Recent advances in the diagnosis and treatment of Menière's disease

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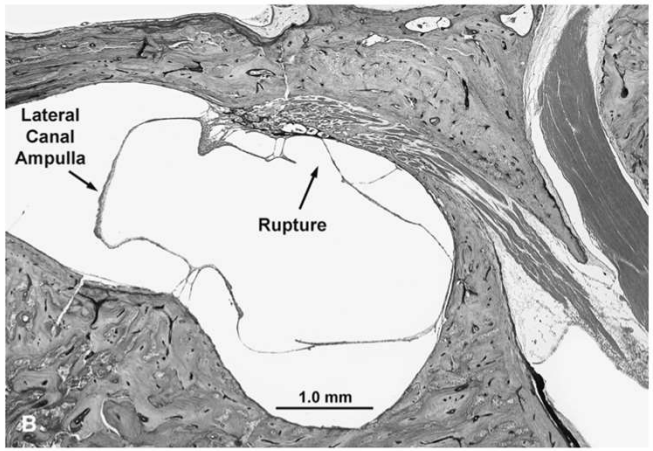
Meniere's Disease

- Meniere's disease (MD) is a syndrome caused by uncommon disorders affecting the inner ear and characterized by episodes of recurrent spontaneous vertigo, tinnitus, sensorineural hearing loss (SNHL), and aural fullness. Since first described in the early 1800s, MD remains a puzzle in etiology, prognosis, and treatment.

- It is a chronic, debilitating condition with an unpredictable course. Initially, it usually afflicts one ear (unilateral MD), but both ears can be involved (bilateral MD)
- Displacement of Reissner's membrane and dilation of the scala media of the cochlea are histological marker of EH.

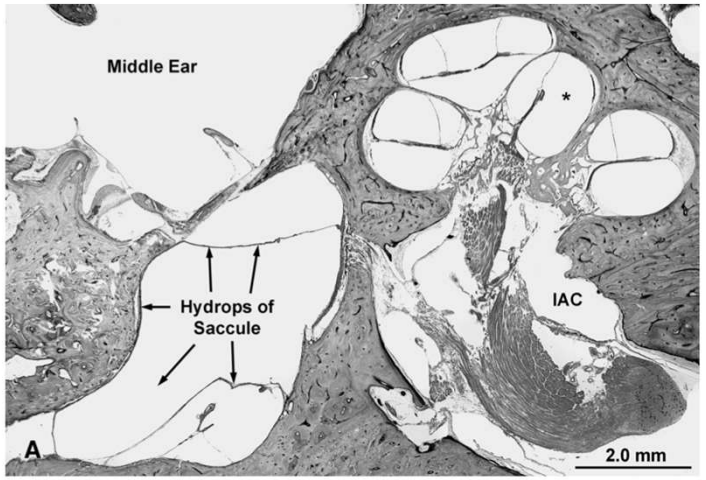
- The condition is associated with endolymphatic hydrops. EH itself does not explains the attacks of vertigo, since histopathological studies have reported EH in individuals without

- **EH may be necessary but not sufficient for MD development**.




Pathophysiology of Ménière's Syndrome: Are Symptoms Caused by Endolymphatic Hydrops?

Saumil N. Merchant, Joe C. Adams, and Joseph B. Nadol, Jr.



Menière Disease: EPIDEMIOLOGY

INCIDENCE
(n° of new cases/year

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

POINT PREVALENCE 190 su 100.000 (Harris, 2010, USA)

PREVALENCE
Number of cases relative to a Number of subjects

- 3.5-513 casi x 100.000 (old data)
- 205 x 100.000 (Celestino-Ralli)
- 190 x 100.000 (USA-2010)

Menière Disease: EPIDEMIOLOGY

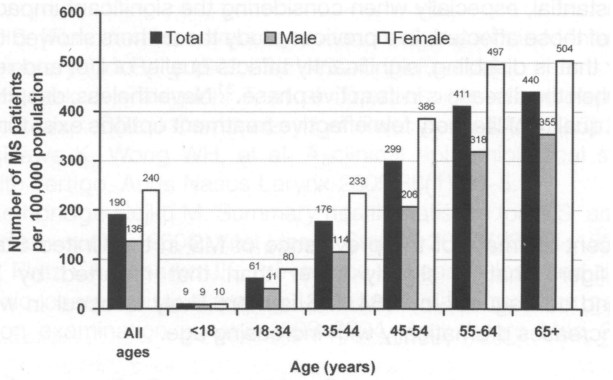
Age of Onset

- **10-15 % MD diagnosed after 65 years of age** *(Uneri e Polat 2008)*
- **Uncommon in childhood**

Table 9
Rate of the elderly MD patients aged 60 or over

Reporters	60–69 years (%)	70 years (%)	Total
1. Mizukoshi (1977)	31(6.0)	7 (1.3)	510
2. Watanabe I (1983)	10 (6.3)	4 (2.5)	158
3. Watanabe Y (1991)	13 (8.8)	0 (0)	148
4. Stahle (1978)		28 (10.9)	257
5. Wladistavosky-Waserman (1984)	50 (27.7)	18 (10.0)	180
6. Kitahara (1981)	27 (6.3)	4 (0.95)	423
7. Ikeda,Watanabe I (1995)		29 (5.0)	584
8. Mizukoshi (1999)	33 (10.1)	6 (1.8)	328

Ratio F/M 1.89 - 1



Mean Age of onset 30-50 years

Mild prevalence in females

Menière's Disease

Hindawi Publishing Corporation
Journal of Aging Research
Volume 2012, Article ID 421596, 5 pages
doi:10.1155/2012/421596

Clinical Study

Does Ménière's Disease in the Elderly Present Some Peculiar Features?

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Table 1: Demographic and clinical data in elderly and younger MD subjects.

	Young MD ($n = 73$)	Elderly MD ($n = 30$)	P value
Age	50.1 ± 12	72 ± 4.3	$P \leq 0.01$
Age at onset of MD	39 ± 9.7	69.3 ± 4.1	$P \leq 0.01$
Migraine	38/73 (51%)	4/30 (20%)	$\chi^2 = 8.93$ $P = 0.03$
Positive autoantibody screening	25/73 (33.8%)	3/30 (20%)	$\chi^2 = 6.31$ $P = 0.02$
Tumarkin	7/73 (9.6%)	11/30 (36-7%)	$\chi^2 = 10.8$ $P \leq 0.01$
Familiar history of vertigo	8/73 (10.9%)	2/30 (6%)	$\chi^2 = 0.5$ $P = 0.5$
Number of spells in the last 6 months	5.5 ± 3.7	10.4 ± 5.4	$P \leq 0.05$

Menière's Disease

BILATERAL MD

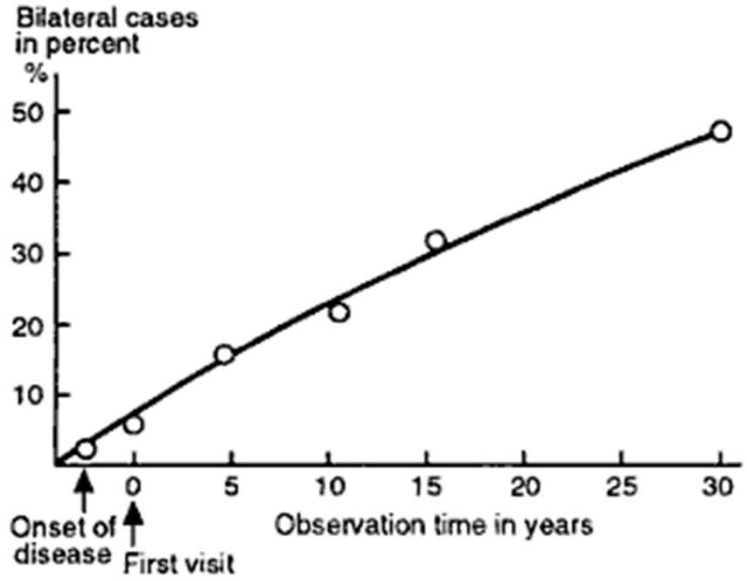
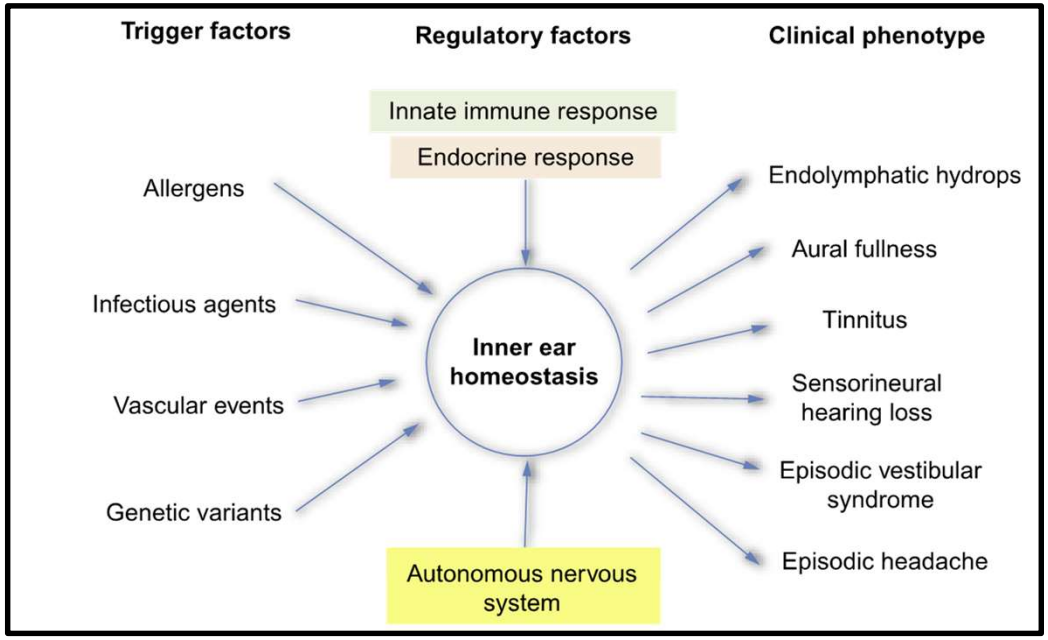


Fig. 1. Number of bilateral cases (in percent) related to duration of disease. (Reproduced from Friberg *et al.*[25], by courtesy of *Acta Otolaryngology (Stockh.).*)

Author	Year of publication	Number of patients	Bilateral cases, %
Castellano	1951	300	2.3
Stahle and Bergman	1967	300	25
Enander and Stahle	1967	334	14
Thomas and Harrison	1971	610	31.8
Diagnostic criteria proposed in 1972 by AAO			
Greven and Oosterveld	1975	292	10
Morrison	1975	330	42.5
Stahle	1976	356	10
Kitahara et al.	1979	265	29
Arenberg et al.	1979	300	56–67
Balkany et al.	1980	226	46
Paparella and Griebie	1984	360	32
Wladislavosky-Waserman et al.	1984	180	34.4
Diagnostic criteria proposed in 1985 by AAO			
Paparella and Mancini	1985	51	14
Brookes	1986	73	40.7
Palaskas et al.	1988	452	20
Charachon et al.	1989	92	7.5
Rosenberg et al.	1991	240	17
Moffat et al.	1992	40	35
Diagnostic criteria proposed in 1995 by AAO			
Shojaku et al.	1995	810	9
Kodama et al.	1995	480	28
Friedrichs and Thornton	2001	100	27
Pérez et al.	2004	101	5
House et al.	2006	232	25

No more than 5% of our MD patients suffer from bilateral MD and the onset of hydropic symptoms appears after many years from the initial diagnosis and usually the clinical picture is characterized by a less intense and frequent crisis with a more prominent audiological involvement

Menière's Disease



- A higher prevalence of autoimmune disorders has been reported in MD supporting the hypothesis of an immune dysfunction in certain patients with MD (especially in bilateral MD)

Gazquez I, Soto-Varela A, Aran I, et al. High prevalence of systemic autoimmune diseases in patients with Menière's disease. PLoS One 2011;6(10):e26759

- The relationship between MD and both respiratory and food allergy has been observed and clinical improvement in MD patients with allergy has been reported after treatment of allergy

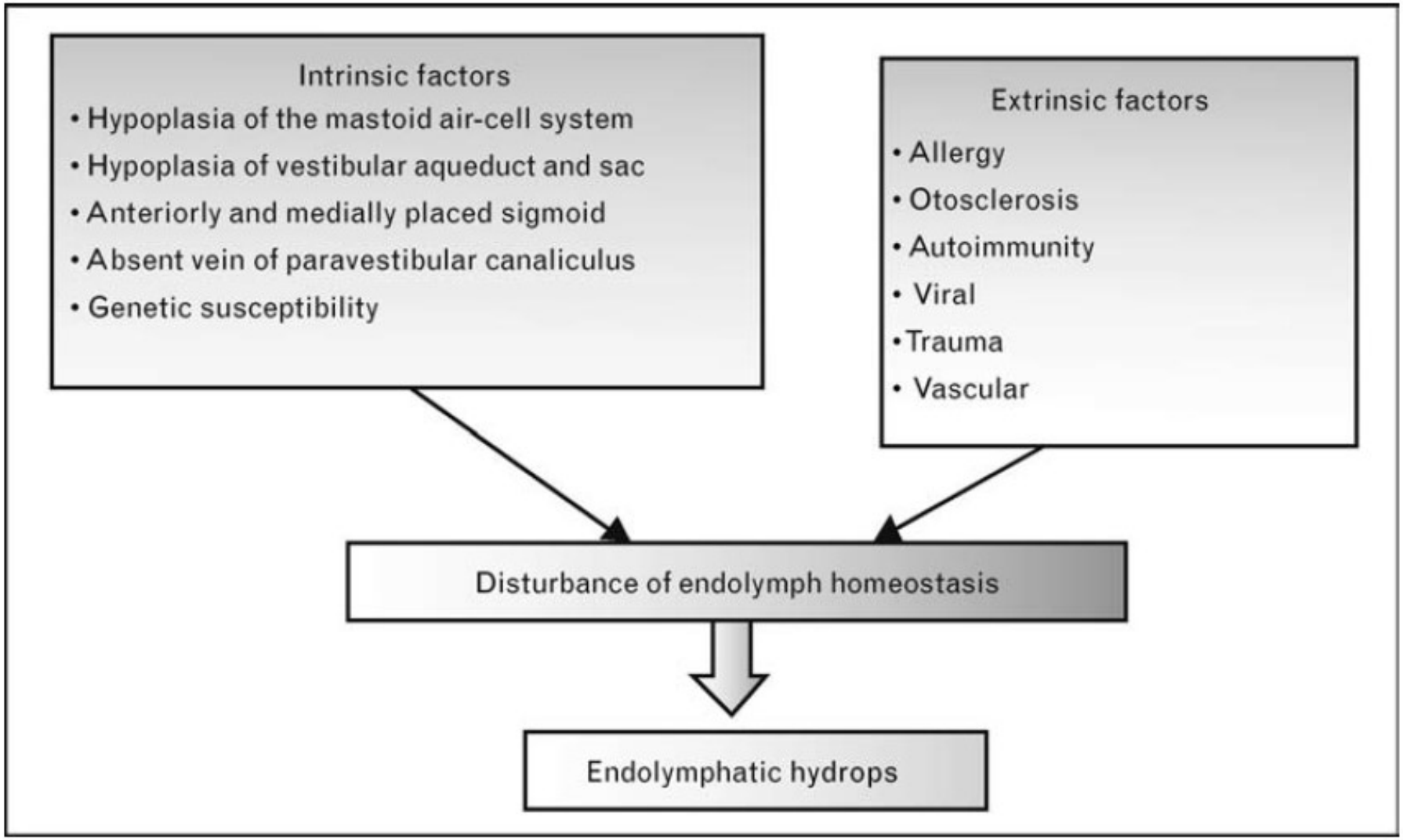
Yang B, Brook CD. The role of allergy in otologic disease. Otolaryngol Clin North Am 2017;50(06):1091–1101

