sections may provide more specific information regarding these interesting observations.

As mentioned earlier, manifestations of Menière’s disease frequently occur during stressful experiences in patients with psychological systems under challenge due to a neurasthenic psychological profile [13,14]. Mediated through the hypothalamus, stress leads to an increased secretion of the adrenocorticotropic hormone (ACTH) from the anterior pituitary gland followed by an increased adrenocortical production of glucocorticoids (cortisol and corticosterone) and mineralocorticoids (aldosterone). The psychological neuro-endocrine response is investigated by cortisol assessment and
dexamethasone suppression test [12]. Sustained elevated levels of glucocorticoids like cortisol can lead to neurotoxic damage of the hippocampal neurons, which play an important role in the feed-back mechanism of the stress regulation system resulting in a decrease in hippocampal volume [17]. Additional magnetic resonance imaging is performed to quantify the hippocampal volume compared to a control group. An extensive psychometric analysis is included in the diagnostic protocol to provide further information with regard to the personality characteristics, coping behaviour and quality of life [22].

Assessment of the symptomatology profile including duration and severity of symptoms using a questionnaire provides relevant additional information. In the population studied the duration of Menière’s disease in bilaterally affected patients was longer than in unilaterally affected patients which was not caused by a change-over from an unilateral start of the disease to a bilateral affection (chapter 4). The ears of each bilaterally affected patient were both affected almost from the beginning of the disease. The severity of symptoms did not correlate with the duration of the disease. The hospital admission caused a release in tinnitus and aural pressure/fullness, possibly by reducing stress, leading to a decrease in endolymphatic hydrops. Concerning vertigo the questionnaire had necessarily to be changed. In the renewed version of the questionnaire the number of attacks will be scored, related to the duration of each attack separately. Concerning the severity of the vertigo a question was added. This severity will be scored retrospectively over the previous three months as ‘none’, ‘mild’, ‘moderate’ or ‘severe’ (appendix).

Correlation between the clinical and histopathological features in Menière’s disease is of extreme importance to further elucidate the etiology and pathogenesis of the disease [23]. Therefore, all patients included in the Groningen Diagnostic Protocol for scientific purposes will be asked to fill out and sign a donor codicil. This codicil provides the possibility to relate post-mortem findings with the individual clinical history of each patient.

References


Mateijsen DJM, Kingma CM, de Jong PE, Wit HP, Albers FWJ. Aldosterone assessment in patients with Menière’s disease. ORL; in press.


Appendix. Symptomatology profile questionnaire (intake+follow-up).

<table>
<thead>
<tr>
<th>Hearing:</th>
<th>AD</th>
<th>AS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complaints during the last 3 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unchanged hearing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changed hearing</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tinnitus:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complaints during the last 3 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aural pressure/fullness:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complaints during the last 3 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vertigo:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complaints during the last 3 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of attacks during the last 3 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

remarks: