MENIÈRE'S DISEASE
PREVALENCE AND CLINICAL PICTURE

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List of Abbreviations

AAO-HNS	American Academy of Otolaryngology — Head and Neck Surgery
AICA	anteroinferior cerebellar artery
AP	action potential
BPPV	benign paroxysmal positional vertigo
COCH	coagulation factor C homolog, cochlin
CT	computerized tomography
DA	drop attack, i.e. Tumarkin otolithic catastrophe
dB (HL)	decibel (hearing level)
ECoG	electrocochleography
ENG	electronystagmography
Hz	hertz
MD	Menière's disease
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
PICA	posteroinferior cerebellar artery
PTA	pure tone average
SP	summation potential
SV	sway velocity
VEMP	vestibular evoked myogenic potential

List of Original Publications

This thesis is based on the following original articles referred to in the text by their Roman numerals:

I **Havia M, Kentala E, Pyykkö I.**
Prevalence of Meniere's disease in general population of Southern Finland.
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II **Havia M, Kentala E, Pyykkö I.**
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III **Havia M, Kentala E.**
Progression of Symptoms of Dizziness in Ménière's Disease.
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IV **Kentala E, Havia M, Pyykkö I.**
Short-lasting drop attacks in Meniere's disease.
Otolaryngol Head Neck Surg 2001;124:526-530.

V **Havia M, Kentala E, Pyykkö I.**
Postural instability in Meniere's disease.
J Vest Res 2004;14:37-46.

The publishers of the original articles have kindly granted their permission to reprint the papers in this thesis. Some unpublished data have also been included.

Introduction

Menière's disease (MD) is a triad of symptoms including episodic vertigo, hearing loss, and tinnitus. The idea of these three symptoms originating from the inner ear was first introduced in 1861 by Prosper Menière, but the etiology and pathogenesis behind the disease bearing his name are still poorly understood (Beasley and Jones 1996).

MD most often affects people in middle age. Only in a small portion of MD patients is the disease established as full triad from the onset. The initial symptoms are often cochlear and they may be attributed to another origin or simply to aging. After the vestibular symptoms join the cochlear symptoms, the long remission periods from vertigo may mask the disease's episodic nature, and the entity of symptoms, and thus, the disease behind the symptoms remains unrecognized (Arenberg et al. 1980; Tokumasu et al. 1996).

The diagnosis of MD has been problematic since no single test exists for definitive diagnosis. Each generation of otologists develops new diagnostic tests for MD, but no definite test has been found and even today many view MD as a diagnosis of exclusion (Levine et al. 1998).

The lack of long-standing consensus on the diagnostic criteria of MD makes it difficult to compare prevalence figures. The American Academy of Otolaryngology – Head and Neck Surgery (AAO–HNS) has redefined the criteria of MD twice since 1972. The most recent criteria, established in 1995, were the ones adopted in this study (AAO–HNS 1995).

Previous estimations of prevalence of MD have been derived from medical databases. The objective of the present work was to study the prevalence of MD in a general population and to evaluate the presence of three major symptoms of MD by duration of disease.

1. Review of the Literature

1.1 Historical Background

1.1.1 Prosper Menière

Prosper Menière was born in Angers, western France, in 1799 — the year Napoleon Bonaparte came into power. After receiving his doctorate of medicine in 1828, Menière worked as a doctor in several different positions, but later serving as Director of the Institute for Deaf-Mutes in Paris, which was one of the largest centers of medicine at that time. In the mid-19th century, the role of the inner ear as an organ of hearing was known since cochlear damage was seen to result in hearing loss, but the functions of the inner ear in maintaining balance and orientation had not yet been discovered. Vertigo, epileptic seizures, hysteria, and brain attacks were all gathered together under the puzzling idiom of "apoplectiform cerebral congestion", a state believed to be caused by congestion of the blood vessels of the brain. In 1861, at the age of 61 years, Menière presented his famous paper before the French Academy of Medicine which postulated that the symptoms of patients with episodic vertigo, hearing loss, and tinnitus originated from the labyrinth instead of the brain (Baloh 2001) .

The most convincing proof of the inner ear being the cause of vertigo was a case of young girl who had suddenly become completely deaf and experienced constant vertigo in conjunction with an influenzal illness. Subsequent autopsy findings revealed that her semicircular canals were filled with bloody exudate, but no intracerebral disease was apparent (Menière 1861). Based on Menière's experience treating many patients with combinated vertigo and hearing loss at the Deaf-Mute Institute, he pointed out that episodic vertigo usually had a benign course and the treatments typically used, including bleeding, leeching,

cupping, and purging, could be more harmful that the disease itself. Menière died of pneumonia in 1862 at the age of 62 years amidst the academic turmoil that his remarks had created (Beasley and Jones 1996; Baloh 2001).

1.1.2 After Menière

In 1874, the term 'Maladie de Menière' was used for the first time by Charcot, who discussed the triad of vertigo, hearing loss, and tinnitus described by Menière. He believed that no treatment existed for the disease but pointed out that its progression ceased upon the occurrence of total hearing loss. The term 'Menière's disease' was used in 1880 in the Edinburgh Medical Journal by McBride and James. They speculated that the cause of the disease was an organic lesion of the semicircular canals, an inflammation of the middle ear or increased pressure in the labyrinth, but one year later McBride specified the reason to be hemorrhage into the semicircular canals (Beasley and Jones 1996).

In 1902, in Vienna, Politzer defined MD as an apoplectiform form of sudden deafness and vertigo arising from the labyrinth. His description of symptoms also included gait disturbances, diplopia, hemianopia, and short episodes of loss of consciousness. In 1928, Dandy recognized the symptom complex consisting of vertigo, nausea, tinnitus, and progressive hearing loss and speculated the underlying cause to be in the vestibular nerve rather than in the semicircular canals since patients had both auditory and vestibular symptoms (Beasley and Jones 1996). In 1938, Hallpike and Cairns in London and Yamakawa in Japan independently described the pathological finding of endolymphatic hydrops in the temporal bones of patients with MD at autopsy.

1.2 Etiology

Although MD has been well characterized histopathologically by the presence of endolymphatic hydrops, the etiology and pathogenesis of the process remain unknown. Recent studies have indicated a possible role of autoimmune processes, endocrine function, infection, allergy, and genetic factors in the etiology. When the causative agent is known, it has been customary to speak about Menière's syndrome, reserving the term MD for the symptom triad of unknown etiology (Hamid and Sismanis 2001).

1.2.1 Autoimmune Processes

McCabe (1979) introduced the idea that autoimmunity might damage the labyrinth, showing that bilateral, progressive sensorineural hearing loss improved following immunosuppressive therapy, namely cortisone and cyclophosphamide. The autoimmune mechanism has also been presented to be etiological factor in MD based on a clinical response to treatment with steroids and immunosuppressive medication, elevated levels of circulating immunocomplexes in serum (Derebery et al. 1991), and increased natural killer cell activity (Fuse et al. 2003).

Using Western blot assays as a test for autoimmune inner ear disorder, antibodies against a 68-kilodalton protein, heat shock protein 70, as well as antibodies of other molecular weights, have been found in sera of MD patients (Billings et al. 1995; Gottschlich et al. 1995; Ryan et al. 2001; Riente et al. 2004). Rauch et al. (1995) found anti-heat shock protein 70 antibodies in 47% of unilateral and in 58% of bilateral MD patients but also observed high prevalence of these antibodies in control subjects. Thus, heat shock protein 70 did not prove useful in diagnosing MD (Rauch et al. 2000). Whether a subgroup of patients has immunomediated MD remains unclear (Ryan et al. 2001).

1.2.2 Endocrine Function

High plasma concentrations of antidiuretic hormone levels in MD patients with bilateral disease compared with a control population have been reported (Takeda et al. 1995; Lim et al. 2003). Exogenous administration of aldosterone results in endolymphatic hydrops in animals, and the secretion of this mineralocorticoid hormone is increased in emotional stress, a state in which MD symptoms often manifest. However, no differences in plasma aldosterone levels between

uni- and bilateral MD patients or between MD patients and normal subjects have been found (Mateijsen et al. 2001a). Brenner et al. (2004) reported a significantly higher rate of thyroid hormone supplement use among MD patients (32%) than among controls matched for age and sex (4%).

1.2.3 Viruses and Allergies

Herpes simplex has more commonly been isolated from the vestibular ganglia of patients with MD than in the general population (100% vs. 81%), suggesting a viral origin of the disease (Vrabec 2003). Latent virus-specific immunoglobulin E-mediated inflammation has been considered to have a role in the initiation and/or sustenance of MD (Calenoff et al. 1995). Duke (1923) was the first to suspect an allergic etiology for MD. An association between MD and food allergy (Clemis 1967; Endicott and Stucker 1977) and subjective improvement in symptoms of MD and allergy after treatment with desensitization and diet modification have subsequently been reported (Derebery 2000).

1.2.4 Genetic Factors

Strong evidence exists of a genetic predisposition to MD, with anticipation, familial occurrence, and an association with migraine and human leukocyte antigens (HLA) (Morrison and Johnson 2002; Oliveira et al. 2002). Morrison found 41 parent-child pairs with a mean 17.5-year difference in age at onset, to possess "anticipation", which means that in addition to earlier onset of the disease in successive generations there is also a tendency towards more severe manifestation. The mode of inheritance has been presented as autosomal dominant, with 60% penetrance of the mutation. The familial frequency of MD has been estimated to be 7% (Morrison 1995; Morrison and Johnson 2002).

The COCH (coagulation factor C homolog, cochlin) gene in chromosome 14 is the only gene identified to cause autosomal dominantly inherited hearing loss associated with vestibular dysfunction in humans. Six different mutations have been reported worldwide, and in some of these, the penetrance of vestibular symptoms is complete, resembling the clinical picture of MD (Usami et al. 2003). Fransen et al. (1999) were the first to report a mutation of a COCH gene leading to symptoms of MD in a significant portion of carriers; more than 25% of patients affected expressed episodic vertigo, tinnitus, hearing loss, and aural fullness. Based on this finding, they stated that COCH mutation should be considered in MD patients.