- Several studies have reported a higher prevalence of migraine in MD and a possible common etiology has been suggested

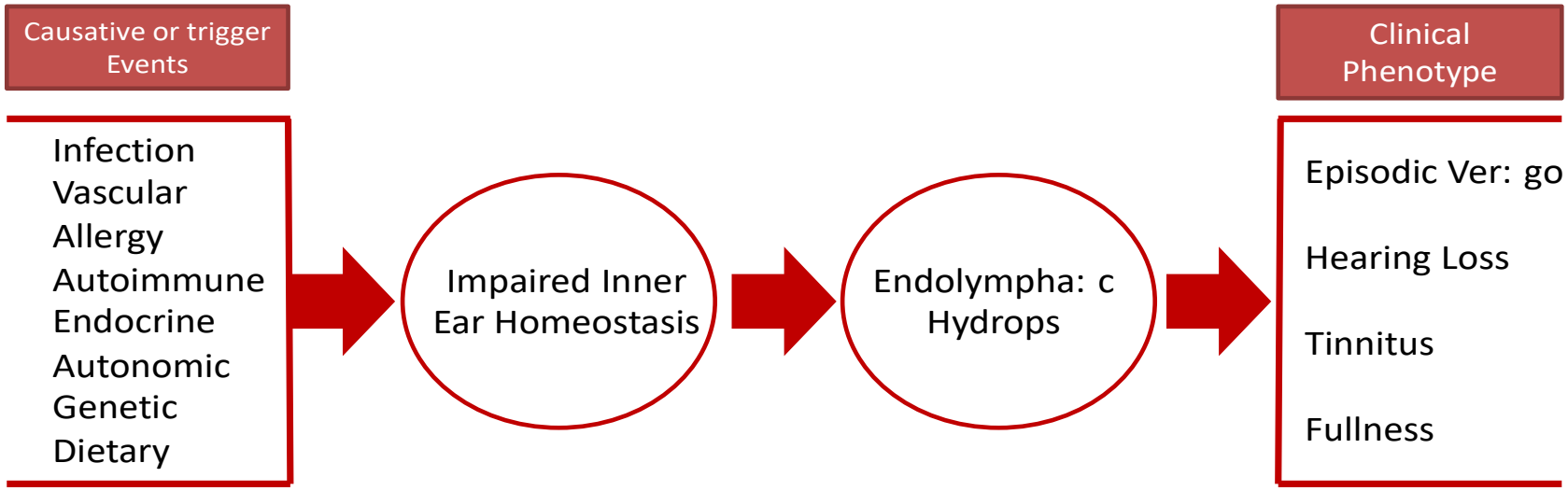
Liu YF, Xu H. The intimate relationship between vestibular migraine and Meniere disease: a review of pathogenesis and presentation. Behav Neurol 2016;2016:3182735

- There is compelling evidence that MD can arise from genetic factors, inflammatory and immunologic dysfunction, infection, trauma, and vasculopathy

Menière's Disease



Menière's Disease



DEFINITE MD

A. Two or more spontaneous episodes of vertigo[1, 2], each lasting **20 minutes to 12 hours**[3]

B. Audiometrically documented low- to medium-frequency sensorineural hearing loss[4,5] in the affected ear on at least one occasion before, during or after one of the episodes of vertigo [6,7]

C. Fluctuating aural symptoms (hearing, tinnitus or fullness) in the affected ear[8]

D. Not better accounted for by another vestibular diagnosis [9]

- The duration of the episodes may last **less than 20 minutes or more than 12 hours**, but this is not a common finding, and other disorders should be considered when such durations are noted.
- When short episodes occur they are usually spontaneous. **Brief episodes** of acute dizziness and unsteadiness with rotational vertigo are more common in the late phase of MD
- **Brief episodes triggered by positional changes** of the head should suggest other causes such as, BPPV, common during all the history of MD.
- The duration of an episode may be difficult to define as patients may have residual symptoms after an episode. Episodic dizziness and unsteadiness are not considered as criteria to define MD, although patients can complain of dizziness.

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The Japan Society for Equilibrium Research
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EAONO

DEFINITE MD

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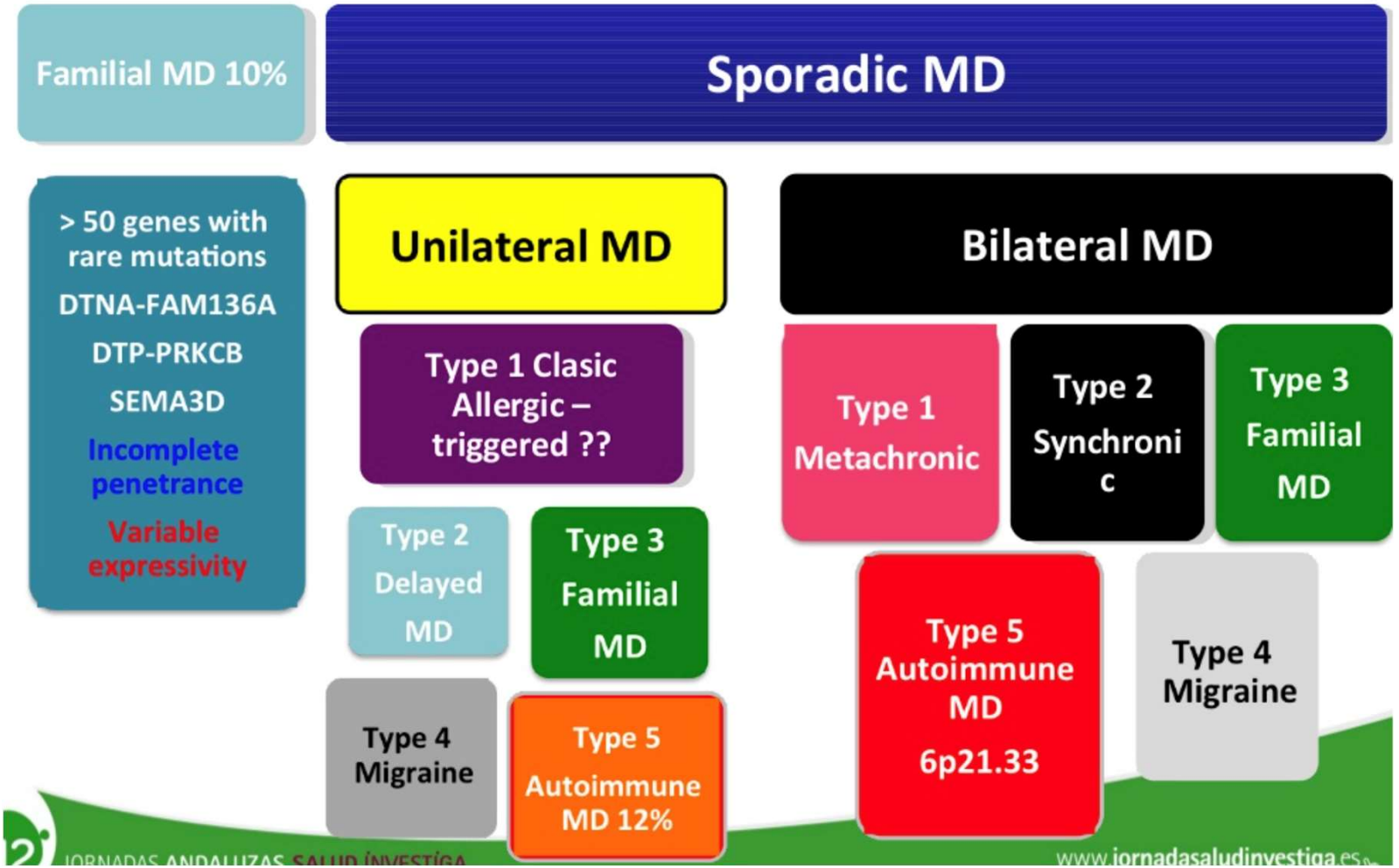
C. Fluctuating aural symptoms (hearing, tinnitus or fullness) in the affected ear[8]

D. Not better accounted for by another vestibular diagnosis [9]

- Although most patients report entirely **spontaneous** spells of vertigo, some patients identify **dietary triggers**, (excessive consumption of sodium or caffeine). (D.D. with acute episode of vestibular migraine)
- Some patients can experience episodes of vertigo lasting seconds to minutes **triggered by high intensity and low-frequency sound** (Tullio phenomenon) and by changes in pressure. These episodes tend to occur later in the disease, perphaps as a result of advanced hydrops bringing the membranous labyrinth in close proximity to the stapes footplate. (**VESTIBULOFIBROSIS**)

Menière's Disease: SubTypes

MD is considered a result of multiple genes interacting with environmental factors. Familial MD has been observed in 5–15% patients and shows a feature of autosomal dominant inheritance



Menière's Disease: Clinical Variants

Delayed endolymphatic hydrops (DEH) consists of new ear symptoms that occur many years after onset of profound deafness.

The damage induced by viral infections trauma or other causes produces the unilateral hearing loss and probably some alterations of inner ear (endolymphatic sac or vestibular aqueduct) that after a variable time could produce an EH in the same ear

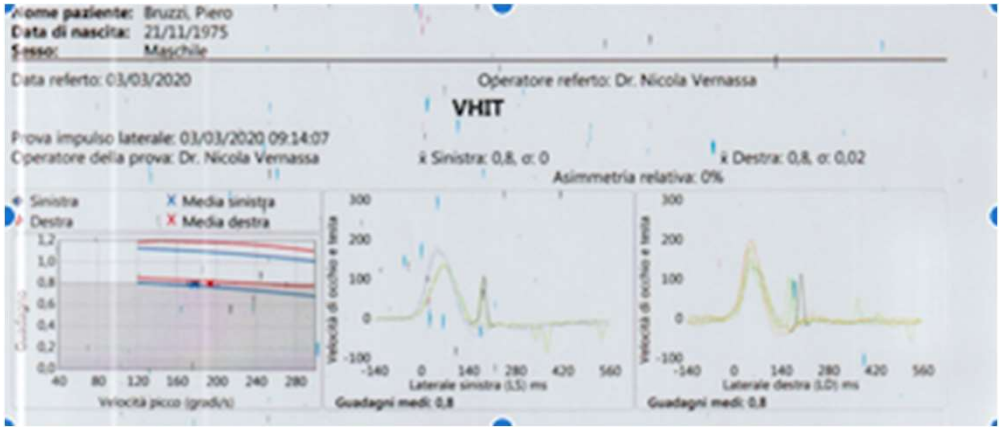
(Ipsilateral DEH) or in the contralateral ear (Contralateral DEH)

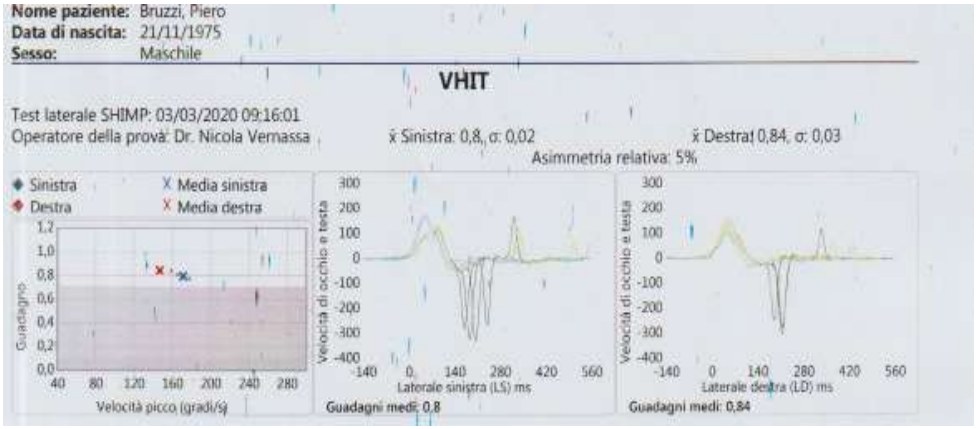
Recurrent Vertigo attacks caused by EH in the deaf ear with no auditory symptoms(the hearing is absent)

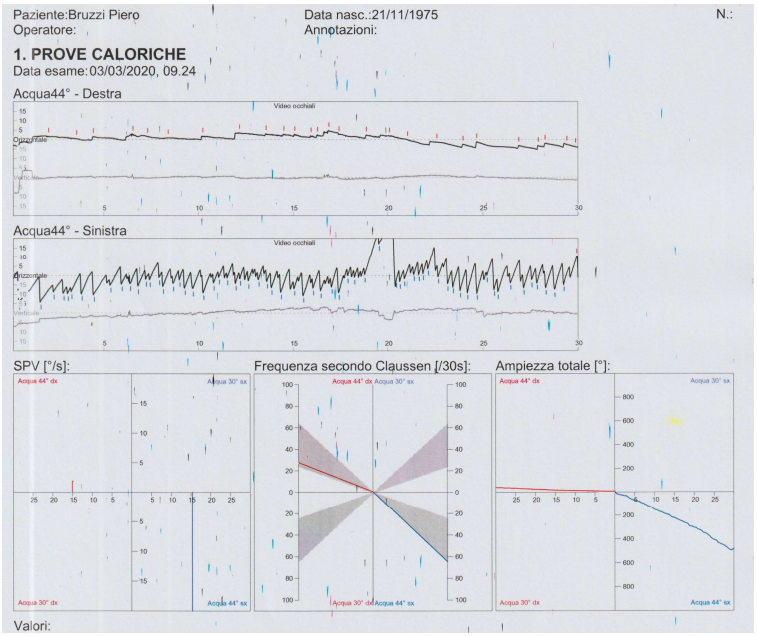
Vertigo attacks and low tone fluctuating hearing loss with fullness and tinnitus caused by EH in the contralateral ear

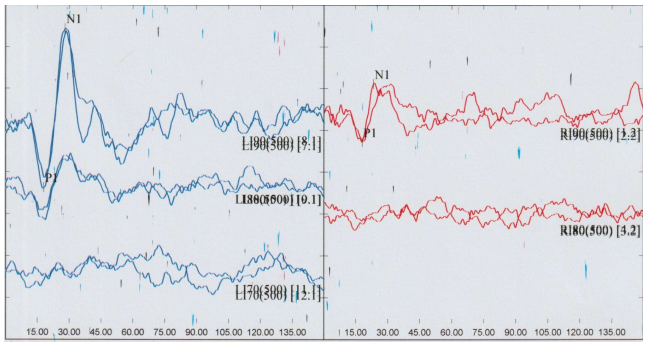
Menière's Disease: Clinical Variants

- B.P. male 45 years, right profound hearing loss from childhood
- From 2010 recurrent verigo attacks lasting 2-4 hours
- Suffering from Migraine with aura
- No response to antimigraneous treatment









Treated with ITG in march 2020
Control on january 2021: no vertigo attacks

TUMARKIN's OTOLITHIC CRISIS

THE OTOLITHIC CATASTROPHE
A NEW SYNDROME
BY
A. TUMARKIN, M.B., F.R.C.S.Ed., D.L.O.

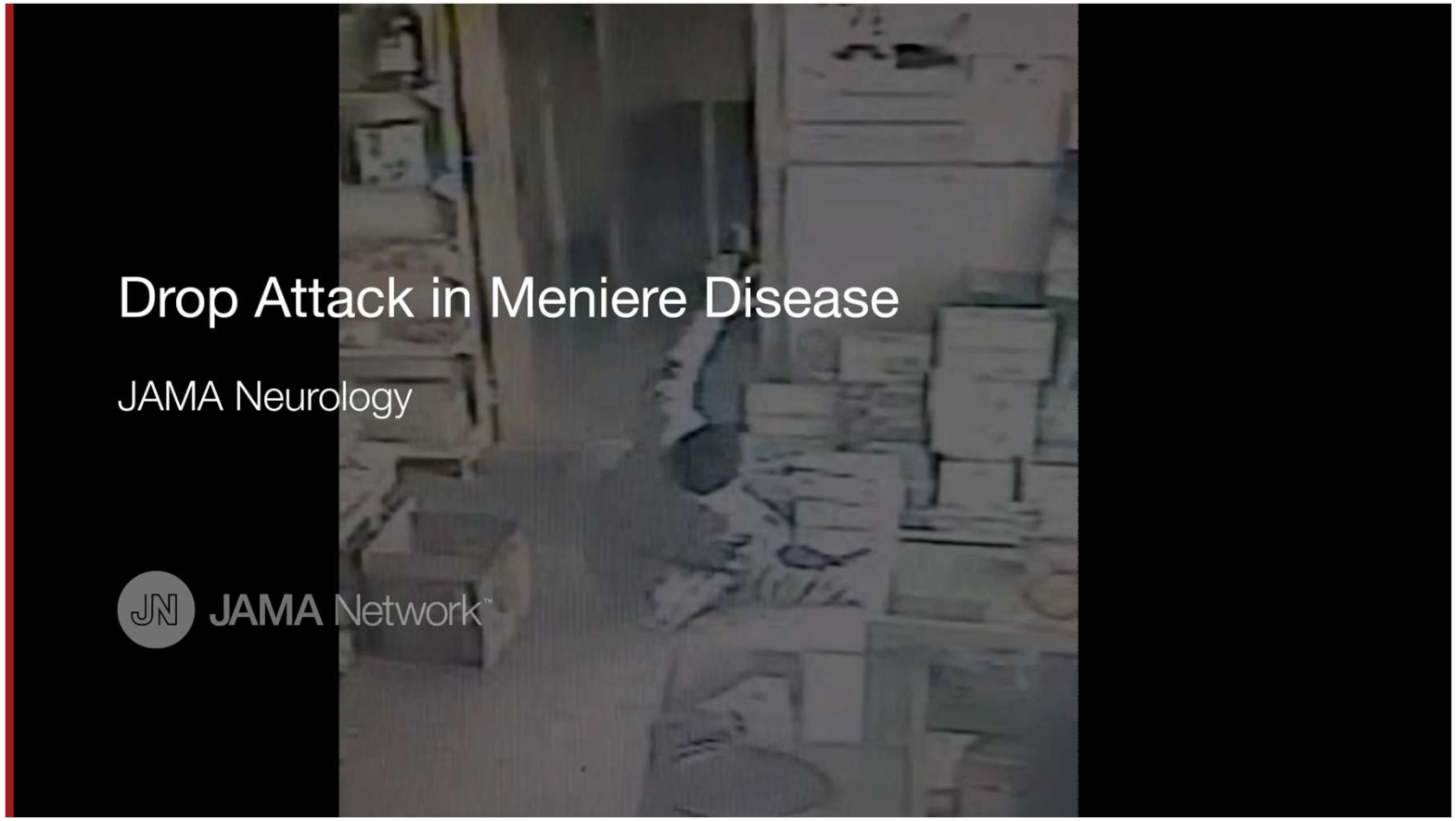
to the fact th
e was known

Sept. 9th	+	
Sept. 11th	+	

but in which he was always able to steady himself by clutching something or by getting to a chair to lie down. These I refer to the semicircular canals. In addition, however, he described an entirely different attack, of which the following is typical. One day he was standing at his desk talking to a client when suddenly he slumped to the floor. He had no vertigo, no loss of consciousness, and no malaise. The thing came like a bolt from the blue, but he was able immediately to assure onlookers that he was all right, and almost

"…. *" … the rare fatal fall which occur in Menière's syndrome is almost certainly to be ascribed to the otolithic apoplexy rather than to the canals…."*

TUMARKIN's OTOLITHIC CRISIS



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Tumarkin's Otolithic Crisis

- Typically Tumarkin's Crisis occur in MD patients in the late stage of the disease or in MD whose onset is over the 6 decades of life.
- In younger MD pts, the saccular structures could be more resistant to the hydropic enlargement and, together to a better postural control, the risks of fall is reduced
- The occurrence of these vestibular drop attacks is variable, although some series report up to 72% (Kentala 2001). But this report wrongly consider as Drop Attacks episodes of tilt and lateropulsion frequently encountered in the late stage of MD when the MD pt rely more on visual and proprioceptive information than on vestibular input to maintain its balance and as such their vertigo attacks are more easily provoked by changes in their visual surrounding or by physical strain.

Tumarkin's Otolithic Crisis

- **This is a very disabling symptom as it occurs without warning and can result in severe injury**
- **The preservation of sensorium clearly distinguishes this from syncope.**
- **Mechanical deformation of the otolithic membrane due to gradient pressure within the inner ear causing a burst of neural impulses from the otolithic organs to the vestibulo-spinal pathways, triggering the fall because an abruptly reduced muscle tone of lower limbs**
- **Similarity with the so called "Otolithic Tullio Phenomenon" (loud sound triggering a fall to the right and forward associated to ocular tilt reaction consistent with ipsilateral otolithic stimulation).**
- **However, in MD Tumarkin's falls there are no precipitating factor and no aura and the falls are more abrupt and violent**
- **In most patients drop attacks remit spontaneously, although other Meniere's symptoms continue to progress. For this reason, the prognosis is relatively benign**

Tumarkin's Otolithic Crisis: TREATMENT

- Conservative Approach; high rate of spontaneous resolution (Jantzen et al)

- Vestibular Nerve Section: benefits of surgery to control Tumarkin crisis have not been demonstrated ; we must keep in mind that, in older patients, co-morbidity plays an important role in compensation mechanism. The older the patient is, the more important is the continuation of the exercises for months after treatment. Another golden rule is that in older patients with DA the search for a possible aetiology rather than MD must to be very careful.

- ITG is an effective alternative and a retrospective study in 24 MD pts supports the use in patients with Tumarkin attacks (Viana et al., 2014)

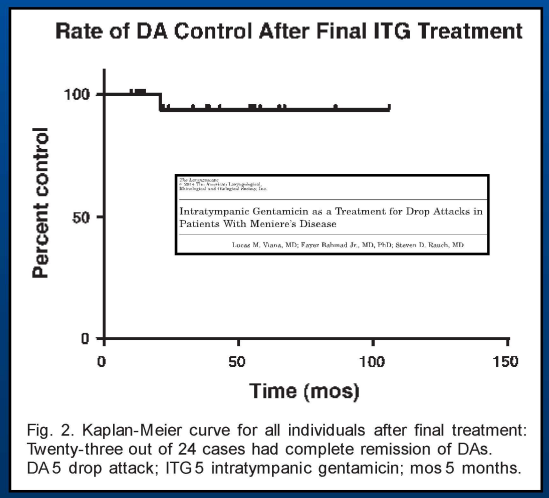


Fig. 2. Kaplan-Meier curve for all individuals after final treatment: Twenty-three out of 24 cases had complete remission of DAs. DA 5 drop attack; ITG 5 intratympanic gentamicin; mos 5 months.

- Recently ITD was also used in 10 pts as a first-line conservative treatment for MD- or DEH-related DA with promising results


Observational Study

Medicine

OPEN

Intratympanic steroids injection is effective for the treatment of drop attacks with Ménière's disease and delayed endolymphatic hydrops

A retrospective study

Bo Liu, MD, Yangming Leng, MD, Renhong Zhou, MS, Jingjing Liu, MS, Dongdong Liu, MS, Su-Lin Zhang, MD*, Wei-Jia Kong, MD*

Menière's Disease: Clinical Variants

VESTIBULAR MD

COCHLEAR MD

- Sometimes in the initial phase hearing loss could be note clearly interpretated by the patients
- Differential Diagnosis with VM

❖ **17-23% SSNHL affects low tones *(Nakashima et al, 2014)***

Hearing Outcome of Low-tone Compared to High-tone Sudden Sensorineural Hearing Loss

George Psillas[1] Aikaterini Rizou[1] Dimitrios Rachovitsas[1] Gabriel Tsiropoulos[1] Jiannis Constantinidis[1]

[1] 1st Academic ENT Department, Aristotle University of Thessaloniki, AHEPA Hospital, Thessaloniki, Greece

Int Arch Otorhinolaryngol 2019;23:65–69.

Address for correspondence Dr George Psillas, MD, 1st Academic ENT Department, Aristotle University of Thessaloniki, AHEPA Hospital, 1, Stilponos Kyriakidi St., GR 546 36 Thessaloniki, Greece (e-mail: psill@otenet.gr).

❖ **More frequent evolution towards definit MD when low tone SSNHL is recurrent**

❖ **Another indicator of possible evolution towards MD is the presence of tinnitus during the first episode**

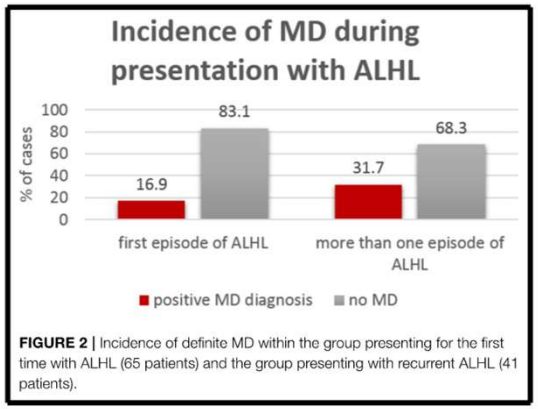


FIGURE 2 | Incidence of definite MD within the group presenting for the first time with ALHL (65 patients) and the group presenting with recurrent ALHL (41 patients).

frontiers in Neurology

ORIGINAL RESEARCH published: 29 October 2018 doi: 10.3389/fneur.2018.00884

Comorbid Symptoms Occurring During Acute Low-Tone Hearing Loss (AHLH) as Potential Predictors of Menière's Disease

Katharina Stölzel, Judith Droste, Linda Josephine Voß, Heidi Olze and Agnieszka J. Szczepek**

Menière's Disease

- Vertigo attacks is the most frequent symptom in the initial phase.
- Less than 30% of MD patients has the three symptoms in the initial phase
- On average the latency between the initial symptom and the development of the classic triad is 1 year
- The so-called cochlear and vestibular variant of MD are probably only particular modalities of onset of MD. A selective hydrops has never been demonstrated

Need of predictive instrumental tests
To evaluate the possible evolution in definite MD

Table 3 Symptoms of Ménière's disease when first seen in a tertiary referral hospital (n=340)

Symptom	Prevalence (%)
Vertigo, tinnitus and hearing loss	38
Vertigo	21
Hearing loss	13
Tinnitus	5
Tinnitus with hearing loss	15
Vertigo with hearing loss	4
Vertigo with tinnitus	4
Total	100%

Table 3. Onset symptom(s) of MD

First symptom	n	%
Vertigo alone	31	13.7
Tinnitus alone	15	6.6
Hearing loss alone	15	6.6
Vertigo and tinnitus[1]	19	8.4
Vertigo and hearing loss[1]	10	4.4
Tinnitus and hearing loss[1]	45	19.8
All three symptoms simultaneously[1]	92	40.5

[1] 'Simultaneous appearance' was recorded in cases where there were fewer than 10 days between the appearance of vertigo and tinnitus, vertigo and hearing loss or tinnitus and hearing loss.

Menière's Disease

Differential Diagnoses in Menière's Disease
➢ Autosomal dominant sensorineural hearing loss type 9 (DFNA9) caused by *COCH* gene
➢ Autosomal dominant sensorineural hearing loss type 6/14 (DFNA6/14) caused by WSF1 gene
➢ Autoimmune inner ear disease
➢ Cerebrovascular disease (stroke/TIA in the vertebrobasiliar system/bleeding)
➢ Cogan's syndrome. Some cases may have recurrences.
➢ Endolymphatic sac tumor
➢ Meningiomas and other masses of the cerebellopontine angle
➢ Neuroborreliosis
➢ Otosyphilis Susac syndrome
➢ Third window syndromes (Perilymph fistula, canal dehiscence, enlarged vestibular aqueduct)
➢ Vestibular migraine
➢ Vestibular paroxysmia (neurovascular compression syndrome)
➢ Vestibular schwannoma
➢ Vogt-Koyanagi-Harada syndrome

TABLE 4: MAIN DIFFERENTIAL DIAGNOSES FOR MENIÈRE'S DISEASE (REPRINTED FROM LOPEZ-ESCAMEZ ET AL., "DIAGNOSTIC CRITERIA FOR MENIÈRE'S DISEASE" [28])

Not all MD are definite…

M.D. 44 years (m): multiple invalidating crises with fullness but no HL, no migraine

P.G. 31 years (m): multiple attacks, sudden and stable HL

S.L. 49 years (f): left severe HL, multiple invalidating crises; which ear is responsible?