Usami et al. (2003) came to the conclusion that mutations in the COCH gene were a frequent cause of autosomal dominant progressive cochleovestibular dysfunction, but not of sporadic MD. This conclusion was based on their study conducted in Japan, in which they detected no mutations in sporadic MD patients. In addition they found a new mutation, the five previous mutations all being found in families of European ancestry.

1.2.5 Other Causes

Otitis media, otosclerosis, acoustic trauma, and developmental factors, such as hypoplasia and narrowing of the vestibular aquaduct, impaired pneumatization of the temporal bone, perisaccular fibrosis, and atrophy or hypoplasia of the sac, have been suggested as etiologic factors in MD (Mancini et al. 2002; Paparella and Djalilian 2002).

1.3 Epidemiology

1.3.1 Prevalence Estimations

Prevalence in Europe

In an early epidemiological study, Cawthorne and Hewlett (1954) reported the occurrence of MD to be 157 per 100 000 individuals in Great Britain. Harrison and Naftalin (1968), by contrast, described the English incidence to be 100/100 000. In Sweden, Stahle et al. (1978) found an incidence of 46/100 000 in their study of inpatients and outpatients possessing the complete triad of MD symptoms. Wilmot (1979) reported an incidence of 10-20/100 000 in Northern Ireland based on his own clinical records. In Italy, the prevalence has been observed to be 8/100 000, with this figure estimated to be 3.4 times higher among hospital personnel (Celestino and Ralli 1991).

Kotimäki et al. (1999) assessed the prevalence of MD in Finland by re-evaluating the hospital records of 306 MD patients treated in 7 different hospitals in Finland. Using the AAO-HNS 1995 criteria, they reported the prevalence of MD to be 43/100 000, but concluded that the prevalence is probably underestimated when using a retrospective method. They chose an investigation period of 5 years to also include those patients not visiting the hospital every year. However, they reported the possibility of some definite MD patients still being missed due the long remission periods in the disease.

Prevalence outside Europe

In the United States, a prevalence of 218/100 000 has been reported (Wladislavosky-Waserman et al. 1984). Their criteria included cases with vestibular, cochlear, and classic MD, and the classic form was defined as having both cochlear and vestibular symptoms with or without tinnitus. Watanabe et al. (1995) described a prevalence of 16-17/100 000 in Japan in a study that was not population-based. A relative frequency of 400/100 000 was found in a Nigerian black community (Okafor 1984). MD is apparently very rare among native Americans, i.e. southwestern American Indians (Wiet 1979). Some of the previous occurrence estimations of MD and criteria used in patient selection are presented in Table 1.

Table 1.
Evaluations of the occurrence of Menière's disease.

Investigator (year)	Occurrence / 100 000	Country	Source of data	Criteria
Cawthorne and Hewlett (1954)	157	Great Britain	Medical records	Undefined
Harrison and Naftalin (1968)	100	Great Britain	Undefined	Undefined
Stahle et al. (1978)	46	Sweden	Medical records	Complete triad
Wilmot (1979)	10-20	Northern Ireland	Clinical records	Undefined
Okafor (1984)	400	Nigeria	Medical records	Rotatory vertigo of an episodic nature, fluctuating cochlear symptoms. Negative findings in other diseases.
Wladislavosky-Waserman et al. (1984)	218	United States	Medical database	Vestibular, cochlear or classic MD with or without tinnitus.
Celestino and Ralli (1991)	8	Italy	Medical records	AAO-HNS 1972
Watanabe et al. (1995)	16-17	Japan	Medical records	Repeated attacks of vertigo, fluctuating cochlear symptoms with vertigo, exclusion of central nervous system diseases.
Kotimäki et al. (1999)	43	Finland	Medical records	AAO-HNS 1995

1.3.2 Age and Gender Distribution

The mean age of patients at onset of disease is 38-50 years (Stahle et al. 1991; Lee et al. 1995; Katsarkas 1996; Tokumasu et al. 1996). Ballester et al. (2002) reported MD to be common in elderly people based on a prevalence rate of 5% among balance-disordered people aged over 65 years. MD has been diagnosed in patients up to 90 years of age. As life span lengthens, the prevalence of MD in the oldest age groups is forecasted to increase (Mancini et al. 2002). Wladislavosky-Waserman et al. (1994) noted a peak in incidence in the age group 45-59 years, but estimated the rate to increase by age, with a small decrease occurring in the oldest age group of more than 75 years. About 3% of all MD patients are reported to belong to the pediatric age group (Meyerhoff et al. 1978). Akagi et al. (2001) found the incidence in pediatric patients with vertigo to be 2.9%. Most often (30.9%), however vertigo in children without otitis media is caused by migraine (Choung et al. 2003). While the disease is often reported to affect both genders equally (Oosterveld 1979; Tokumasu et al. 1995; Katsarkas 1996),

some authors have found a slight female predominance (Stahle et al. 1991; Lee et al. 1995).

1.3.3 Bilaterality

No difference is present in the involvement of the right and left ears in MD (Lee et al. 1995), but the prevalence of bilateral disease has been reported to increase with duration of illness (Green et al. 1991; Stahle et al. 1991). Forty-seven percent of patients have bilateral disease after 20 years of follow-up (Friberg et al. 1984). The time interval for symptoms to start in the second ear can vary from zero to more than 20 years (Haye and Quist-Hanssen 1976). Age at onset is not correlated with bilaterality of MD (Lee et al. 1995). Electrocochleography (ECoG) has revealed endolymphatic hydrops in the contralateral asymptomatic ear in 10% of MD patients regarded as having unilateral disease (Conlon and Gibson 1999).

1.4 Diagnostics of Menière's Disease

The cornerstone in the diagnosis of MD is the history given by the patient, with the audiologic evaluation being of secondary importance. It is, however, commonly accepted that after patient's history the audiologic data provide most relevant information for the diagnosis of MD (Lee et al. 1995; Mancini et al. 2002).

Advances in technology have resulted in a series of otoneurologic tests that increase clinicians' ability to evaluate vestibular function in patients with balance disorders. There is, however, no spesific clinical test for MD (Baloh 1998), and in diagnostics, the otoneurologic tests have a tertiary position. Diagnostic imaging studies are used principally to rule out other diseases (Mancini et al. 2002).

In the symptom history given by the patient, it is important to distinguish vertigo from other types of dizziness. The physical examination should include complete otorhinolaryngologic and neurologic evaluation, the latter in particularly, if the main complaint is balance disorder (Kumar and Petchenik 1990; Baloh 1995).

The variability in MD presentation, with its remissions and exacerbations, can sometimes make the disease difficult to recognize. This has prompted the development of guidelines to increase accuracy in reporting and diagnostics (Devaiah and Ator 2000).

1.4.1 Diagnostic Criteria of Menière's Disease

AAO-HNS published guidelines for the diagnosis in MD in 1972 (Alford 1972). These criteria were revised in 1985, when the Committee excluded the variants "cochlear" and "vestibular" MD based on an absence of documentation that these variants were related to the same pathologic disorder as MD (Pearson and Brackmann 1985). The criteria were revised a second time in 1995, diagnosis now requiring both cochlear and vestibular symptoms. These criteria still in use today are presented in Table 2 (AAO-HNS 1995).

Hearing loss in MD is easily documented but hard to define precisely. The AAO-HNS criteria offer few options in the diagnostics of hearing loss. The most useful for unilateral cases being criteria, where hearing loss is defined as the average of threshold values at 0.5, 1, 2, and 3 kHz being ≥ 20 dB poorer in the ear in question than on the opposite side. Diagnosis in bilateral cases, involves the average of threshold values at 0.5, 1, 2, and 3 kHz being > 25 dB poorer in the studied ear.

Table 2.
Criteria for diagnosis of MD (AAO-HNS 1995).

Certain MD	• Definite MD, plus histopathologic confirmation
Definite MD	• Two or more definitive spontaneous episodes of vertigo lasting 20 minutes or longer • Audiometrically documented hearing loss on at least one occasion • Tinnitus or aural fullness in the treated ear • Other causes excluded
Probable MD	• One definitive episode of vertigo • Audiometrically documented hearing loss on at least one occasion • Tinnitus or aural fullness in the treated ear • Other causes excluded
Possible MD	• Episodic vertigo of the Menière type without documented hearing loss, or • Sensorineural hearing loss, fluctuating of fixed, with dysequilibrium but without definitive episodes • Other causes excluded

Hearing stages

Because hearing is the most readily measured variable, a staging system based solely on hearing has been devised by the Committee on Hearing and Equilibrium of AAO-HNS (Table 3). This staging is based on the four-tone average of the pure-tone thresholds at 0.5, 1, 2, and 3 kHz of the worst audiogram. Staging should, however, be applied only in cases of definite or certain MD (AAO-HNS 1995).

Table 3.
Hearing stages by AAO-HNS 1995 criteria.

Stage	Four-tone average of hearing thresholds at 0.5, 1, 2, and 3 kHz
1	< 26 dB
2	26–40 dB
3	41–70 dB
4	> 70 dB

1.4.2 Audiologic Tests

Audiometry

Sensorineural hearing loss has to be documented audiometrically on at least one occasion to justify the diagnosis of MD. The determination of hearing change

should be based on the four-tone average of hearing thresholds at 0.5, 1, 2, and 3 kHz. A change of 10 dB or more is considered clinically significant in determination of hearing change. The four-tone average of 0.5, 1, 2, and 3 kHz has been chosen by AAO-HNS because it takes into account the importance of high frequencies in normal hearing (AAO-HNS 1995). Loudness recruitment and reduced speech discrimination are frequently noted in MD patients (de Sousa 2002). In case of bilateral hearing loss with a pure-tone average (PTA) worse than 70 dB or word recognition worse than 50%, the diagnosis of MD should be questioned (AAO-HNS 1995) .