Initial contralateral involvement unrecognizable with clinical criteria

never treat a bilateral form with ITG !!!

If you do not get a diagnosis…

you will not get a therapy

Menière's Disease

The diagnosis of MD is primarily a clinical diagnosis.

Which role for instrumental assessment?

- vestibular techniques could be able to to find out any instrumental feature able to characterize the disease
- The delineation of an instrumental profile of MD would be of great interest to clinicians:
  - **when the diagnosis is doubtful**
  - **when a MD does not meet all international criteria**
  - **when a bilateral involvement is suspected.**

Menière's Disease

AAO-HNSF Scale:

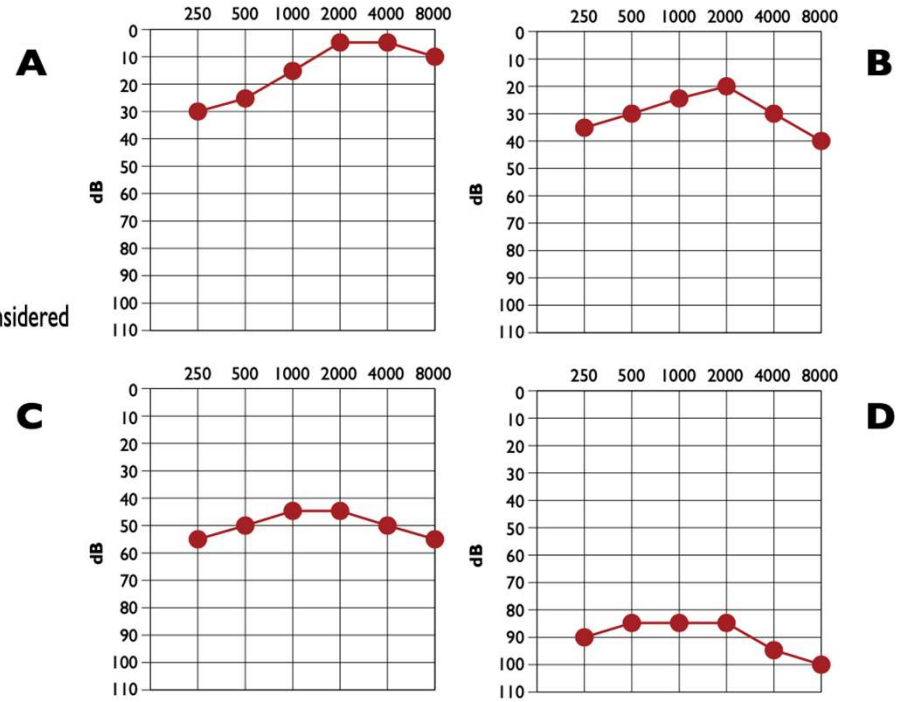
Class A: Discrimination 70-100%; PTA <30 dB

Class B: Discrimination 50-69%; PTA 31-50 dB

Class C: Discrimination 50-69%; PTA >50 dB

Class D: Discrimination <50%; any PTA

Most clinicians consider Class A and B/C to be useable or serviceable hearing; Class D not considered serviceable hearing.



On the basis of the level of HL, a staging of MD has been proposed

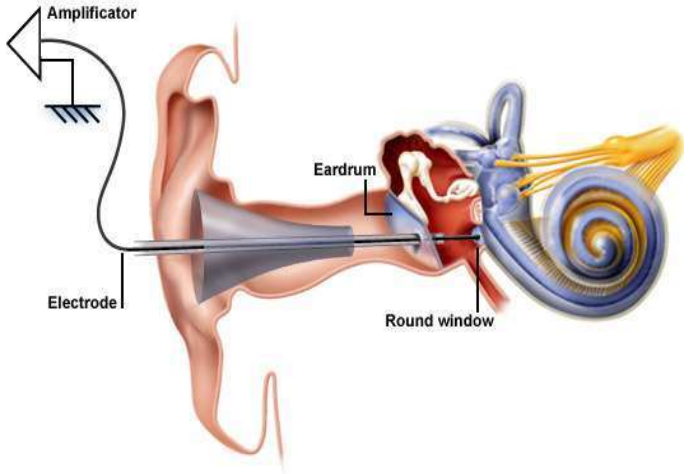
Tabella II - Stadiazione della MdM in base all'entità dell'ipoacusia.

PTA	STADIO			
	I	2	3	4
	≤ 25	26-40	41-70	> 70

Menière's Disease: ElectroCochleoGraphy

- It measures electrical potentials arising in the cochlea and VIII nerve in response to auditory stimuli within first 5 millisec
- Response is in the form of
  - Cochlearmicrophonics (CM)
  - Summation potential (SM)
  - Action potentials (AP)

• Enlarged SP reflects pathologic condition of EH. SP-AP amplitude ratio is more consistent with the presence of meniere's disease. On average, SP-AP ratio of 0.45 or greater is considered abnormal.



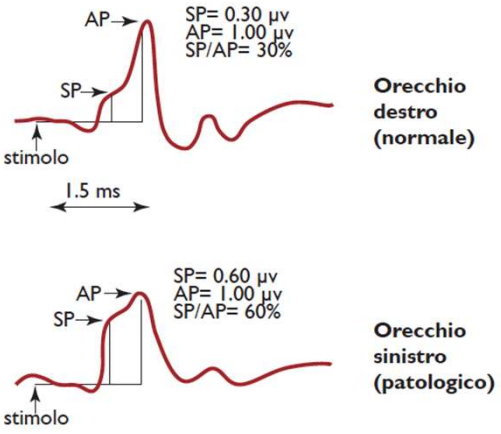
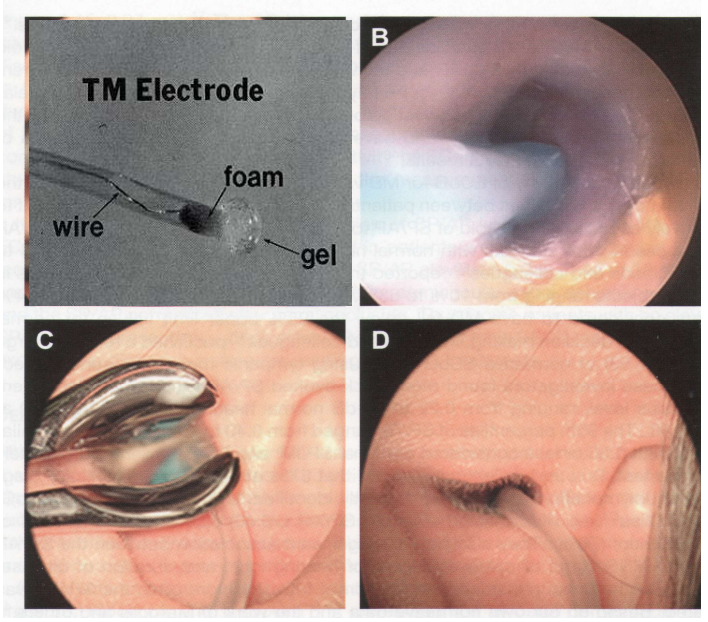


Figura 6 - EcoG nel normale (in alto) e nella MdM (in basso). AP: potenziale d'azione; SP: potenziale di sommazione.



Menière's Disease

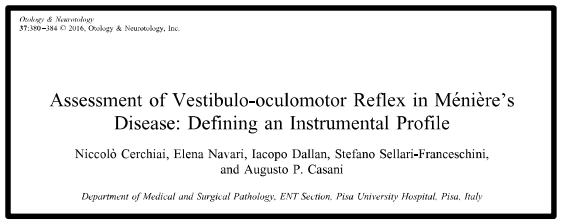
VESTIBULAR Tests

- Bedside examination for spontaneous and positional nystagmus
- Caloric test
- Video Head Impulse test
- Cervical and Ocular Vemps

Meniere's Disease: vHIT versus Caloric test

Video Head Impulse Test

- 70 MD patients between March 2014 and February 2015
- 2 separate groups: 16 patients (**Group 1**) had been previously ***treated with ITG***, while 54 (**Group 2**) had undergone a ***conservative therapy.***



Otology & Neurotology
37:380–384 © 2016, Otology & Neurotology, Inc.

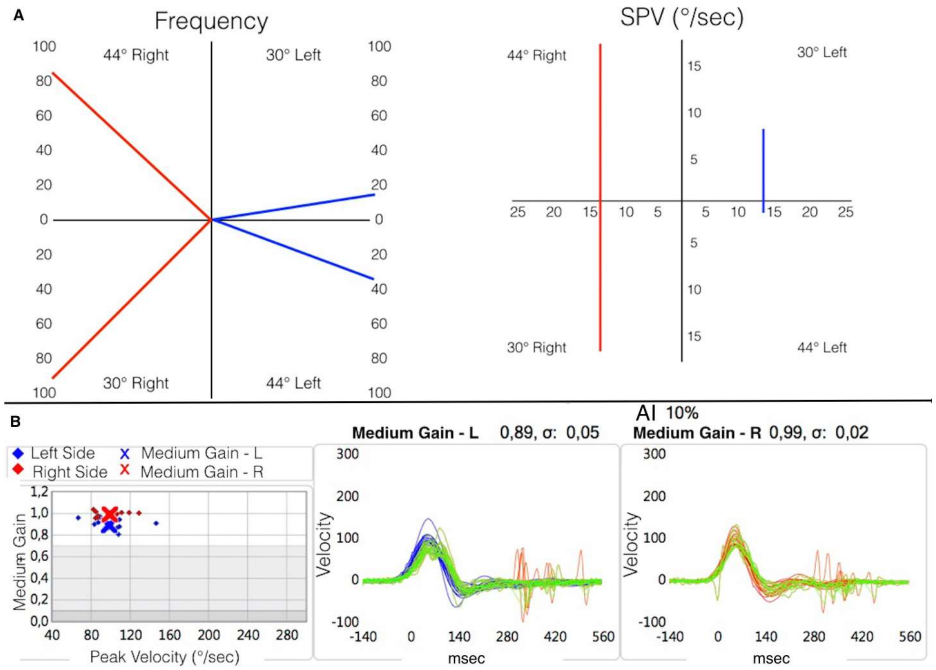
Assessment of Vestibulo-oculomotor Reflex in Ménière's Disease: Defining an Instrumental Profile

Niccolò Cerchiai, Elena Navari, Iacopo Dallan, Stefano Sellari-Franceschini, and Augusto P. Casani

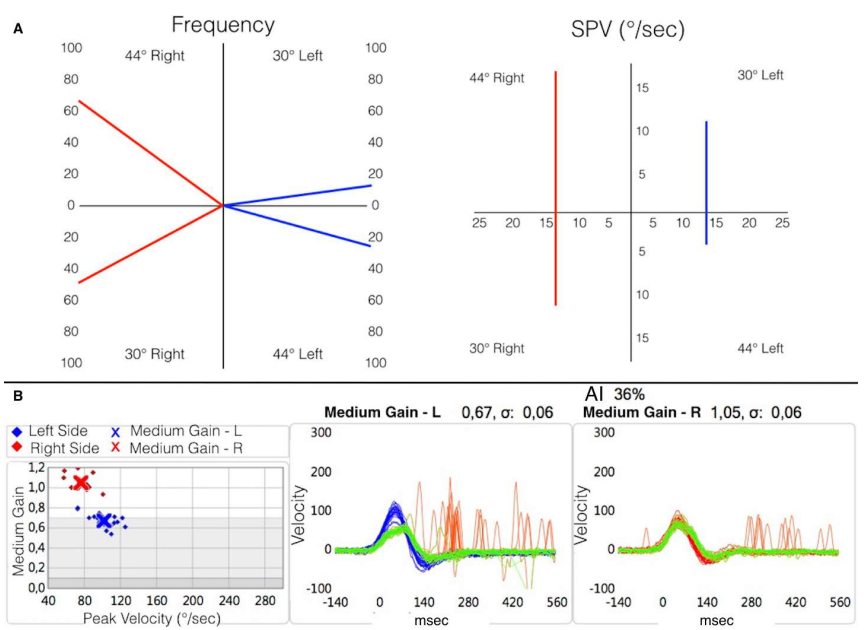
Department of Medical and Surgical Pathology, ENT Section, Pisa University Hospital, Pisa, Italy

- HF-VOR is naturally preserved even in the late stage of MD (Group 2)
- The dissociation between CP and vHIT findings could be considered as an instrumental hallmark of MD.
- ITG reduces HF-VOR gain and can be considered as an endpoint of the treatment (Group 1)

Meniere's Disease: vHIT versus Caloric test



Group 2: Dissociation



Group 2: ITG treated

Journal of Neurology
https://doi.org/10.1007/s00415-019-09431-9

REVIEW

Dissociation of caloric and head impulse tests: a marker of Meniere's disease

I. P. Hannigan[1,2] · M. S. Welgampola[2,3] · Shaun R. D. Watson[1,4]

Received: 7 April 2019 / Revised: 5 June 2019 / Accepted: 11 June 2019

Meniere's Disease: vHIT versus Caloric test

- Differential effects on different types of hair cells. However, recent studies on human fresh tissue show that both type I and type II hair cells are affected about equally (*McCall BMC Ear Nose Throat Disord 2009*).

- In the caloric test, unilateral weakness is due more to the hydropic expansion of the lateral canal membranous duct, rather than, as is widely assumed, to a loss of vestibular receptor hair cell function. In other words, the non physiological fluid drive generated by the caloric thermal gradient across the temporal bone dissipates owing to local convective flow as the duct expands, reducing the hydrostatic driving force across the cupula.

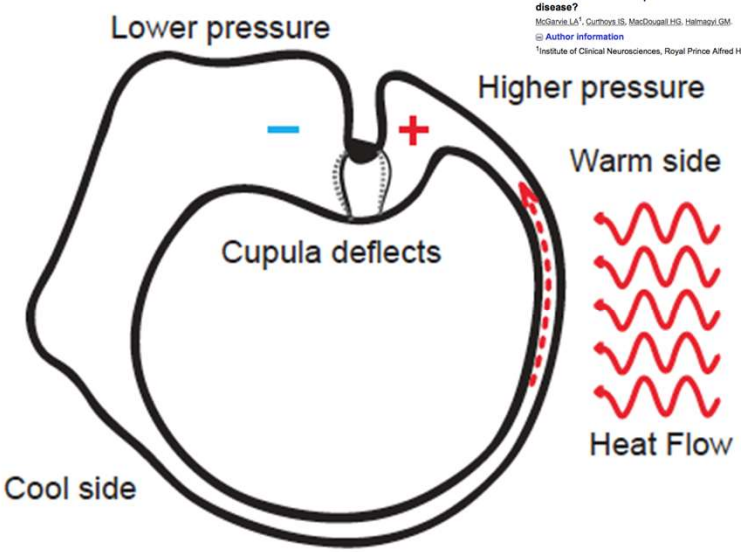
Ann N Y Acad Sci. 2015 Apr;1343:58-62. doi: 10.1111/nyas.12687. Epub 2015 Feb 26.

What does the head impulse test versus caloric dissociation reveal about vestibular dysfunction in Ménière's disease?

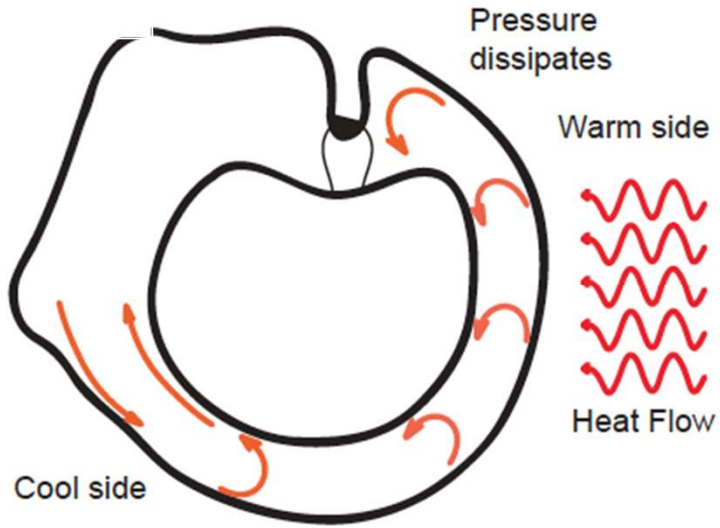
McGarvie LA[1], Curthoys IS, MacDougall HG, Halmagyi GM.

Author information

[1]Institute of Clinical Neurosciences, Royal Prince Alfred Hospital, Camperdown, NSW, Australia.



Normal Duct: No local flow, hydrostatic pressure drive retained and Cupula bent.



Hydropic Expansion of Duct: Local convective flow dissipates hydrostatic pressure across Cupula.

Meniere's Disease: Caloric test

BVC in definite MD

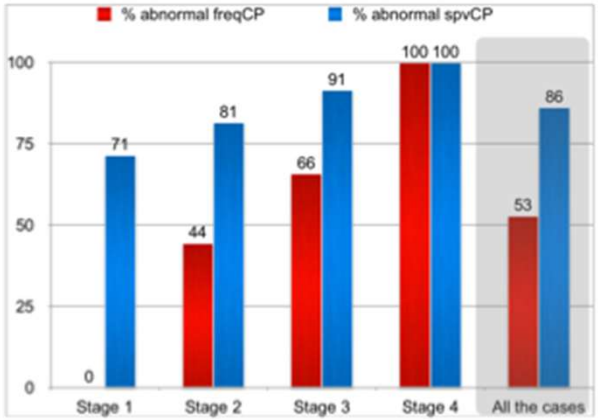
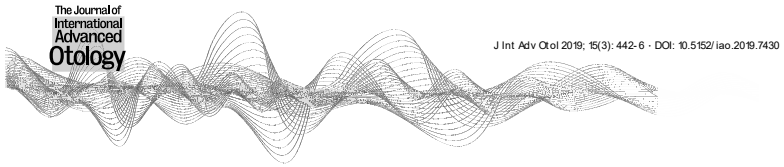


FIGURE 8: HISTOGRAMS SHOWING PERCENTAGES OF ABNORMAL FREQCP AND SPVCP IN DMD GROUP



Original Article

Menière's Disease and Caloric Stimulation: Some News from an Old Test

Niccolò Cerchiai[1], Elena Navari[1], Mario Miccoli[2], Augusto Pietro Casani[1]

Department of Medicine and Surgery, Pisa University Hospital, Pisa University Hospital, Pisa, Italy (NC, EN, APC)
Department of Clinical and Experimental Medicine, Pisa University Hospital, Pisa University Hospital, Pisa, Italy (MM)

- **Slow-phase velocity** of thermally-induced nystagmus is early reduced in MD.
- In definite MD pts high % of pathologic sSPV canal paresis parameters were detected **in all the stages.**
- However, the most important aspect is given by a **dissociation between freqCP and spvCP especially during the early stages of disease**
- This trend characterizes also **pMD**, suggesting that these pathological findings are detectable also in a not fully-developed MD
- **The study showed that Definite MD and Probable MD are potentially similar from an instrumental point of view**

Meniere's Disease: Vemps

SPECIAL ARTICLE

AMERICAN ACADEMY OF NEUROLOGY

Practice guideline: Cervical and ocular vestibular evoked myogenic potential testing

Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology

Conclusion. On the basis of multiple conflicting or inconclusive studies, neither cVEMP nor oVEMP testing was found to be useful in diagnosing Ménière disease, but the studies possibly demonstrate that vestibular loss as assessed by VEMP may be seen in Ménière disease.

Clinical context for using VEMP in Ménière disease. The diagnosis of Ménière disease has long been a clinical one,[e19] and only recently has audiometry been added to the diagnostic criteria.[e20] There is no demonstrable role of VEMP in diagnosis of Ménière disease.

A lot of papers analyzed the role of Vemps for the diagnosis of MD with heterogeneous results

Interestingly, the frequency tuning in some patients shows a shift towards the 1000 Hz

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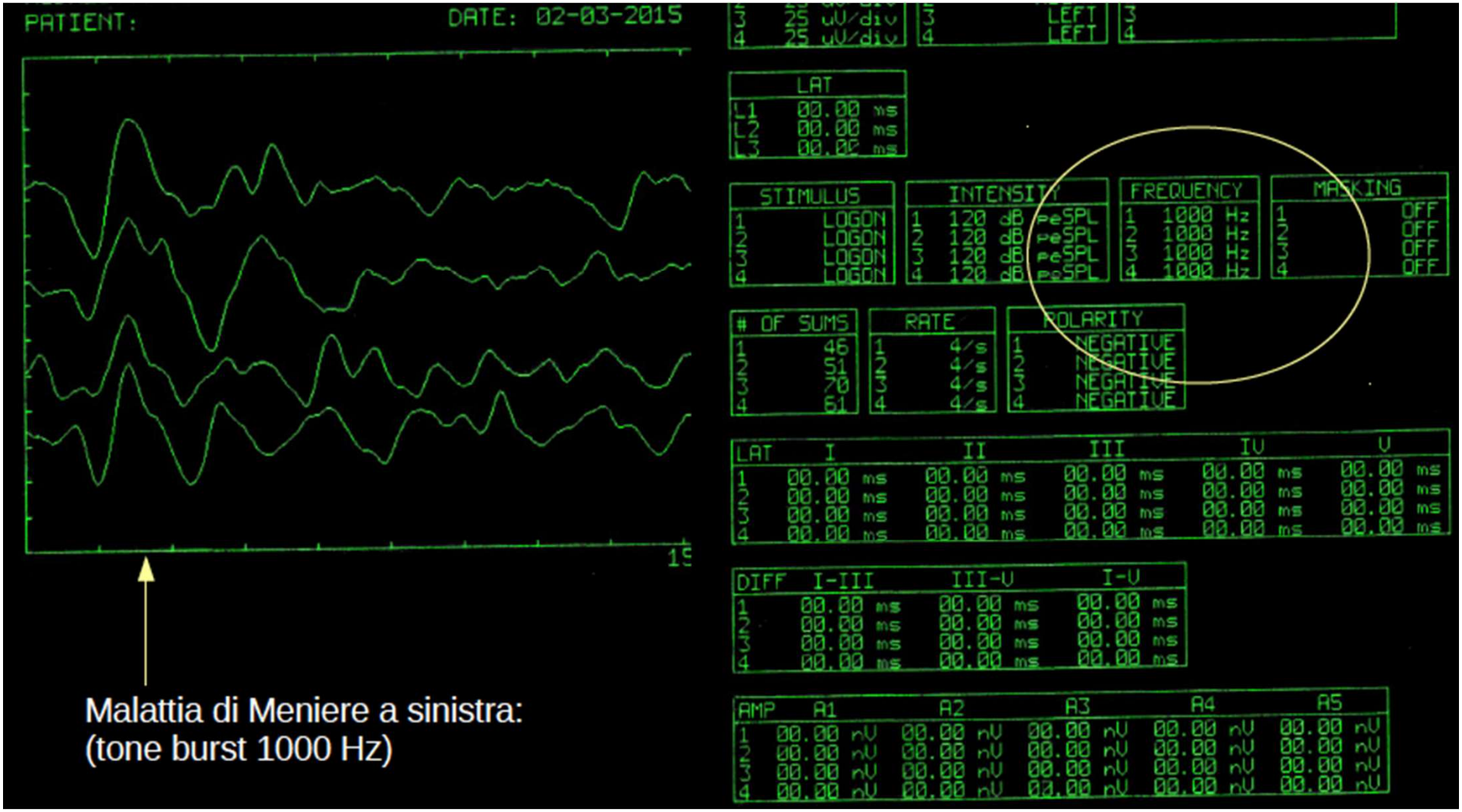
Università degli Studi di Pisa

Meniere's Disease: VEMPs

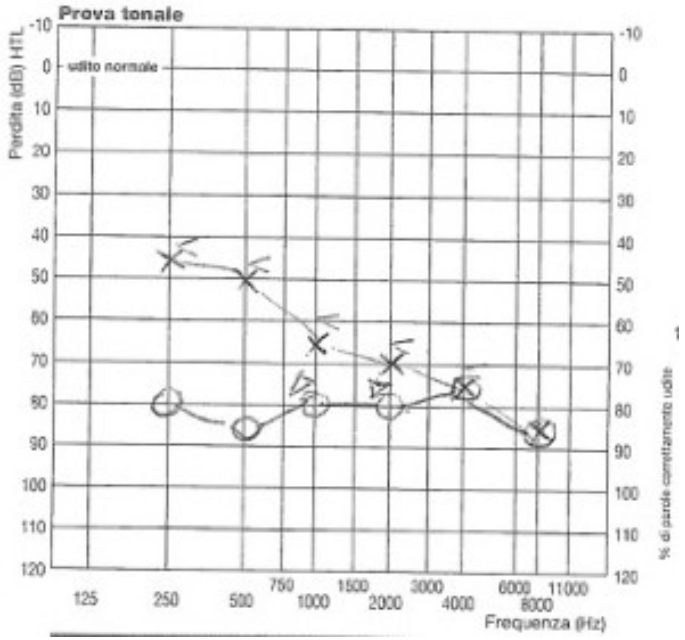
Malattia di Meniere a sinistra:
nessuna onda ai cVEMPs
(tone burst 500 Hz)

Meniere's Disease: Vemps



Meniere's Disease: Instrumental Assessment

- **Female, 86 years,** diagnosed as right MD 30 years ago treated with betahistine and benzodiazepine with relatively good results
- Reappareance of vertigo attacks in October 2019; last episode december 2020



Meniere's Disease: Instrumental Assessment

CNG-Analyser

Licenza concessa per:GN Otometrics

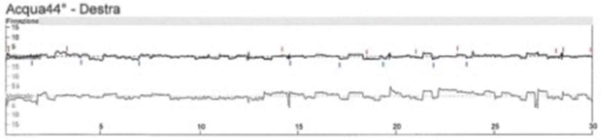
Paziente:CarisioTeresa
Operatore:

Data nasc.:05/10/1932
Annotazioni:

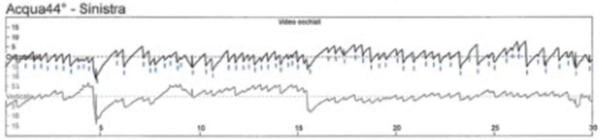
N.:

1. PROVE CALORICHE
Data esame:05/01/2021, 11.47

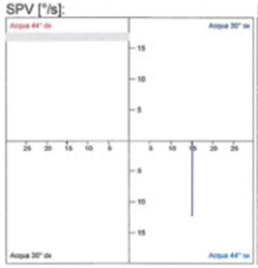
Acqua44° - Destra



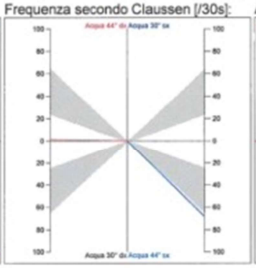
Acqua44° - Sinistra



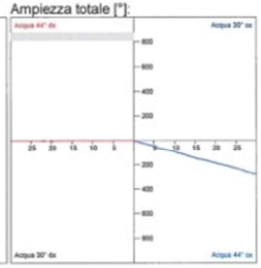
SPV [°/s]:



Frequenza secondo Claussen [/30s]:



Ampiezza totale [°]:



Valori:

	SPV [°/s]	t [s]	Frq [/30s]	t [s]
SPN				
Acqua 44° dx	-0,4	15,2	1	15,2
Acqua 44° sx	-12,3	15,2	-68	15,1
PV [%]				
PD [%]				

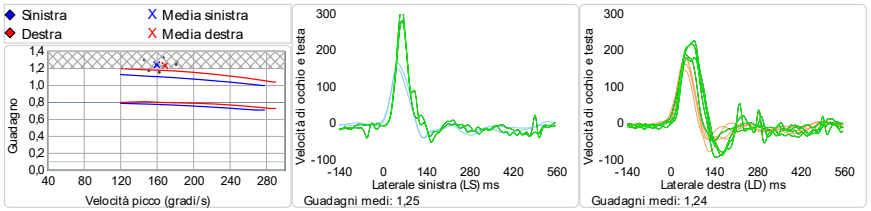
VHIT

Prova impulso laterale: 05/01/2021 11:07:00
Operatore della prova: Dr. Nicola Vernassa

x̄ Sinistra: 1,25, σ: 0,08

x̄ Destra: 1,24, σ: 0,06

Asimmetria relativa: 1%

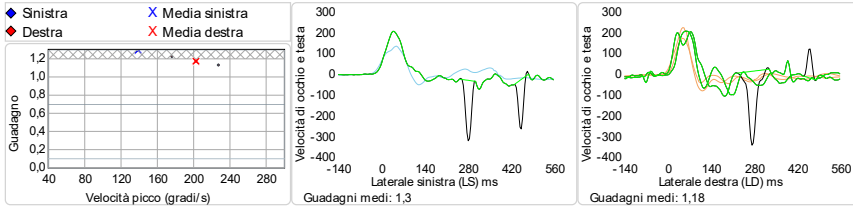


Test laterale SHIMP: 05/01/2021 11:10:08
Operatore della prova: Dr. Nicola Vernassa