Electrocochleography

ECoG is a method used for measuring stimulus-related electrical potentials generated in the cochlea and auditory nerve (Odabasi et al. 2000). The three most important electrical phenomena in ECoG evaluation are cochlear microphonics, summating potential (SP), and action potential (AP). An elevated SP/AP ratio has been reported to be important in diagnosing MD (Gibson et al. 1983; Eaton et al. 2003). SP enlargement has been described as the physiological manifestation of endolymphatic hydrops and sensitive in diagnosing MD (Gibson and Prasher 1983; Conlon and Gibson 2000). However, Levine et al. (1998) found ECoG to have limited value in diagnosing MD but they noted a correlation between duration of MD and audiometric findings. Pappas et al. (2000) in turn noticed no relationship between disease duration and ECoG results but found a significant relationship between hearing loss and elevated SP/AP ratio.

Transtympanic promontory placement of the electrode has been reported to produce the best recording conditions. However, the invasive procedure needed in the transtympanic approach limits its clinical usefulness. The results of extratympanic ECoG have been found to correlate well with the transtympanic measurements. Mori et al. (1987) found extratympanic ECoG useful in diagnosing MD patients and an increased SP/AP amplitude ratio to be much more common among MD patients than among those with hearing loss of other origin. However, pathological SP/AP ratios are also observed in such diseases as sudden deafness and Lyme disease (Selmani et al. 2002). This decreases the specificity of the pathologic finding. Recently, the SP/AP area curve ratio was reported to be more sensitive than the conventional SP/AP amplitude ratio in detecting MD patients, and a combination of ECoG and glycerol tests was effective in identifying patients with atypical MD whose disease would ultimately progress to definite MD (Devaiah et al. 2003; Kimura et al. 2003).

Auditory brainstem response

In auditory brainstem response, an auditory stimulus, usually a click, is given to the tested ear, after which an electric response is recorded. The ascending auditory pathways connect with the central nervous system nuclei, creating a complex system of auditory pathways. Auditory brainstem response is used in differential diagnostics of MD to rule out retrocochlear reasons for vertigo and hearing loss such as vestibular schwannomas and vascular anomalies (de Sousa et al. 2002).

1.4.3 Otoneurologic Tests

Posturography

Postural sway has been used as an indicator of balance function (Monsell et al. 1997). Postural sway too small to be observed in everyday life can be recorded by force platform posturography (Terekhov 1976), which measures forces needed to maintain balance and support body weight (Aalto et al. 1988). The two types of clinical posturography used are static and dynamic posturography (Black 1982). Static platform posturography measures body sway while the subject stands still on a stationary platform, whereas dynamic platform posturography also measures the subject's ability to stand in situations where balance is disturbed by a sway-referenced platform and/or visual surroundings (O'Neill et al. 1998; Evans and Krebs 1999). The sensitivity of static posturography has been reported to be 57%, as opposed to 38% for dynamic posturography, in diagnosing all patients with peripheral vestibular deficit. However, sensitivity of posturography increases to 66% with regards to MD patients alone (Di Fabio 1996). Asai et al. (1993) in turn found dynamic posturography to be better than other postural tests in the detection of pathology in patients with vestibular deficient. MD patients were relatively unstable or fell in dynamic posturography when they were dependent on a vestibular system only (platform sway-referenced and vision absent or distorted) (Black 1982). Evans and Krebs (1999) stated that posturography would only modestly enhance the diagnosis of vestibular deficit and that it could be utilized best in evaluating the effect of rehabilitation, and thus, assessing the functional status of balance-impaired subjects. Persons over 75 years have been reported to sway significantly more than younger people (Baloh et al. 1998). Postural sway is found to be most stable between the ages of 30 and 60 years, with sway velocity (SV) thereafter increasing due to degenerative changes in the body (Hytönen et al. 1993).

Electronystagmography

Electronystagmography (ENG) is a electrical method consisting of a set of vestibular tests for monitoring eye movements using the direct current potential naturally existing between the cornea and the retina. ENG can provide site-of-lesion information in case of vestibular deficit. With regards to MD, the most important component of ENG is caloric test. The most frequent abnormality noticed in caloric testing is unilateral weakness (Bhansali and Honrubia 1999). Most tests on vestibular function only provide information about the asymmetry of the vestibular lesion affecting the horizontal semicircular canals and they reveal nothing about patient's functional status since the tests are carried out in passive position. Abnormal caloric test results also tend to remain abnormal if the symptoms resolve (Asai et al. 1993).

In unilateral MD, caloric weakness has been demonstrated in 58% of patients on the involved side and in 19% on the normal side. Complete paralysis has been found in 7% of MD patients. With duration of MD, caloric responses have been reported to become weaker in 26% and stronger in 11% of patients. Twenty-six percent of the MD patients have had both increased and decreased values in their caloric tests when tested more than twice (Proctor 2000). Fifty-four percent of definite MD patients have had abnormal tests results in ENG with caloric irrigation (Kotimäki 2003).

Saccades are the fastest possible eye movements, reaching peak velocities of up to 700 per second. They are used to capture visual targets in the periphery of the visual field onto the fovea. Normal voluntary saccadic eye movements are very exact and overshooting rarely happens. Disorders of the saccadic system are categorized into three groups: velocity, accuracy, and latency. Abnormally slow saccades appear in many degenerative and metabolic diseases of the central nervous system (Bhansali and Honrubia 1999). Inaccurancy has been reported in association with cerebellar (Baloh et al. 1977) as well as with cerebellobrainstem (Dahlen et al. 1980) and frontal lobe lesions (Wennmo et al. 1983). Latency disorders occur in people with abnormal vision, Parkinson's disease, or Alzheimer's disease (Bhansali and Honrubia 1999).

Pursuit eye movements are smooth traching movements of the eyes that match the speed of the target and make it possible to analyze the moving target (Bhansali and Honrubia 1999; Haarmeier and Thier 1999). In case of an impaired smooth pursuit system corrective saccades are needed in order to keep up with the target. Abnormal smooth pursuit eye movements are seen in disorders throughout the central nervous system (Bhansali and Honrubia 1999).

Vestibular evoked myogenic potentials

The vestibular evoked myogenic potential test is a new method used to assess the inner ear (Magliulo et al. 2004). Loud clicks, short tone burst, head taps, and short duration of transmastoid currents have been shown to activate vestibular receptors and evoke reflex changes in tonic electromyogram activity within the sternocleidomastoid muscles that can be recorded by a electromyogram (Colebatch 2001). The vestibular evoked myogenic potential test has been reported to be beneficial in identifying endolymphatic hydrops of the inner ear and, when combined with the glycerol test, it can diagnose early-stage endolymphatic hydrops (Magliulo et al. 2004). Young et al. (2003) found vestibular evoked myogenic potentials to correlate with the stage of MD.

1.4.4 Imaging Studies

More detailed imaging of the inner ear and auditory pathways has been made possible by advancements in magnetic resonance imaging (MRI) and computerized tomography (CT) (Casselman 2002). MRI rules out vestibular schwannomas (Rosenberg 2000; Somers et al. 2001). Congenital inner ear malformations can often be seen on CT, but submillimetric MRI images are essential in diagnosing the defects between scalae inside the cochlea as well as possible asymmetry between scalae seen in endolymphatic hydrops (Davidson et al. 1999; Casselman et al. 2001). In animal studies, high-resolution MRI can visualize and quantify the extent of endolymphatic hydrops (Zou et al. 2003). Silver et al. (2002) reported that in using a 9.4 Tesla magnetic resonance scanner, the most powerful magnetic resonance magnet currently available, the most specific structures, including Reissner's membrane, can be analyzed in detail; the experience received via cadaver tests will eventually be extended to examining MD patients. In differentiating between MD and vascular-origin syndromal vertigo, the use of MRI and MRA (magnetic resonance angiography) is recommended (Welsh et al. 1996).

1.4.5 Laboratory Tests

Although laboratory tests are seldom positive in MD, they are cost-effective and yield information on the general health of the patient. The laboratory test panel should include a hemogram and determinations of erythrocyte sedimentation rate, C-reactive protein, thyroid function, and cholesterol, triglyceride, and glucose levels. A fluorescent treponemal antibody absorption test is used to rule out otosyphilis (de Sousa 2002).

1.4.6 Differential Diagnostics

Migraine

Migraine is a cause of recurrent vestibular symptoms, and in differential diagnosis, it should be taken into consideration. Migrainous vertigo includes episodic vestibular symptoms lasting from minutes to several days, an individual or family history of migraine, migrainous symptoms during the attack with or without headache, and migraine aura (Johnson 1998; Neuhauser et al. 2001). Vertigo and sensorineural hearing loss have been stated to occur in migraine in 12% (Johnson 1998) to 38% (Olsson 1991) of cases. Differentiation between MD and migraine is complicated because the prevalence of migraine in MD patients is 56% vs. 25% in patients without MD, and in less than half of patients a fixed association exists between headache and vertigo. The prevalence of migraine is increased in both men and women with MD. Forty-five percent of MD patients have vertigo attacks that are invariably accompanied by at least one migrainous symptom, such as migrainous headache, phonophobia, or aural symptoms (Neuhauser et al. 2001; Radtke et al. 2002).

The association between MD and migraine was already suggested by Prosper Menière in 1861. The high prevalence of migraine in MD patients and of vestibulo-cochlear symptoms in migrainous vertigo raises the possibility of some common etiology (Neuhauser et al. 2001; Radtke et al. 2002), but no generally accepted mechanism to explain the connection has been presented (Baloh 1997, 1998). Migraine has been demonstrated to damage the inner ear, causing permanent hearing loss and impairment of vestibular function (Lee 2000). Endolymphatic hydrops presented to be the cause of MD attack (Hallpike and Cairns 1938) has also been suggested to develop in a ear previously compromised by a vasospasm in the cochlear or vestibular branch of the internal auditory artery due to a migrainous mechanism (Baloh 1997; Lee et al. 2000, 2003). The efficacy of antimigrainous therapy in migraine-related dizziness has been shown to directly correlate with the therapy's ability to alleviate headache, and this correlation was maintained regardless of the temporal relation between headache and vertigo (Bikhazi et al. 1997).