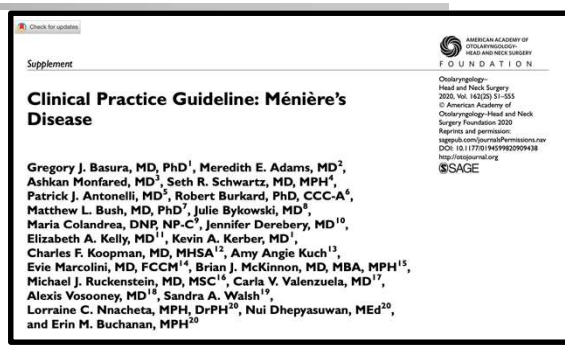
x̄ Sinistra: 1,3, σ: 0

x̄ Destra: 1,18, σ: 0,05

Asimmetria relativa: 9%



Meniere's Disease: Instrumental Assessment



Supplement

Clinical Practice Guideline: Ménière's Disease

Gregory J. Basura, MD, PhD[1], Meredith E. Adams, MD[2], Ashkan Monfared, MD[3], Seth R. Schwartz, MD, MPH[4], Patrick J. Antonelli, MD[5], Robert Burkard, PhD, CCC-A[6], Matthew L. Bush, MD, PhD[7], Julie Bykowski, MD[8], Maria Colandrea, DNP, NP-C[9], Jennifer Derebery, MD[10], Elizabeth A. Kelly, MD[11], Kevin A. Kerber, MD[1], Charles F. Koopman, MD, MHSA[12], Amy Angie Kuch[13], Evie Marcolini, MD, FCCM[14], Brian J. McKinnon, MD, MBA, MPH[15], Michael J. Ruckenstein, MD, MSC[16], Carla V. Valenzuela, MD[17], Alexis Vosooney, MD[18], Sandra A. Walsh[19], Lorraine C. Nnacheta, MPH, DrPH[20], Nui Dhepyasuwan, MEd[20], and Erin M. Buchanan, MPH[20]

AMERICAN ACADEMY OF OTOLARYNGOLOGY-HEAD AND NECK SURGERY FOUNDATION

Otolaryngology–Head and Neck Surgery 2020, Vol. 163(3S) S1–S55

DOI: 10.1177/0194599820909438
http://otojournal.org
SAGE

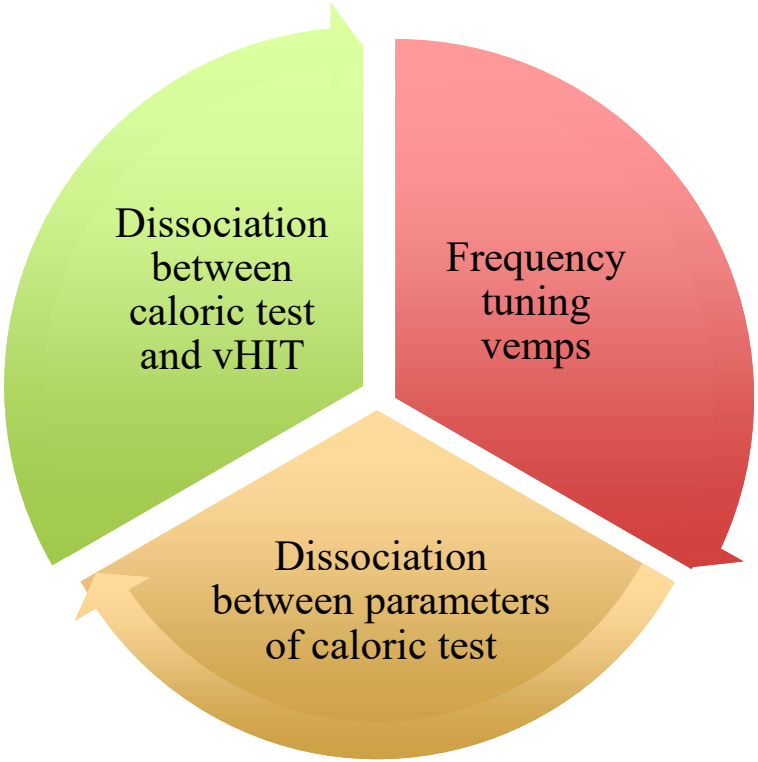
- the tests may provide information beneficial to the evaluation and management of specific individuals.
- These tests may provide a supportive role in the diagnosis of MD, specifically when patients present with atypical symptoms or when there is difficulty determining the affected ear, which may be helpful when considering ablative interventions.
- The tests are most appropriately used when the results will be utilized to alter patient management.

Table 4. Summary of Guideline Key Action Statements.

Statement	Action	Strength
Statement 1. Diagnosis of Ménière's disease	Clinicians should diagnose definite or probable Ménière's disease in patients presenting with 2 or more episodes of vertigo lasting 20 minutes to 12 hours (definite) or up to 24 hours (probable) and fluctuating or nonfluctuating sensorineural hearing loss, tinnitus, or pressure in the affected ear, when these symptoms are not better accounted for by another disorder.	Recommendation
Statement 2. Assessing for vestibular migraine	Clinicians should determine if patients meet diagnostic criteria for vestibular migraine when assessing for Ménière's disease.	Recommendation
Statement 3. Audiometric testing	Clinicians should obtain an audiogram when assessing a patient for the diagnosis of Ménière's disease.	Strong recommendation
Statement 4. Utility of imaging	Clinicians may offer magnetic resonance imaging (MRI) of the internal auditory canal (IAC) and posterior fossa in patients with possible Ménière's disease and audiometrically verified asymmetric sensorineural hearing loss.	Option
Statement 5. Vestibular or electrophysiologic testing	Clinicians should not routinely order vestibular function testing or electrocochleography to establish the diagnosis of Ménière's disease.	Recommendation against
Statement 6. Patient education	Clinicians should educate patients with Ménière's disease about the natural history, measures for symptom control, treatment options, and outcomes.	Recommendation

- Specifically, vestibular testing should be performed to assess the integrity of the vestibular system prior to completing an inner ear ablative procedure for MD treatment. As bilateral peripheral vestibular hypofunction has a significant impact on QOL full assessment of the vestibular function in the contralateral ear is warranted to determine the risks prior to permanent vestibular ablation.
- Vestibular testing may also be used to assess the effectiveness of ablative treatment

Meniere's Disease: Instrumental Assessement



Early Diagnosis

↓

Early Treatment

↓

Better management and prognosis of MD

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Meniere's Disease: MR IMAGING

There are potential benefits of further confirmation of EH with imaging:

(1) in clinically unilateral MD, it may provide evidence of bilateral EH, which could influence choice of therapeutic approaches and provide prognostic information;

(2) with incomplete phenotypes or atypical clinical features, it may provide an objective assessment which helps distinguish MD from other diagnoses (e.g.VM or AIED)

(3) and allows earlier diagnosis prior to manifestation of the complete diagnostic clinical criteria.

Clinical indications for EH imaging.

Clinical indication	Rationale/comments
Unilateral MD, when invasive therapies are being considered (30%)	Vestibular-destructive treatments such as intratympanic gentamicin would be ill advised if the contralateral inner ear was hydropic and less able to compensate
MD with bilateral aural symptoms (9%)	Knowledge of hydropic change in the contralateral ear maybe helpful for prognosis and in planning therapy
Incomplete phenotypes and in particular monosymptomatic presentations (61%)	Monosymptomatic presentations are typically: a) episodic vertigo alone, where an alternative or overlapping diagnosis is being considered such as vestibular migraine b) sudden onset SNHL or fluctuating aural symptoms alone

TABLE 1. *Comparison of intratympanic versus intravenous contrast agent application for MR imaging of endolymphatic hydrops*

IT Contrast	IV Contrast
High signal intensity	Low signal intensity
Excellent image quality	Good image quality
Total dose about 1:1,000 compared with IV	Usually double-dose
Puncture of ear drum	Puncture of vein
20–28 hours interval	3–5 hours interval
Off-label	Off-label?
One ear	Both ears
Depends on healthy middle ear	Depends on blood-labyrinth-barrier

THE RADIOLOGICAL FEATURES OF EH MAY BE APPROACHED IN DIFFERENT WAYS

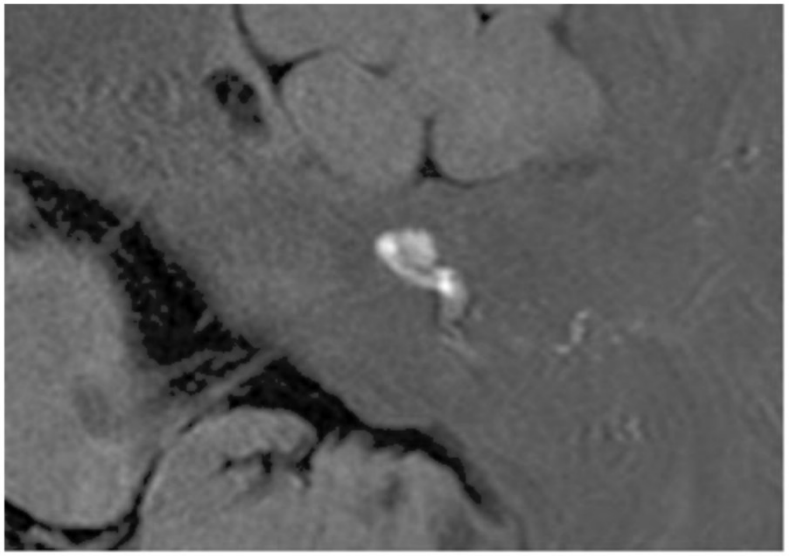
Magnetic resonance imaging features of endolymphatic hydrops (EH).

	Details	Advantages	Disadvantages/pitfalls
Endolymph to perilymph Semiquantitative area grades	Nakashima *et al.* (Nagoya) grading[14] *Vestibular*: Recorded at inferior aspect of LSCC as % area of endolymph relative to total fluid area Grade 1: 33–50% Grade 2: >50% *Cochlear*: Displacement of Reissner's membrane Grade 1: cochlear duct < scala vestibuli area Grade 2: cochlear duct > scala vestibuli area Barath *et al.* grading[16] *Vestibular*: Recorded at widest part of the vestibule >50% area of endolymph relative to total fluid area Grade 1: perilymphatic space still visible Grade 2: vestibule entirely replaced *Cochlear*: Dilated cochlear duct Grade 1: spares part of scala vestibuli Grade 2: replaces scala vestibuli	Simple and quick Good correlation with volumetric quantification of EH volume.[42,43]	Endolymphatic area is dependent on TI, section thickness[44] and angle of reformat Mismatch between the grading systems due to different levels and criteria. Vestibule: area is markedly influenced by minor change in section selection due to orientation of utricle in axial plane[30,44] Cochlea: non-enhancing endolymph may be mimicked by artefact from interscalar septa and the grade may vary along length of cochlea (EH usually involves middle and apical turns first: maximum grade recorded)[39] Limited number of grades although range extended by some authors[6,39]
Ratio of the saccule to utricle area (SURI)	Assessed on double oblique reformat along the longest axial and coronal vestibular dimensions on two references sections	SURI≥1 is very specific Utricle and saccule areas vary concomitantly when parameters of the 3D-FLAIR sequence are modified	Structures may be fused when hydropic; unable to assess SURI Only 50% sensitive Dichotomised outcome and does not provide a "grading"
Asymmetry between the inner ears	Compare each ear for asymmetric cochlear (and possibly LSCC) perilymphatic enhancement Asymmetric increase in size of vestibular and cochlear endolymphatic structures ipsilateral to symptoms		Increased labyrinthine enhancement is not specific The smaller sized structure may be pathological The contralateral asymptomatic ear has higher rates of EH: suboptimal control
Endolymphatic extension to vestibular orifices	Extension of endolymphatic structures to posterior limb of SCC or the oval window	Specific	Limited descriptions and evaluation Only applies to vestibular structures
Hybrid systems	Mainly combining grading systems with SURI and cochlear perilymphatic enhancement[33,40]	Maximises diagnostic accuracy. Addition of cochlear perilymphatic enhancement helps distinguish from other vertigo associated inner era pathology[23]	

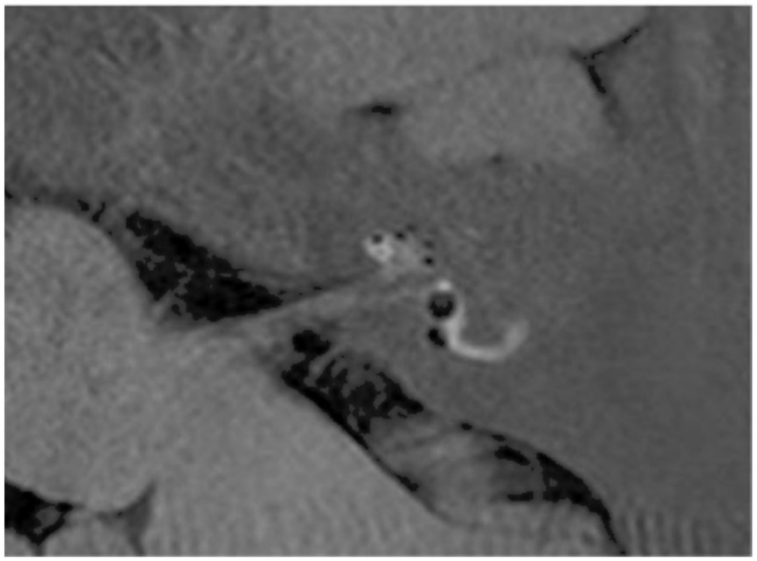
SURI, saccule to utricle area ratio inversion; FLAIR, fluid attenuated inversion recovery; LSCC, lateral semi-circular canal.

Meniere's Disease: MR IMAGING

- The best MR technique to evaluate EH is 24-hour delayed three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) following intratympanic contrast. If this is not available, a 4-hour delayed 3D-FLAIR sequence after intravenous gadolinium could be used.
- With either method, the perilymphatic, but not endolymphatic, space enhances with gadolinium. This enables imaging either of an enlarged scala media (in cochlear hydrops) or an enlarged saccule (in vestibular hydrops). In late-stage Menière's disease, this imaging may show almost complete obliteration of the perilymphatic space.



A



B

MR scan of the left inner ear with contrast enhancement.

(A) Normal labyrinth.

(B) Endolymphatic hydrops (dilated endolymphatic space in black).

Menière's Disease: Therapeutic Options

- Therapy in MD primarily aims to prevent attacks and, if possible, also to avoid the progression of vestibulocochlear deficits. More than 3.500 papers have been published on MD treatment

- The spectrum of therapy recommendations ranges from a salt-free diet, diuretics, pulsed low-pressure delivery, endolymphatic sac surgery, and intratympanic administration of gentamicin or steroids to oral application of steroids or Betahistine

- Treatment prescribed for the intercritical phase aims to: (**i**) reduce the number and severity of vertiginous crises; (**ii**) relieve chronic symptoms (instability and tinnitus); and (**iii**) prevent the progression of the disease, with specific focus on hearing loss and disordered balance.
- Maintenance therapies are able to achieve sufficient control of vertiginous crises in at least two-thirds of patients, especially when associated with a healthy lifestyle (i.e., no alcohol, no tobacco, no coffee, no stress), dietary measures (sodium restriction) and diuretics; **however, there is no effective therapy for long-term preservation of hearing.**

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Menière's Disease: Therapeutic Options

- **Endolymphatic hydrops** (EH) can exist without ever producing symptoms of MD. There must be an additional factor(s) combining with EH to give rise to the symptomatic disease.
- Therefore, medical treatment can be directed at both the formation of EH itself and possible cofactors that "activate" the disease.
- **Potential MD cofactors** include chronic cerebrovascular disease, episodes of reduced blood flow, and/or activation of the inflammatory processes within the inner ear.
- **Possible contributors** to these cofactors include migraine, sleep apnea, hypertension, atherosclerosis, autoimmune disease, immunologic dysfunction, food and environmental intolerances and allergy.
- **A primary goal of medical treatment should be identifying and treating these underlying conditions.**

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Dipartimento di Patologia Medica, Chirurgica, Molecolare e Area Critica
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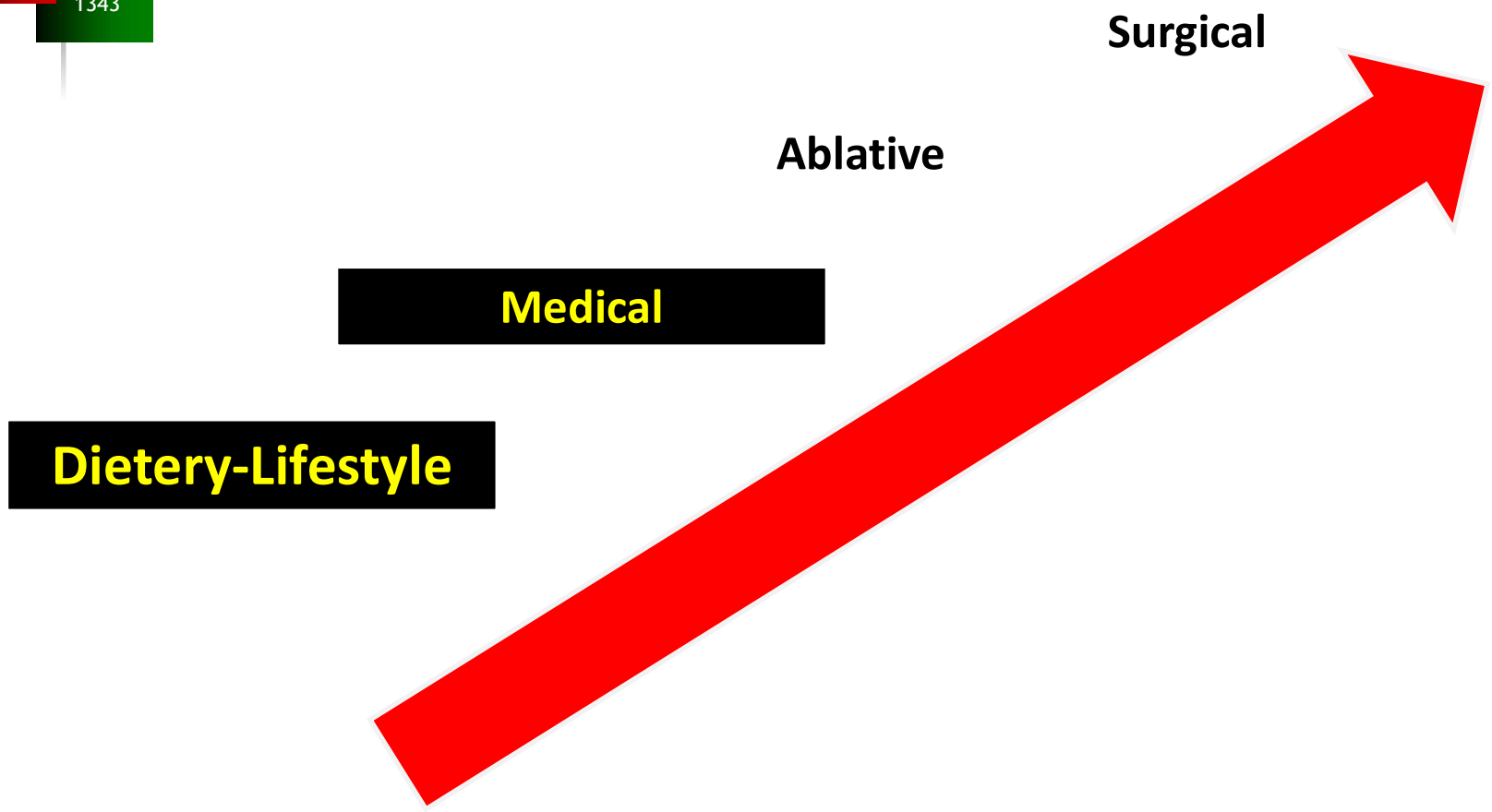
Meniere's Disease



Firstly the treatment must be customized according with different factors like age, duration of the disease, comorbidities, impact of the disease upon the quality of life, presence of psyco-pathological disturbances, etc.

Meniere's Disease

- Meniere's disease is a ''phenotype''; that is, it is a clinical presentation of unstable hearing and balance that may arise from many different insults to the inner ear. A normal ear has a host of homeo- static systems. These systems regulate the production, maintenance, and recycling of endolymph and perilymph.
- Under normal circumstances, these homeostatic systems are so robust that inner ear functions of hearing and balance are impervious to changes in the rest of the body or the external environment.
- In Meniere's disease one or more of these systems is dysfunctional. As a consequence of impaired homeostasis, hearing and balance functions become vulnerable to myriad of internal and external factors, such as stress, sleep deprivation, dietary indiscretion, hormonal change, allergies, and barometric pressure change

Fragile Ear

Conservative treatments must include lifestyle and dietary adjustments,

Menière's Disease: Therapeutic Options

- Due to the fluctuating nature of symptoms and poor understanding of disease etiology, treatment of MD is very challenging.
- The problem of assessing the efficacy of treatments is that MD is prone to prolonged remissions and it is impossible to be sure that the remission was due to the treatment or just occurred spontaneously.
- This is further complicated by data showing that vertigo resolves in 57% of patients after 2-years and 71% after 8-years with the disease (*Silverstein et al., 1989*).
- Moreover, as bilateral involvement could increase with disease progression, so ablative treatment must be given with caution.
- **However only ablative treatment had been proven to achieve significant vertigo control under strict scientific conditions**.

TOROK 1977; RUCKENSTEIN 1991

60-80% OF POSITIVE THERAPEUTIC RESPONSE TO ANY TYPE OF INTERVENTION IN SHORT OR INTERMEDIATE TERM

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Menière's Disease: Acute Management

Vestibular suppressants and anti-emetic agents have been used to control acute vertigo attack

TABLE V.
Medical Management of Ménière's Disease.

Acute management

- Vestibular suppressants
- Anti-emetics
- Rehydration
- Electrolyte adjustment

- **Benzodiazepines**
  - Additional beneficial anxiolytic effects
- **Anticholinergics with Antihistamic effect**
  - **Prometazine**
    - Antihistaminic, Anticholinergic, Antidopaminergic
  - **Meclizine**
  - **Tietilpirazine**
    - Anti-emetic properties
- **Steroids**
  - Prednisone 1 mg/Kg/ tapered
    - Antonio e Friedmann, 2005
- **Osmotic Diuretic Drugs**
  - Glycerol or Mannitol

Side effects and Contraindications
- Reduction of saliva
- Glaucoma, Prostatic diseases
- Extra-pyramidal Effects

- Haematuria
- Congestive Heart Failure

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Menière's Disease: Acute Management

Management of the acute attack of MD
The Italian Experience

European Archives of Oto-Rhino-Laryngology
https://doi.org/10.1007/s00405-019-05423-7

OTOLOGY

Check for updates

Therapeutic strategies in the treatment of Menière's disease: the Italian experience

Nicola Quaranta[1] · P. Picciotti[2] · G. Porro[1] · B. Sterlicchio[1] · G. Danesi[3] · P. Petrone[4] · Giacinto Asprella Libonati[5]

Treatment of the acute phase

83.5% of respondents used diuretics in the acute phase, 66.7% steroids, and 22% vasodilators. Mannitol was the most commonly described diuretic (36%), followed by glycerol (25.2%), acetazolamide (16.2%), and hydrochlorothiazide (14.4%). Statistical analysis did not show a correlation

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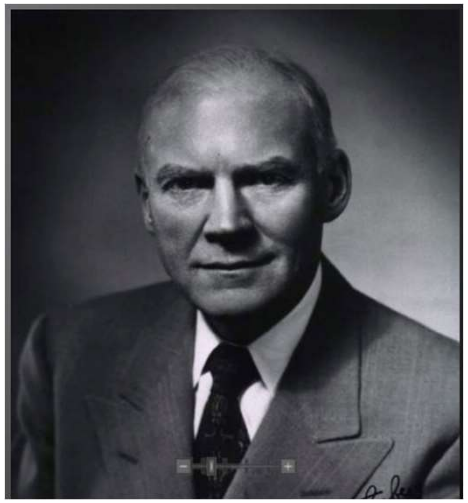
LYFESTYLE CHANGES

Some triggers of Meniere's attacks include caffeine, chocolate, stress, visual stimuli, and dropping barometric pressure.
Trigger avoidance is recommended through dietary modifications with strong recommendation for **low-salt (daily sodium less than 1500 mg) diet**, limiting stimulants including caffeine, and regular sleep cycle with adequate sleep. *caffeine can provoke modifications in the endolymph volume with its sympathomimetic action*



LXXXIV.

MÉNIÈRE'S SYMPTOM COMPLEX: MEDICAL TREATMENT.*

A. C. Furstenberg, M. D.,
F. H. Lashmet, M. D.,
Frank Lathrop.
Ann Arbor.

Recommendation to **restrict sodium intake** was originally conceived as a way of reducing ''fluid retention'' in the inner ear. Although this notion might seem simplistic and improbable, the fact is that many patients with Meniere's disease are sensitive to sodium intake and do better on a restricted diet.

A **fragile ear** may be intolerant of variations in sodium levels. If so, it is likely that a low sodium level is not actually the important feature of treatment. **A constant sodium level is the critical feature.**

LYFESTYLE CHANGES

How is the compliance of MD patients to dietary modifications and how could impact on the clinical course?

This study suggests that compliance with the dietary recommendations may have had a relationship to reduction in vertigo symptoms. Number of spells per month and AAO-HNS functional level both significantly improved, and degree of improvement showed some relationship to the degree of compliance with the reduced sodium and/or caffeine-free diet.

Nutrition can play a role in the management of MD

Otology & Neurotology
34:1438–1443 © 2013, Otology & Neurotology, Inc.

Dietary Modification as Adjunct Treatment in Ménière's Disease: Patient Willingness and Ability to Comply

*Emily Luxford, †Karen I. Berliner, ‡Jacqueline Lee, and §William M. Luxford

*VA Medical Center, Los Angeles; †House Research Institute, Marina del Rey; ‡Nutrition and Dietetics, California State University, Long Beach, and §House Clinic and House Research Institute, Los Angeles, California, U.S.A.

TABLE 2. *Reported compliance to dietary recommendations*

Question	Percent of respondents
Diet currently followed	
Reduced sodium diet	79.5
Caffeine-free diet	68.0
Both diets	58.0
Neither diet	11.8
Compliance level*	
100% compliant	21.8
75% compliant	53.2
50% compliant	17.7
25% compliant	4.8
Not compliant	2.4
Compliance duration	
>2 yr	67.2
1–2 yr	10.7
7–12 mo	4.1
3–6 mo	12.3
1–2 mo	3.3
Never	2.5
Difficulty of low-sodium diet/caffeine-free diet	
Easy to follow	12.7/37.9
Manageable	65.1/46.8
Difficult to follow	21.4/12.9
Impossible to follow	.8/2.4

*100% = all meals and snacks; 75% = 3 meals/day; 50% = 2 meals/day; 25% = 1 meal/day.

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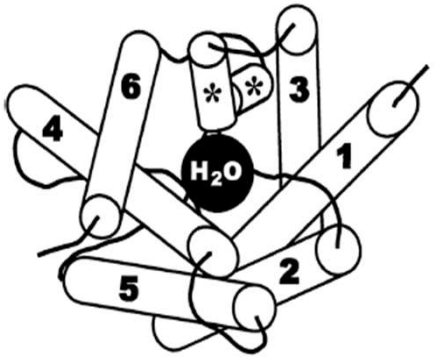
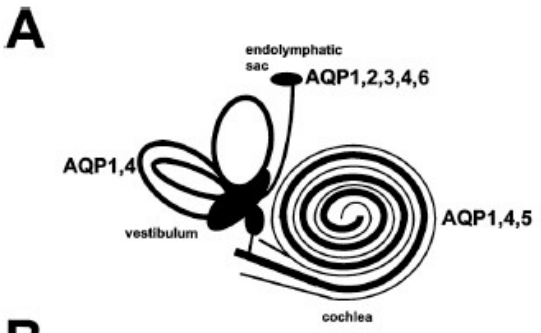
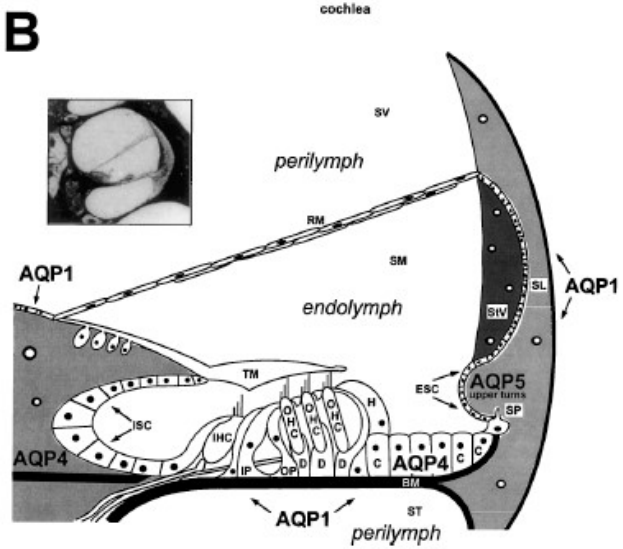
LYFESTYLE CHANGES

INCREASE OF WATER INTAKE

- AQs transport water through the membranes and inhibit the passage of ions maintaining the intracellular pH
- AQP 2 are highly represented in the ES and are closely related to ADH receptors
- Receptors were also found (especially in the ES) for AVP and Aldosterone that could play an important role in the hydro-electrolyte balance of inner ear
- An increase in these hormones (stress) could activate AQPs favoring EH







- Takeda et al. reported evidence of elevated plasma AVP levels in patients with MD.
- High levels of AQP-2 mRNA in the cochlea and the chronic administration of AVP induced EH.
- Thus, we could speculate that elevated levels of AVP may cause EH.
- **An increase of water intake could reduce the level of APV reducing the activity of AQP in inner ear so preventing the onset of EH**

Meniere's Disease

Università di Pisa 1343

The Laryngoscope
Lippincott Williams & Wilkins, Inc.