Central nervous system causes

Vertigo associated with other neurologic symptoms, such as facial weakness and gait ataxia, is generally attributed to vertebrobasilar ischemia, but when presented as an isolated phenomenon vertigo is frequently of more benign origin, often linked to peripheral vestibular disorders (Troost 1980; Grad and Baloh 1989). Isolated vertigo has, however, also been reported to be the only symptom

of vertebrobasilar ischemia (Gomez et al. 1996). Vertigo and cochlear symptoms can result from ischemia in different branches of the vertbrobasilar territory, such as the posteroinferior (PICA) and anteroinferior cerebellar arteries (AICA), the posterior cerebral artery, and the basilar artery (Welsh et al. 1996). Adams (1943) was the first to describe association between acute ischemic stroke in the AICA distribution and vertigo, hearing loss, and tinnitus. Lee et al. (2002) found vertigo to be the initial symptom in all 12 patients with AICA in their prospective study. The patients had concomitant nausea and/or vomiting, and in the clinical examination, they all had spontaneous (horizontal-rotatory) nystagmus beating toward the healthy side (i.e. directed away from the side of infarction). Four patients (25%) had vertigo and/or auditory symptoms as an isolated manifestation from days to 2 months before infarctation. These transient symptoms lasted minutes, which is the typical duration of transient ischemia within the anterior or posterior circulation.

Grad and Baloh (1989) have also emphasized that brief episodes (minutes) of audiovestibular symptoms can be a warning of upcoming brainstem stroke. Sudden deafness and tinnitus can result from cochlear ischemia (Matsushita et al. 1993; Lee et al. 2002). A cochlear site for hearing loss with AICA infarction is understandable because the labyrinthine artery is an end-artery without collateral circulation (Grad and Baloh 1989). AICA infarction is most commonly caused by formation of an atheroma or thrombus in the parent basilar artery which blocks the orifice of AICA (Caplan 1989). Hinojosa and Kohut (1990) reported a loss of sensory epithelium of the cochlea and vestibular labyrinth consistent with inner ear infarction based on their histopathologic study of temporal bone of a patient with complete AICA infarction. MRA has been demonstrated to be superior in differentiating between central perfusion and vestibular disorders (Welsh et al. 2000).

Fluctuating hearing loss associated with vertigo and tinnitus can also be the initial symptom of multiple sclerosis. Other central nervous system causes that have to be taken into account in differential diagnostics are epilepsy, vascular loop compression syndrome, Arnold-Chiari malformation, arachnoid cysts, and tumors of the cerebellum and brainstem (Harrison and Naftalin 1968, Weber and Adkins 1997, Buongiorno and Ricca 2003).

Vestibular schwannoma

Hearing loss and tinnitus are the main symptoms of vestibular schwannoma, also known as acoustic neurinoma. Since vestibular schwannomas grow slowly or their growth is arrested, they often go undiagnosed for years. Advancements

in imaging studies have enabled vestibular schwannomas that would never have become clinically significant to be detected (Rosenberg 2000). Only half of the patients with vestibular schwannoma have vertigo (Kentala and Pyykkö 2001). However, 38% of patients have the full triad of vertigo, hearing loss, and tinnitus, and when vertigo is present it has been reported to mimic the vertigo seen in MD in 14% of patients. The mean duration of vertigo attacks range from 5 minutes to 4 hours, and they most commonly occur in acute phase once or twice a day. Caloric asymmetry > 25% has been detected in 61% of patients (Kentala and Pyykkö 2000). The majority of patients aged over 65 years with vestibular schwannomas do not need surgery, with MRI considered to be reliable in following their tumor growth (Rosenberg 2000).

Traumatic vertigo

Traumatic endolymphatic hydrops is a clinical entity caused by a history of head trauma. The clinical picture is characterized by episodic vertigo, fluctuating hearing loss, tinnitus, and aural fullness (Shea et al. 1995). Fluctuations in hearing after head trauma typically occur during the first year, after which the hearing loss stabilizes (Segal et al. 2002). Pulec (1972) reported head trauma to be the cause of endolymphatic hydrops in 3% of patients. Temporal bone fractures are capable of interrupting the endolymphatic duct in humans, leading to Menière's syndrome, which includes symptoms typical of MD. Trauma-induced hydrops without temporal bone fractures has also been reported (Ylikoski et al. 1982; Paparella and Mancini 1983). Obstructive hydrops can result not only from disruption of the endolymphatic duct because of fractures, but also from a block in flow caused by blood and debris (Fitzgerald 1996).

The symptoms, which are predominantly vestibular rather than auditory, often start several years after the trauma (Ylikoski et al. 1982). As time increases between the trauma and the MD-like symptoms, the causative relationship can be difficult to recognize. Reduced vestibular response in ENG has been found to be more common in trauma-induced Menière's syndrome than in MD, but auditory tests are often normal in traumatic Menière's syndrome. MD does not appear to be causally related to previous acoustic trauma (Fitzgerald 1996; Segal et al. 2003)

Labyrinthine fistula

Labyrinthine fistulae are anomalous communication routes between the inner ear and surrounding structures, leading to clinical symptoms of vertigo, hearing loss, and tinnitus resembeling MD. In addition, however, patients often feel per-

sistent disequilibrium and motion intolerance, with their symptoms being exacerbated by visually unstable surroundings (Fitzgerald 1996; Minor 2003). Labyrinthine fistula is an entity consisting of perilymphatic fistula and superior semicircular canal dehiscence syndrome. Perilymphatic fistula can be due to an excessive pressure change, trauma, erosion caused by chronic infection, or complications after an ear operation (Minor 2003; Baloh 2004). In 1998, Minor et al. presented superior semicircular canal dehiscence syndrome, which is caused by bony dehiscence of the affected canal. Loud sounds (Tullio phenomenon) and pressure changes (Hennebert sign) were noted to result in nystagmus in the plane of the superior semicircular canal. Patients with this syndrome have sound- and pressure-induced vertigo attacks, and a positive finding in fistula testing. Their air conduction thresholds are normal, but they may have an air bone gap - a finding in audiogram which distinguishes them from MD patients (Baloh 2004). Diagnosis of the syndrome is confirmed by high-resolution CT scans (Minor et al. 1998).

Benign paroxysmal positional vertigo

Benign paroxysmal positional vertigo (BPPV) is reported to be the most common peripheral vestibular deficit (Nedzelski et al. 1986). BPPV is characterized by a nystagmus that starts after a short latency, has limited duration, and is fatigued in repeated testing. Nystagmus results from free-floating otoliths in the endolymph of the posterior semicircular canal (Parnes and McClure 1992). Canalith reposition maneuvers have been reported to give good treatment results (Epley 1992), but many people recover from their symptoms after days or months with no intervention (Perez et al. 2002).

Patients with BPPV have a 2–5% increased prevalence of MD, and the MD symptoms typically start 2–5 years before the onset of BPPV (Baloh et al. 1987; Gross et al. 2000). The prevalence of migraine in BPPV patients is also higher than in the normal population (Ishiyama et al. 2000; Lempert et al. 2000). The prevalence of BPPV in MD patients has been reported to be 10% (Perez et al. 2002). BPPV can establish in the same or opposite ear as MD, or it can be bilateral, but when these two vestibular deficits are present simultaneously the resultant disability is higher than with BPPV alone (Dornhoffer and Colvin 2000).

1.5 Clinical Course in Menière's Disease

MD is diagnosed when the classic triad of symptoms is established. At the time of diagnosis, patients have often had audiologic or vestibular symptoms alone for months or even years (Mancini et al. 2002). The initial symptom in MD has been reported to be cochlear in 61%, vestibular in 18%, and a combination of the two in 21% of patients (Tokumasu et al. 1996).

1.5.1 Hearing Loss

MD is characterized by progressive, sensorineural hearing loss, usually accompanied by a history of hearing fluctuation, loudness intolerance, diplacusis, and aural pressure (Lee et al. 1995). Hearing often fluctuates early in MD, but fluctuation is not always present (AAO-HNS 1995). Hearing loss is considered to be low-frequency dominated (Antoni-Candela 1976), but the most common audiometric pattern can also be flat (Meurman and Grahne 1956; Enander and Stahle 1967). The duration of MD can influence the audiometric pattern. The pattern can be up-sloping (27%) or flat (55%) early in the disease but become downsloping as the disease progresses (Antoni-Candela 1976). Lee et al (1995) reported the predominant audiogram to be a peak type (50%), followed by a falling type (26%) and a dip type (9%). After 15 years of observation, 74% of patients were reported to have a flat audiogram (Friberg et al. 1984). Recently, the audiogram has been found to most frequently be up-sloping or peak type, with the shape of audiogram being independent of duration of MD (Mateijsen et al. 2001b).

Enander and Stahle (1967) observed the main loss of hearing to occur during the early years of the disease, after which the hearing level appears to stabilize, with the median for pure-tone audiogram, speech reception, and speech discrimination scores being 56 dB, 60 dB, and 54%, respectively (Stahle 1976). After 21 years of follow-up, Friberg et al. (1984) found no patients with a mean hearing loss of < 30 dB. Early in MD, hearing becomes impaired linearly with disease duration, but after the age of 50 years, both aging and duration of the disease apparently affect the hearing level (Kotimäki et al. 2001).

Profound hearing loss occurs in 1-6% of severely affected MD patients (Stahle 1976; Shojaku et al. 1995). Patients with bilateral profound sensorineural hearing loss have been found to benefit from cochlear implantation (Lustig et al. 2003).

1.5.2 Tinnitus

Hägnebo et al. (1997) reported tinnitus to cause the most discomfort to the MD patients. Tinnitus in MD can shift from a low pitched to a higher pitch but often is of low-frequency type, and thus, is difficult to mask with environmental sounds (Vernon et al. 1980; Kolbe et al. 2000). Patients describe it as a roaring, buzzing, ringing, or popping sound (Stouffer and Tyler 1990). Tinnitus may increase during or preceding a vertigo attack and continue so for some time after the attack (Alford 1972). Tinnitus in MD is often severe, and its intensity is reported to increase with duration of the disease (Kolbe et al. 2000). During the course of MD tinnitus has been reported to be easier to mask by a low level of external sounds, and in some patients it is also believed to disappear eventually (Vernon et al. 1980).

MD patients with tinnitus regard their tinnitus as more disturbing than patients with tinnitus due other causes, such as vestibular schwannoma, sudden deafness, noise-induced hearing loss, or presbyacusis (Stouffer and Tyler 1990; Kentala 1996). Surgery does not eliminate tinnitus, but gentamicin treatment offers some relief (Kaasinen et al. 1995; Feenstra 1997).

1.5.3 Vertigo

The vertigo in MD tends to be rotational, occurring in well-defined episodes. The attacks are often accompanied by nausea and sometimes vomiting and persist from 20 minutes to 24 hours (Alford 1972; AAO-HNS 1995). The vertigo attack in MD typically reaches a peak within a few minutes, remains severe for an hour or two, and then slowly resolves over the next few hours (Baloh 1995). Many people with MD experience and are adapted to low levels of vertigo and disequilibrium between vertigo attacks (Cohen et al. 1995), but the actual attacks have been reported to be most problematic of the three main symptoms of MD (Meyerhoff et al. 1981). The first vertigo attack has been regarded as the onset of the disease by some authors (Haye and Quist-Hanssen 1976).

Early in MD, vestibular symptoms dominate. During the active periods 1/3 of patients were reported to have more than 30 vertigo attacks per year (Haye and Quist-Hanssen 1976). After the first year of the disease, nausea-associated vertigo attacks become less frequent (Oosterveld 1979). In a study consisting of 514 MD patients, vertigo attacks lasted less than 10 minutes in 20%, 10–59 minutes in 36%, 1–4 hours in 36%, and more than 4 hours in 28%. In most cases (65%), the attacks occurred irregularly, in 23% during the daytime, in 7% in the evenings, and in 5% during the night-time. Sixty-five percent of patients had to dis-

continue their activities during the attacks (Hägnebo et al. 1997).

Vertigo attacks disappear or at least diminish over time (Stahle 1976; Friberg et al. 1984; Green et al. 1991). Up to 20 years, the mean number of annual attacks has been found to be 6-11, with this figure declining to 3-4 per year after that (Friberg et al. 1984). Silvestein et al. (1989) reported 57% of MD patients to have complete control of their vertigo after 2 years and 71% after 3 or more years since onset of the disease. Haye and Quist-Hanssen (1976) found that in 48% of the MD patients, the longest period without vertigo attacks was more than 5 years and in 19% 10 years or more. The impact of vertigo on the ability to work has been estimated to be moderate, and the annual working days lost because of MD to lie between 0 and 4 (Friberg et al. 1984).

Drop attacks

Drop attacks (DA) in MD were initially reported by Tumarkin (1936), and thus, they are also known as Tumarkin otolithic catastrophes. DA are abrupt attacks of falling without loss of consciousness. They occur most often in patients with severe and long-lasting MD, but they can also initiate the disease (Black et al. 1982; Baloh et al. 1990). DA usually last only from a few seconds to no more than a minute and are accompanied by cochlear symptoms, including hearing loss, tinnitus, and aural pressure (Tumarkin 1936). The patients characteristically feel as though they had been pushed and sometimes report a sudden tilting of their surroundings simultaneously with the fall. DA are supposed to result from mechanical deformation of otolithic organs, causing a burst of neural impulses, which activates vestibulospinal reflexes (Baloh et al. 1990; Ishiyama et al. 2001).

The incidence of DA is not known, but they have been reported to occur in 6–7% of MD patients (Black et al. 1982; Baloh et al. 1990). Ballester et al. (2002) found that in MD patients aged over 65 years the incidence of DA depended on the type of disease: the incidence was 11% for longstanding MD but 26% when the diagnosis had been set after the age of 65. Moreover they reported that 8% of elderly MD patients had initially been misdiagnosed mainly because of DA as having had a stroke or brainstem ischemia.

DA resolve spontaneously in the majority of MD patients, and for the remainder vestibular nerve section or destruction of the labyrinth - either surgically or chemically can eliminate the attacks (Janzen and Russell 1988; Ödkvist and Bergenius 1988). Ishiyama et al. (2003) reported DA that were related to non-MD otologic cause and found the incidence of migraine to be high in this group of patients with normal hearing.

2. Aims of the Study

1. To study the population-based prevalence of MD.

2. To characterize progression and level of hearing loss and tinnitus by duration of MD and to determine their relation to vertigo.

3. To evaluate the progression of vertigo by duration of MD with special reference to patients with a long history of persisting symptoms.

4. To assess the prevalence of DA in MD patients and to determine whether an association exists between DA and other symptoms of MD.

5. To evaluate postural stability and otoneurologic findings by duration of MD.

3. Materials and Methods

The study protocol was approved by the Ethics Committee of the Helsinki University Central Hospital.

3.1 Subjects

In Study I, a questionnaire was sent to 5000 randomly selected persons aged 12 years or more living in the Helsinki University Hospital area. These people were randomly selected from the population register data. Forty-seven percent of the recipients were men and 53% women. Their mean age was 44 years (range 12-99 years). The response rate after one postal reminder was 63% (n=3138). After exclusions the final study group consisted of 3116 people. Forty-three percent of the them were men and 56% women. Their mean age was 45 (range 12-99) years.

A sample of 243 consecutive patients with MD was examined in the Studies II–IV. The group consisted of 69 men and 174 women, and their mean age at onset of symptoms was 44 (range 17–79) years. Their mean age at the time of testing was 50 (range 20-80) years.

A subgroup of 180 patients underwent posturography testing in Study V. After excluding one male patient, 179 patients were analyzed for postural stability. Their mean age at the time of testing was 51 (range 22–80) years for men and 49 (range 20-78) years for women.

3.2 Methods

In audiological evaluation, pure-tone audiometry at frequencies of 0,125 kHz to 8 kHz was performed by trained audiology assistants using Madsen OB-822 diagnostic audiometer and TDH-39 headphones. The audiometers were calibrated according to ISO standards. The four-tone average of hearing thresholds at frequencies of 0.5, 1, 2, and 3 kHz (AAO-HNS 1995) was used to quantify the hearing loss.

In Study I, the recipients of questionnaires were asked whether they had experienced vertigo together with a moving sensation, hearing loss or tinnitus. For exclusion purposes, we also enquired about general illnesses, ear infections, former head and ear traumas, noise exposure, medication, and use of tobacco and alcohol. Patients with vertigo attacks were asked about their frequency, intensity, and duration. They were also asked about provoking factors for vertigo, their age at onset of vertigo symptoms, and whether nausea was present during the attacks. Finally, they were asked to estimate the time elapsed since their last vertigo attack. To assess the validity of the population-based study, we randomly selected a 100-subject sample among the people reporting vertigo. The sample was clinically examined in our vestibular unit. The clinical examination included complete otorhinolaryngologic and neurologic examinations supplemented by audiologic and otoneurologic tests. The following tests were used: 1) posturography; quiet stance, eyes open and closed (Starck et al. 1991, 1992), 2) ENG; caloric excitability at 44°C and 37°C, asymmetry (>25% considered being abnormal), spontaneous nystagmus, saccadic eye movements; peak velocity (degree per second), accuracy (degree), and reaction time (milliseconds) (Juhola 1986), and pursuit eye movements; gain (as percentage) and latency (milliseconds) (Juhola 1988). MRI or ABR were done when needed.

In Studies II-V, the patients completed a questionnaire concerning vertigo, hearing loss, tinnitus, earlier diseases, head and ear traumas, and use of tobacco and alcohol. This information was supplemented by clinical examination data and the results of audiologic, otoneurologic, and imaging studies. The otoneurologic tests consisted of ENG and posturography.

3.3 Statistical Analysis

Data were analyzed with SPSS statistical programs 8.0 and 10.0. Frequencies, means, ranges, and standard deviations were calculated for most of the variables in Studies I–V. In Study V, when data were skewed, medians and ranges were expressed. Spearman correlation coefficients were calculated to determine

whether associations existed between different symptoms in Studies I–V. The correlation was considered significant at the 0.01 level. The distributions of symptoms and findings in patient subgroups were determined by error bar of means using 95% confidence intervals. The group means were compared with one-way analysis of variance, significantly ($p=0.05$) different means were determined with Tukey's test in Studies III and V and Duncan's test in Study IV. In Studies III and V, the relationship between variables and duration of MD was studied by cross-tabulation and the χ^2 test. In Study IV, factor analysis was performed to establish the relationship among variables, and logistic regression analysis to group the patients likely to have DA.

4. Results

4.1 Prevalence of Menière's Disease in General Population of Southern Finland (I)

The prevalence of MD was assessed in a general population aged 12 years or more. A group of 5000 people aged 12 years or more and living in the Helsinki University Hospital area was randomly selected from the population register data. This group was sent a questionnaire on symptoms of vertigo, tinnitus, and hearing loss. The final study group consisted of 3116 persons. A subgroup of 100 individuals reporting vertigo was randomly selected among the respondents for further clinical evaluation to assess the validity of the population-based study.

Of the group of 3116 responders 7% (n=216) reported the triad of vertigo, hearing loss and tinnitus, but 61% (n=128) of these had not been examined for their vertigo symptoms. Subjects with more intense, more frequent, and longer lasting vertigo attacks with concomitant nausea were more likely to have visited a doctor for their symptoms. Cochlear symptoms preceded vertigo in 61% of subjects. After excluding subjects who might have another reason for their symptoms, 28 possible, 31 probable, and 16 definite MD patients remained and are presented in Table 4. The group of 16 definite MD patients consisted of 13 women and 3 men. Nine of them had previously been given a MD diagnosis that could be confirmed by medical records. Their mean duration of disease was 19 (range 2–41) years and their mean age at the onset of symptoms was 44 (range 19-77) years.

Table 4.
Number of MD patients in the final group of 3116 persons and their mean age at the time of attending the study.

MD	Total	Women	Men	Mean age and range (years)
Definitive	16	13	3	61 (39-79)
Probable	31	15	16	51 (20-79)
Possible	28	21	7	54 (23-83)

Based on the 16 definite MD patients found here, the population-based prevalence of MD is 513 per 100 000 individuals aged 12 years or more. If we are extremely conservative and include only the 10 patients for whom MD diagnosis could be confirmed (9 by medical records and one by clinical examination), the rate would be 321 per 100 000 inhabitants. The highest prevalence (1709/100 000) was seen in the age group 61–70 years. After excluding the definite MD patients and subjects who might have another reason for their symptoms, the prevalence rates for probable and possible MD were 995/100 000 and 899/100 000 respectively.

4.2 Hearing Loss and Tinnitus in Menière's Disease (II)

A group of 243 definite MD patients was evaluated to characterize the progression and level of hearing loss and tinnitus by duration of MD and to determine their relation to vertigo.

For analysis of progression of MD symptoms by duration of disease, the patients were divided into 6 groups based on the time elapsed since the onset of MD. The duration groups were 1) <1 week (n=6), 2) 1-4 weeks (n=14), 3) 1–4 months (n=32), 4) 5–12 months (n=37), 5) 1- 4 years (n=56), and 6) >4 years (n=98).

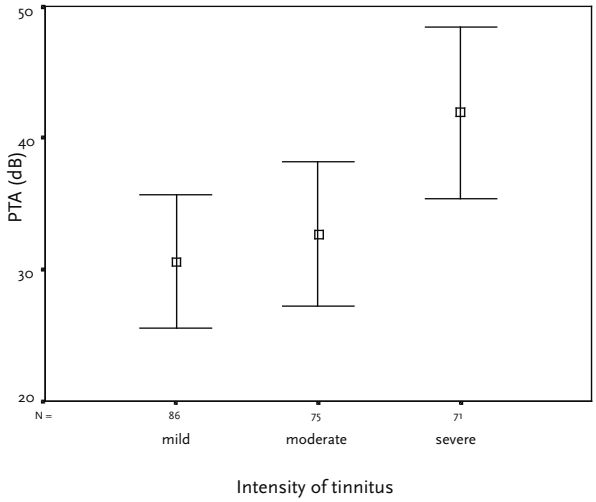
Hearing loss alone initiated symptoms in 13% of patients. Hearing loss combined with tinnitus was seen in 15% and combined with vertigo in 4% of patients as the initial symptom. In 5% tinnitus alone and in 4% tinnitus combined with vertigo were the initial symptoms. In 38% of patients, the disease started with the full triad.

Longer duration of the disease was associated with more profound hearing loss. Progression of hearing loss was most rapid at the 500 Hz frequency. Fluctuation of hearing was reported by 44% of patients and deterioration of hearing

during vertigo attacks by 55%. Increased intensity of vertigo attack was linked to the deterioration in hearing during the attack. Fluctuation of hearing was significantly more common during the first year of symptoms. Patients with more profound hearing loss performed worse on posturography, both with eyes open and closed. Level of hearing loss did not correlate with frequency, duration, or intensity of vertigo attacks.

Bilateral tinnitus was more common than bilateral MD in our material, and it was experienced as more disturbing and intense than unilateral tinnitus. Thirty-eight percent of patients scored intensity of their tinnitus as mild, 32% as moderate, and 30% as severe. The intensity of tinnitus increased with duration of disease as well as with decrease of hearing (Figure 1).

Figure 1.
Means of PTA of hearing thresholds at 0.5, 1, 2, and 3 kHz by intensity of tinnitus with 95% confidence intervals.



Intense tinnitus was linked specifically to hearing loss at 500 Hz ($p<0.05$). Tinnitus was unaffected by the frequency or duration of vertigo attacks. However, patients with intense tinnitus more often had vertigo provoked by head positioning, physical activity, or pressure changes than those with less intense tinnitus. Unsteadiness, moving difficulties outside vertigo attacks, and DA were more common among the patients reporting intense tinnitus. Intense tinnitus was common in MD and, along with deteriorated hearing, it increased in the later stages of the disease.

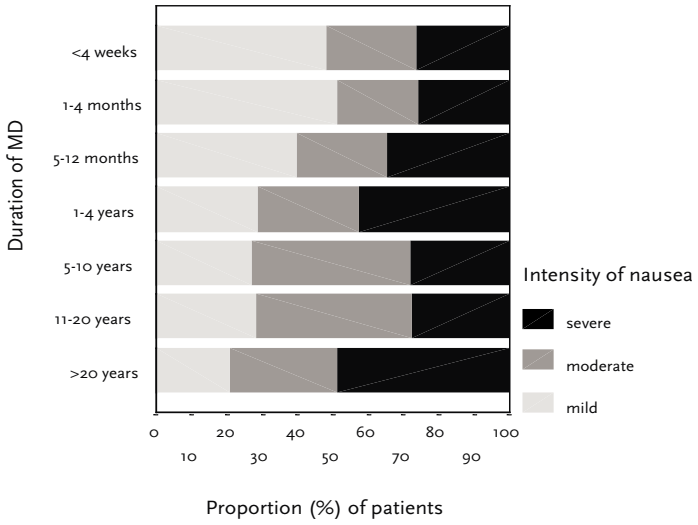
4.3 Progression of Symptoms of Dizziness in Menière's Disease (III)

The progression of symptoms of dizziness was studied by duration of MD with special attention being paid to patients with long disease duration.
Patients were allocated into the following 7 duration groups: 1) <4 weeks (n=20), 2) 1–4 months (n=32), 3) 5–12 months (n=37), 4) 1–4 years (n=56), 5) 5–10 years (n=49), 6) 11–20 years (n=32), and 7) >20 years (n=17).

No differences were found in frequency, intensity, or duration of vertigo attacks between the duration groups. However, the number of patients reporting continuous vertigo began to grow after a disease duration of 10 years, reaching 21% among patients who had had MD for 20 years. Vertigo attacks most commonly lasted between 5 minutes and 4 hours. The duration of vertigo attacks increased as the disease progressed. More than half of patients scored the intensity of their vertigo attacks as moderate or severe, i.e. attacks either forced them stop their activity or lie down. The proportion having severe or very severe attacks increased with disease progression. The increase in intensity of nausea by disease duration is presented in Figure 2.

Surgically treated patients reported longer, more intense, and more frequent vertigo attacks than those who had not been operated on. Ninety percent of the

Figure 2.
Increase in intensity of nausea felt by the patients during vertigo attacks by MD duration.



surgically treated patients considered their attacks to be severe or very severe.

The prevalence of bilateral disease increased with disease duration, being highest among those with symptoms for more than 20 years. No statistical differences were present in intensity, frequency, or duration of vertigo attacks between patients with bilateral and those with unilateral MD or between the genders. A subgroup of patients with MD had severe symptoms of dizziness even after a 20-year disease history.

4.4 Short-lasting Drop Attacks in Menière's Disease (IV)

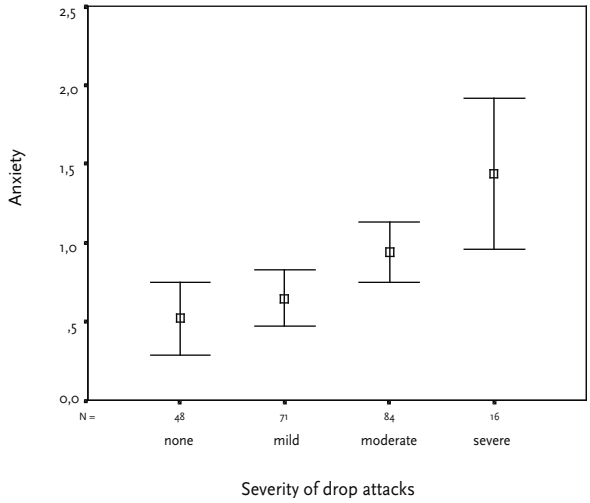
This study assessed the prevalence of DA in MD and determined whether associations exists between DA and other symptoms of MD.

For analysis of progression of MD symptoms by duration of disease, the patients were divided into 6 groups based on the time elapsed since the onset of MD. The duration groups were 1) <1 week (n=6), 2) 1–4 weeks (n=14), 3) 1–4 months (n=32), 4) 5–12 months (n=37), 5) 1–4 years (n=56), and 6) >4 years (n=98).

DA were defined as rapid attacks of falling or slips without loss of consciousness. The occurrence together with description of attacks and severity of attacks were specifically enquired about in the questionnaire. To assess the daily disturbance caused by DA, the frequency of attacks was divided into the following 3 classes: 1) mild disturbance with DA appearing seldom or being mild, 2) moderate disturbance with more frequent DA or DA being moderate, and 3) severe disturbance with DA occurring several times a day or being severe.

DA were experienced by 72% (n=173) of MD patients. They were mild in 42% (n=72), moderate in 49% (n=85), and severe in 9% (n=16) of patients. No difference was seen in mean duration of MD, age at onset of symptoms, intensity of vertigo, or gender between the DA and non-DA groups. In patients with DA, tinnitus was more severe and vertigo attacks were more likely provoked by visual factors (e.g. rapid movement in surrounding), pressure changes (e.g .flying or sneezing), head positioning, or physical strain than in patients without DA. DA patients also had more moving difficulties outside vertigo attacks than did non-DA patients. Patients with DA had more anxiety than those without DA (Figure 3.) They also had more cranial nerve symptoms, including facial sensitivity disturbances, visual blurring, and dysarthria, than non-DA patients. In the otoneurologic tests, no differences were present between the DA and non-DA groups.

Figure 3.
Relationship between anxiety and drop attacks with 95% confidence intervals. Anxiety rated as 0) none, 1) mild, 2) moderate, or 3) severe.



4.5 Postural Instability in Menière's Disease (V)

The Study V evaluated the progression of postural stability in MD patients by both hearing stage and disease duration.

Patients were divided into following 7 duration groups: 1) <4 weeks (n=15), 2) 1–4 months (n=28), 3) 5–12 months (n=28), 4) 1–4 years (n=50), 5) 5–10 years (n=30), 6) 11–20 years (n=19), and 7) >20 years (n=20).

We used static computerized platform posturography to measure postural stability. The measurements were done with eyes open and closed, the latter to exhibit visual control. The SV were expressed as the length of the path of the center point of force divided by the time (mm/sec). To examine the relationship between patients' hearing level and their SV values, we further divided the patients by their PTA of hearing thresholds (0,5, 1, 2, and 3 kHz) into 4 hearing stages defined by AAO-HNS as I <26 dB, II 26-40 dB, III 41-70 dB, and IV >70 dB. The mean age of the patients at the time of testing was 51 (range 22-80) years.

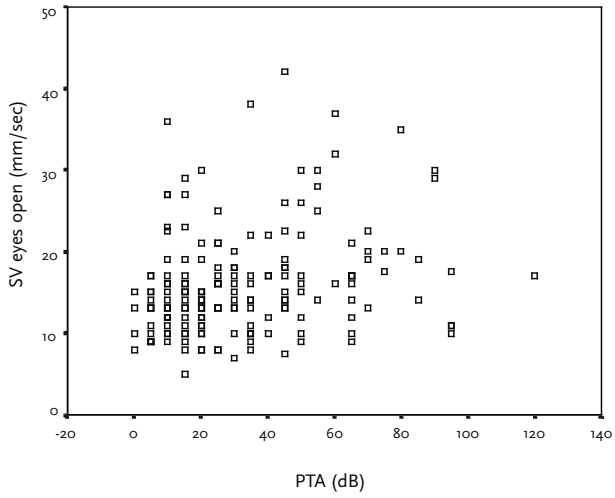
No significant difference was observed in mean SV between the seven dura-

tion groups. Neither was there any difference in caloric asymmetry (≤25%) between the different duration groups. Caloric response was normal 65% of the patients, and in this group 60% had a normal SV with eyes open and 57% with eyes closed.

The SV values measured with eyes open and eyes closed correlated well with each other (r=0.76). The SV values in the entire group were within the normal range in 58% (n=103) of the patients, with eyes open and in 55% (n=99) with eyes closed. No statistical difference was present in mean SV between the different duration groups of MD. Patients affected with bilateral MD swayed slightly more with eyes open as well as closed than unilaterally affected patients, but the difference was not significant.

In the group with more severe disease (severe or very severe attacks lasting more than 4 hours, at least 1-4 times a month), SV was within the normal range in 63% of cases, both with eyes open and closed. The patients belonging to hearing stage III (PTA 41-70 dB) swayed significantly more than patients in stage I (PTA <25 dB). Since mean age and age range were alike in these two groups, the result cannot be explained by age. The large variability in SV between the subjects having same PTA is presented in Figure 4.

Figure 4.
Scatter plot of SV with eyes open by PTA of hearing thresholds at 0.5, 1, 2, and 3 kHz.



5. Discussion

5.1 General Discussion

A large population-based data was collected to assess the prevalence of MD in a general population (I). The progression of cochlear symptoms, including tinnitus and hearing loss, their relationship with vertigo, and characteristics of tinnitus in MD were evaluated (II). The symptoms of dizziness in MD were studied by duration of disease, with special reference to patients with a long history of the disease (III). The occurrence of DA was examined and the relationship between DA and other symptoms of MD was evaluated (IV). Postural instability was assessed by both hearing stage and duration of MD (V).

The mean age of 44 years at the onset of MD symptoms in Studies II-IV was the same as the mean age at onset in the 16 definite MD patients of the population study (I). The clear female predominance seen in Studies II-V (70% women vs. 30% men) was also seen in 16 definite MD patients (80% vs. 20%) (I).

The proportion of patients with bilateral MD increased with duration of the disease (III). While patients with bilateral disease did not have more severe vertigo symptoms than patients with unilateral disease, bilateral tinnitus was experienced as more disturbing than unilateral tinnitus (II). Forty-two percent of subjects with severe tinnitus reported having DA quite often or several times a day. Black et al. (1982) reported DA to be more common in severe and long-lasting MD, a finding confirmed here.

5.2 Prevalence of Menière's Disease

The population-based prevalence of MD was calculated to be 513 per 100 000 individuals. This finding is much higher than earlier estimations of prevalence

based on hospital registers (Stahle et al.1978; Watanabe et al.1995; Kotimäki et al.1999). Wladislavosky-Waserman et al (1984) reported a fairly high figure of 218/100 000 in Rochester, Minnesota, for the period 1951-1980. Their material included 436 MD or Menière's syndrome patients. However, only 180 of their patients met the diagnostic guidelines of that time (1972). With respect to the revised 1995 criteria, the prevalence would have been much lower (Wladislavosky-Waserman et al. 1984). Our prevalence rate for definite MD using the most recent criteria (1995) is twice the figure of Wladislavosky-Waserman et al. (1984) and more than ten times that of Kotimäki et al. (1999).

Hospital registers have weaknesses. Data collected in routine clinical work vary in quality and are limited in consistency, accuracy, availability, and completeness of medical records (da Costa et al. 2002). We encountered this dilemma in the case of a MD patient diagnosed during the examination of the vertigo sample. Despite her several visits to the outpatient polyclinic of the Department of Otorhinolaryngology in the 1970s, no mention of her vertigo symptoms was found in her medical records. Her auditory symptoms appeared to be the main problem at the time because she received a diagnosis of cochlear degeneration and was given a hearing aid but no treatment for her vertigo attacks, which continued after her last visit to the clinic.

Arenberg et al. (1980) claimed that mostly moderate and severe cases of MD are found in the studies based on hospital material; we agree with this. When evaluating the group with the triad of symptoms, we noticed that the longer, the more intense and the more frequent the vertigo attacks, the more probable the previous examinations were because of vertigo symptoms.

Tokomasu et al. (1996) reported cochlear symptoms to precede the onset of vertigo attacks in 61% of patients. In Study I, cochlear symptoms preceded vertigo ones in 61% of subjects with the triad of symptoms and in 54% of patients with definite MD. When the cochlear signs appear first there is the risk that they become attributed to another cause and when the vestibular symptoms become apparent the triad of symptoms may go unrecognized particularly, due to episodic nature of the vestibular symptoms (Arenberg et al. 1980). It is harder to link the new vestibular symptoms to persisting hearing loss.

We found only 3 men in the group of 16 definite MD patients, which might suggest that the actual prevalence rate is even higher than we reported. MD has, after all, been considered to affect both genders equally (Tokomasu et al. 1995; Katsarkas 1996). Kotimäki et al. (1999) in their prevalence study did not give separate prevalence figures for men and women. We speculate that men are less eager than women to participate in questionnaire-based studies, although 43%

of our responders were men. The possibility also exists that women are more affected by MD than men in Finland.

Wladislavosky et al. (1984) reported a peak incidence in the age group 45-59 years, but estimated that the rate would increase with age with a small decrease occurring in the oldest age group of 75 years and over. We noticed a peak in prevalence of 1709/100 000 in the age group 61–70 years and a small decline in the age group over 70 years. The possibility of MD should be kept in mind regarding these age groups which are also affected by presbyacusis and whose vertigo might easily be diagnosed as being of central origin.

Patients reporting a history of brain ischemia were excluded from our prevalence calculations and this might have affected (lowered) the prevalence rates. Some of these patients who had been diagnosed as having brain ischemia might actually be MD patients with DA or MD patients with later occurring ischemic disease. However, without the possibility for a clinical examination, we had to exclude these patients. Patients reporting headache symptoms, by contrast, were included in the prevalence calculations due to the high prevalence rate of migraine in MD patients. Some of these patients might actually be afflicted with migraineous vertigo, but because they met the criteria of MD, they were considered MD patients with migraines.

The small number of men in our prevalence calculation and the strict criteria used for exclusion may underestimate the actual prevalence rate. On the other hand, children under the age of 12 years were not included in the study, and if the assumption that those more affected by the symptoms in question were more eager to answer the questionnaire is held to be valid, these would lower the calculated prevalence rate. These two aspects may to some degree compensate each another.

5.3 Hearing Loss and Tinnitus in Menière's Disease

Our MD patients were collected from the vestibular unit of Helsinki University Hospital. They filled in a questionnaire concerning their symptoms. Of the 243 patients, cochlear symptoms started the disease in 33%, supporting the view that MD patients whose disease starts with vestibular symptoms are more likely to receive a correct diagnosis. In our population-based study (I), 54% of the definite MD patients had started their disease with cochlear symptoms. Tokomasu et al. (1996) reported 61% of MD patients in Japan start their disease with cochlear symptoms.

Katsarkas (1996) found that hearing degreases at a more or less fixed rate but some variation is present in the decline of vestibular function. In our study, no correlation was seen between the degree of hearing loss and caloric asymmetry in ENG.

Bilateral tinnitus was more often, than unilateral tinnitus experienced as severe. One-third of patients scored their tinnitus as severe. More intense tinnitus has been reported in the late stages of MD (Kolbe et al. 2000). This finding of increased intensity can be explained partly by increased hearing loss and bilateral tinnitus with disease duration.

5.4 Vertigo in Menière's Disease

Vertigo attacks in MD were reported to resolve in 30% or disappear in 54% of patients in a 9- year follow-up (Green et al.1991). A decline in the frequency of attacks has been estimated to occur after two decades have elapsed since onset of the disease (Friberg et al.1984). Nausea-associated vertigo attacks are rarer after the first year of MD has passed (Oosterveld 1979). In our study, when evaluating a group of MD patients, whose disease duration varied from recent onset to 41 years, we did not find frequency, intensity or duration of vertigo attacks to decrease with disease duration. Seventy-five percent of patients who had had MD for more than 20 years considered their vertigo attacks to be severe, and 36% still had attacks 1-4 times a week. Nausea associated with vertigo attacks was most common among those with a long disease history. Our hospital is a tertiary referral clinic which attends to patients with the most persistent and severe symptoms, and 20% of our sample had had symptoms for more than 10 years. This tertiary nature of our clinic presumably also had an influence on the high number of severe symptoms found in the group of patients who had had MD more than 20 years. Many people apparently are freed of their MD symptoms over time since there were considerably less patients in the late-disease duration groups than the earlier duration groups would have suggested. Surgically treated patients reported longer, more intense, and more frequent attacks than those who had not been operated on. This can be explained by them having more severe symptoms overall, with this being the reason for their operation. It also supports what has earlier been reported: endolympatic sac surgery does not alter the long-term natural course of MD or modifies it slightly (Silverstein et al. 1989, Filipo and Barbara 1997).

Consistent with earlier studies, we found bilateral illness to increase with duration of MD (Stahle 1976; Friberg et al. 1984 and Tokomasu et al. 1995).

Compared with 47% reported by Friberg et al. (1984), we found 43% of patients to have bilateral disease after 20 years had elapsed since onset of the disease. The overall proportion of patients with bilateral disease was 16%.

5.5 Drop Attacks in Menière's Disease

DA, i.e. sudden falls without loss of consciousness, have been speculated to account for a considerable proportion of potentially dangerous falls in older people (Ishiyama et al. 2001). Ballester et al. (2002) reported that 8% of elderly MD people aged over 65 years had initially being misdiagnosed as having had a stroke or brainstem ischemia because of DA.

We found DA in 72% of MD patients, in stark contrast to the much lower figures 6-7% reported earlier (Black et al. 1982; Baloh et al. 1990). The high prevalence can be explained by the fact that all of the patients reporting DA probably would not had reported DA that caused only mild or moderate disability had it not been specifically inquired about. Only 9% of our patients had severe DA - a figure similar to the prevalence rates of the authors above. Black et al. (1982) reported DA to be more common in severe and long-lasting MD, a finding consistent with ours. Our hospital being a tertiary referral clinic may increase the prevalence of DA found in MD patients.

In 65% of MD patients with DA, vertigo attacks were provoked by rapid movements in the environment and in 71% by head movements. These patients no longer rely on vestibular information to maintain their balance, instead relying on visual and proprioseptive information. In their study on conservative management of DA patients, Janzen and Russell (1988) concluded that this patient group can benefit from visually secure surroundings.

5.6 Postural Instability in Menière's Disease

MD patients are thought to be more dependent on visual input than people with normal vestibular function (Black 1982), and thus, measuring SV with the patient's eyes closed is considered to be a tool to remove this visual control. We found, however, that eyes-open and eyes-closed SV values correlated well with each other (r=0.76).

Declined hearing was linked to worse performance on the platform. Our study did not, however, provide evidence that posturography would be helpful in evaluating progression of MD. There was a large subject to subject variability in posturography performing. Evans and Krebs (1999) stated that posturography

and ENG findings do not correlate with each other and at its best posturography only modestly enhances the diagnosis of peripheral vestibular hypofunction. Most useful posturography could be in evaluating the effect of rehabilitation and thus receiving objective information on the functional status of balance impaired patients. Paparella (1991) found that up to 50% of MD patients have normal reactions in caloric tests even when affected by severe vestibular symptoms. This is in agreement with our results.

5.7 Future Aspects

The link between MD and migraine is interesting and worthy of further investigations. The medication used in migraine patients has already shown to alleviate migraine-related dizziness. If its efficacy extends to MD patients, this would help a group that has thus sufferred from an intractable disease. The development of imaging studies enables detailed information to be collected on the inner ear and the brain that could previously be only obtained postmortem. These advanced imaging studies will improve differentiation between MD and symptoms of vertigo, tinnitus, and hearing loss of central origin, and thus, should be used more.

6. Conclusions

Based on the findings of Studies I–V the following conclusions were drawn:

1. The population-based prevalence of definite MD is 513 per 100 000 individuals aged 12 years or more. A peak in prevalence (1709/100 000) was seen in the age group 61–70 years (I).

2. Hearing loss and tinnitus intensity progress in MD patients with disease duration. More intense tinnitus was seen in bilateral cases who had longer disease duration (II).

3. A subgroup of patients with MD continues to have severe symptoms of dizziness 20 years after onset of the disease. The prevalence of bilateral disease increases with duration of illness, but patients with bilateral MD did not have more severe vertigo symptoms than those with unilateral disease (III).

4. DA are common in MD patients and are especially seen in the advanced stage of the disease. DA patients are more dependent on visual and proprioceptive information than MD patients without DA (IV).

5. Postural stability did not deteriorate with the duration of MD. Patients with more advanced hearing loss performed worse on the platform, and this finding was not age-dependent (V).

6. The enhancement of imaging studies is important in differentiating MD symptoms from the central causes of symptoms.

7. Summary

Objectives: The prevalence of Menière's disease (MD) in a general population and the presence of three major symptoms of MD, vertigo, hearing loss, and tinnitus, by duration of disease were evaluated.

Subjects and methods: To study the prevalence of MD in a general population, a questionnaire was sent to 5000 randomly selected people aged 12 years or more living in the Helsinki University Hospital area. The individuals receiving the questionnaire were asked whether they had experienced vertigo associated with a moving sensation, hearing loss, or tinnitus. For exclusion purposes, we also enquired about general illnesses, ear infections, former head and ear traumas, noise exposure, medication and use of tobacco and alcohol. The response rate after one postal reminder was 63%. To assess the validity of the population-based study, we randomly selected a 100 subject-sample among the people reporting vertigo. The sample was clinically examined in our vestibular unit. A total of 243 consecutive MD patients were evaluated to clarify the clinical picture of MD.

Results: The population-based prevalence of definite MD was 513 per 100 000 inhabitants aged 12 years or more, with a peak prevalence of 1709 per 100 000 inhabitants seen in the age group 61–70 years. If we are extremely conservative and include only the 10 patients for whom MD diagnosis could be confirmed, the rate would still be 321 per 100 000 inhabitants. The true prevalence can, however, be considered to be 513 per 100 000 inhabitants. The cochlear symptoms of hearing loss and tinnitus severity increased with disease duration. In 54% of definite MD patients, the disease started with cochlear symptoms. A subgroup of patients still had severe symptoms of dizziness 20 years after disease

onset. The prevalence of bilateral MD was most common late in the disease, but patients with bilateral disease did not have more severe vertigo symptoms than patients with unilateral disease. Short-lasting drop attacks were experienced by 72% of the MD patients, and they were typically seen in the advanced stage of the disease. Postural stability did not deteriorate with duration of MD, but patients with advanced hearing loss were found more unstable.

Conclusions: The prevalence of definite MD here was much higher than previous reports based on hospital records have suggested. A peak in prevalence was seen in the age group 61–70 years. The possibility of MD should be considered in this age group also affected by presbyacusis and whose vertigo might be diagnosed as being of central origin. When cochlear symptoms start the disease, there is a risk that they may be misattributed to another cause or presumed to be due to aging, and triad of symptoms may go undiagnosed. Imaging studies should be used to differentiate between MD patients and patients with vertigo because of vascular disorder. Although MD symptoms may resolve with time, a subgroup of patients continues to have severe symptoms 20 years after onset of the disease.

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10. Appendix

Population Questionnaire

Please answer the following questions and circle the most appropriate alternative.

Surname:
First name:
Social security number:

Sex:
Woman / Man

Age:
Height:
Weight:

Place of residence (e.g. town, countryside):

Smoking:
Yes / No

Does your skin get easily burned by the sun?:
Always / Often / Sometimes / never

Occupation (also the previous one):
Education:
a) elementary school
b) trade school
c) college
d) secondary school graduate
e) university

Have you been exposed to noise in your work?
Yes
No

Has the use of hearing protection been recommend or is the noise level in your work over 85 dB?
Yes
No

How long have you been exposed to noise in your work?

Noise level at work?

Have you had a
1) head trauma
Yes
No

2) sudden acoustic trauma
Yes
No

Have you had recurrent (more than 3) middle ear infections?
Yes
No

Do you consider your hearing to be normal for a person of your age?
Yes
No

If your hearing is impaired, please answer the following questions:
Is there a specific reason for your hearing loss?

Is your hearing impaired:
In the Right
Left
Both ears?

Does your hearing fluctuate?
Yes
No

Do you suffer from your impaired hearing?
Not at all
A little
Quite a lot
Very much

Has your hearing level been measured?
Yes
No

Do you know your hearing level?

Do you suffer from ringing or humming in your ears?
Not at all
A little
Quite a lot
Very much

If ringing or humming occurs, is it in your
Right
Left
Both ears?

Do you suffer from headaches?
Not at all
A little
Quite a lot
Very much

Do you ever faint?
Never
Seldom
Sometimes
Very often

Are you on medication on a regular basis?
What medication?
Yes
No

Do you have any of the following diseases?
Hypertonia
Diabetes
Coronary artery disease
Brain circulation disorder
Thyroid disorder
Another disease:

Is your cholesterol level above normal?
Yes
No

What is your cholesterol level?

Have you experienced sudden falls or staggered without loss of consciousness?
Yes
No

Have you experienced vertigo together with a moving sensation?
Yes
No

If you answered "yes" to the previous question, please answer the following questions. If you answered "no", we thank you for your participation and for returning the questionnaire.

How long have you experienced vertigo?

How old were you when your vertigo symptoms began?

How much do you suffer from your vertigo?
Not at all
A little
Quite a lot
Very much

How often does vertigo occur?
a) only one time
b) less than once a year
c) 1-2 times a year
d) 3-12 times a year
e) 1-4 times a month
f) 2-7 times a week
g) several times a day
h) constantly

How long does the sensation of vertigo last?
a) less than 15 seconds
b) 15 seconds-5 minutes
c) more than 5 minutes-4 hours
d) more than 4 hours-24 hours
e) several days

Does nausea occur concomitantly with vertigo?
a) never
b) seldom
c) often
d) always

How intense is your attack?
a) mild (can continue working)
b) moderate (have to stop working)
c) severe (have to rest)
d) very severe (have trouble even in rest)

Have you noticed anything that might provoke vertigo? If yes, what?

When did you have your last episode of vertigo?

Have you been examined by a doctor for vertigo?
Yes
No

Does vertigo affect your work ability?
Yes
No

If you have more than one of the above symptoms (vertigo, hearing loss, tinnitus), which was the first to appear?