Water May Cure Patients With Meniere Disease

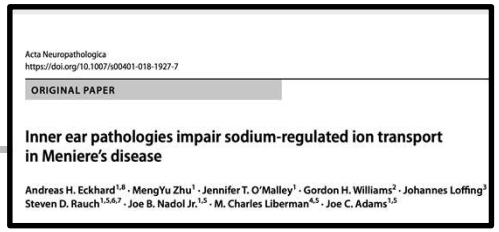
Hideaki Naganuma, MD; Katsumasa Kawahara, MD; Koji Tokumasu, MD; Makito Okamoto, MD

Eighteen patients with MD in group 1 drank 35 mL/kg per day of water for 2 years.

Objectives/Hypothesis: **We examined whether sufficient water intake is effective in the long-term control of vertigo and hearing activity in patients with Meniere disease (MD) for whom conventional therapy has proven unsuccessful.** ***Study Design:*** **The authors conducted a time-series study with historical control.** ***Methods:*** **Eighteen patients with MD in group 1 drank 35 mL/kg per day of water for 2 years. Twenty-nine patients with MD treated with the conventional dietary and diuretic therapy for more than 2 years during 1992 to 1999 at the same hospital were enrolled in a historical control of group 2.** ***Results:*** **Patients in group 1 dramatically relieved vertigo and significantly improved in the hearing of the worst pure-tone average of three frequencies (0.125, 0.25, and 0.5 kHz) (low PTA) during the last 6 months of the study period. In contrast, patients in group 2 became worse in both the four- (0.5, 1, 2, and 4 kHz) frequency PTA and the low PTA, although their vertigo did improve. The number of patients whose hearing were improved, unchanged, and worse were 4, 12, and 2 in group 1 and 2, 11, and 16 in group 2, respectively.** ***Conclusion:*** **Deliberate modulation of the intake of water may be the simplest and most cost-effective medical treatment for patients with MD. Larger studies will be needed to confirm these results in a larger patient cohort.** ***Key Words:*** **Meniere's disease, water intake, VP-V2 receptor, vasopressin aquaporin (AQP).**

Laryngoscope, **116:1455–1460, 2006**

Meniere's Disease

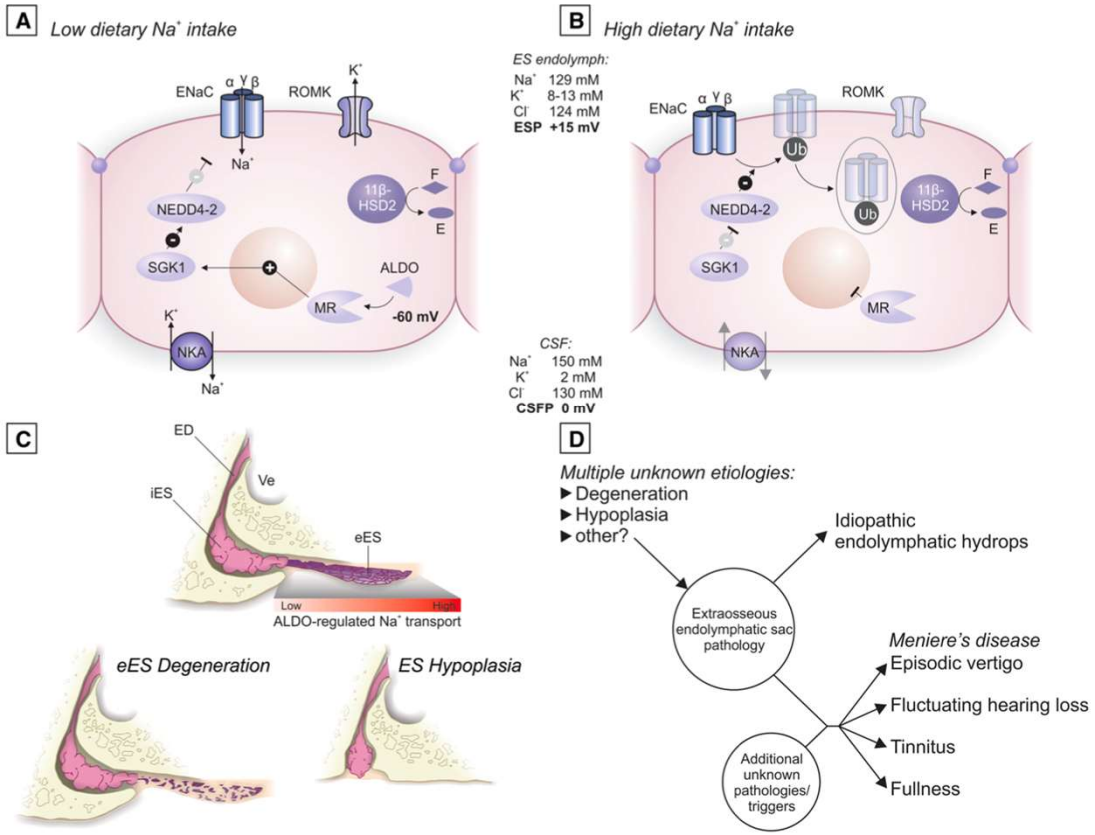

Acta Neuropathologica
https://doi.org/10.1007/s00401-018-1927-7

ORIGINAL PAPER

Inner ear pathologies impair sodium-regulated ion transport in Meniere's disease

Andreas H. Eckhard[1,8] · MengYu Zhu[1] · Jennifer T. O'Malley[1] · Gordon H. Williams[2] · Johannes Loffing[3] · Steven D. Rauch[1,5,6,7] · Joe B. Nadol Jr.[1,5] · M. Charles Liberman[4,5] · Joe C. Adams[1,5]

- we demonstrate mineralocorticoid-controlled sodium transport mechanisms in the epithelium of the **extraosseous portion of the endolymphatic sac (eES)** in the murine and human inner ears.
- Histological analysis of the eES revealed pathological changes (**hypoplasia or degeneration of epithelium in the eES in cases with iEH and a clinical history of MD**, but no such changes were found in cases with "secondary" EH due to other otological diseases or in healthy controls.



From the results of the present study, it can be concluded that ES surgical procedures for MD cannot work as hypothesized, since the eES epithelium in the dura of the posterior cranial fossa is either inaccessible due to ES hypoplasia or functionally compromised due to degenerative changes (present study). This finding is in line with the ambiguous clinical outcome that these procedures were shown to have with regard to control of acute MD symptoms

Meniere's Disease

- In the last decade, the use of specially processed cereals (SPC) has been proposed to increase endogenous antisecretory factor (AF) synthesis to improve symptoms of MD with controversial results.

13. Leong SC, Narayan S, Lesser TH (2013) Antisecretory factor-inducing therapy improves patient-reported functional levels in Meniere's disease. Ann Otol Rhinol Laryngol 122(10):619–624

12. Ingvardsen CJ, Klokker M (2016) Antisecretory therapy with no improvement in functional level in Meniere's disease. Acta Otolaryngol 136(3):232–235. https://doi.org/10.3109/00016489.2015.1115551

- AF is a 41 kDa protein, originally characterized as a pituitary substance, that acts as a regulator of water and ion transport across the cellular membrane.
- Immunohistochemical studies have demonstrated the presence of AF in the rat's inner ear and in the man's saccule; evidence showed that endogenous AF activity increases after exposure to bacterial toxins and can be also induced in humans and animals by a diet with SPC

European Archives of Oto-Rhino-Laryngology (2020) 277:77–83
https://doi.org/10.1007/s00405-019-05682-4

OTOLOGY

Food-induced stimulation of the antisecretory factor to improve symptoms in Meniere's disease: our results

Alfonso Scarpa[1] · Massimo Ralli[2] · Pasquale Viola[3] · Claudia Cassandro[4] · Matteo Alicandri-Ciufelli[5] · Maurizio Iengo[6] · Giuseppe Chiarella[3] · Marco de Vincentiis[2] · Michele Cavaliere[6] · Ettore Cassandro[1]

Conclusion Our study shows a reduced number of vertigo attacks and a positive effect on the discomfort generated by tinnitus and quality of life in patients with unilateral MD treated with SPC and when compared to patients treated with intravenous glycerol and dexamethasone. No effects on hearing thresholds were noted in both groups.

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DIURETICS IN MD

- In their comprehensive review of medical management of MD, Coelho et al. recommended diuretics as a second-tier treatment for persistent vertigo following the failure of life-style modifications such as low salt diet and abstaining from caffeine, tobacco, and alcohol.

- Given the episodic nature of MD with periods of recurrent symptoms followed by prolonged quiescence of disease, the authors recommended that cessation of diuretic therapy be considered after 3 months of treatment if vertigo subsides.

- Subsequently, a Cochrane Database review in 2006 and an update from 2009 reviewing the effect of diuretics treatment in MD found that there were no trials of high enough quality to meet the standard set for their systematic review.

Rosenbaum A, Winter M. Are diuretics effective for Meniere's disease? *Medwave* 2018;18:e7187.

- On other hand, the use of diuretics could be considered as relatively safe. We found moderate certainty of evidence to support that diuretic use was associated with minimal adverse effects.

DIURETICS IN MD

- **Diuretics represent the most commonly used first-line medical treatment for MD**.
- **The studies that support using diuretics have a low level of evidence.**
- The drug chosen differs from one author to another but, according to the literature, **hydrochlorothiazide** (*It should be avoided or used cautiously in patients with hypotension, renal disease, diabetes mellitus, and gout*), **acetazolamide** (*even in case of migraine association; causes cerebral vasodilation and carbonic anhydrase inhibition. Both of these mechanisms are thought to play an important role in migraine prophylaxis, Typical side effects include paresthesia and increased risk for kidney stones*) and **chlorthalidone** are used in decreasing order.
- We recommend their use that may decrease vertigo spell frequency (Grade C). A special attention must be payed to their respective contraindications and side-effects.
- **It is our view that until a definitive study can be performed, diuretic therapy provides, at a minimum, a safe and inexpensive opportunity for patients to exert control over the disease, thereby enhancing non-specific treatment effects.**

Betahistine

The most widely used drug for MD in Europe is betahistine, a histamine-like molecule that acts as a weak agonist for the H1 receptor and, at the same time, as an effective antagonist for the H3 receptor

- **Originally conceived as a vasodilator**
  - MD caused by vasospasm of stria vascolaris
- **Weak histamine H1 agonist and stronger H3 antagonist**
  - Both preclinical and clinical studies suggest a wide range of potential effects for Betahistine.
  - First, it modulates histaminergic neurotransmission by partially agonizing the activity of the histamine H1 receptor.
  - Betahistine has however more potent antagonistic properties at the histamine H3 receptor, inducing an increased histamine turnover and release.
  - Second, Betahistine has vascular effects both in the cochlea and in the brain.
  - Third, Betahistine has effects on neuronal excitability and spike generation of neurons in the lateral and medial vestibular nuclei. It has been recently demonstrated that histamine induces an excitatory modulation by depolarizing both spontaneous firing neurons and silent neurons in the rat inferior vestibular nucleus via the histamine H1 and H2 receptors.
  - It is possible that the Betahistine antivertigo activity is firstly achieved by Betahistine itself and then sustained by its metabolite aminoethyl-pyridine .
  - Finally, several studies and reviews indicate that the histamine H3 receptor plays a key role in vestibular compensation, behavioral recovery, and reduction of symptoms.

BETAHISTINE

Betahistine is administered orally in divided doses; the total daily dose usually lies between 24 and 48 mg. In the 12 studies the total daily dose varied between 24 mg (1 study), 32 mg (2 studies), 36 mg (1 study), 24–48 mg (1 study) and 48 mg (7 studies), thereby representing current clinical practice.

Eur Arch Otorhinolaryngol (2014) 271:887–897
DOI 10.1007/s00405-013-2596-8

REVIEW ARTICLE

Meta-analysis of clinical studies with betahistine in Ménière's disease and vestibular vertigo

Jozef J. P. Nauta

Publication/ report	Indication	Total daily dose betahistine (mg)	Treatment duration	No. of patients betahistine/ placebo	Design
Elia [42]	MD	16	14 days	10/10	Cross-over
Burkin [43]	MD	16	14 days	11/11	Cross-over
Canty [44]	VV	32	8 weeks	18/19	Cross-over
Kastein [32]	MD	36	12 weeks	26/24	Parallel group
Nury [47]	VV	48	12 weeks	20/19	Parallel group
Fischer [48]	VV	48	3 months	43/40	Parallel group
Ricci [50]	MD	24	10× mean duration of the interval between episodes	5/5	Parallel group
Legent [51]	MD	48	3 months	39/42	Parallel group
Conraux [53]	MD	24–48	3 months	36/34	Parallel group
Oosterveld [55]	MD or VV	48	5 weeks	38 +/44+	Cross-over
Maisonneuve [57]	VV	48	3 months	27/27	Parallel group
Salden [58]	VV	48	8 weeks	50/50	Parallel group
KirkPatrick [59]	MD or VV	48	30 days	119/117	Parallel group
Mira [61]	MD or VV	32	3 months	75/69	Parallel group

This meta-analisys supported also the therapeutic benefit of betahistine on vertiginous symptoms in both Meniere's disease and vestibular vertigo patients

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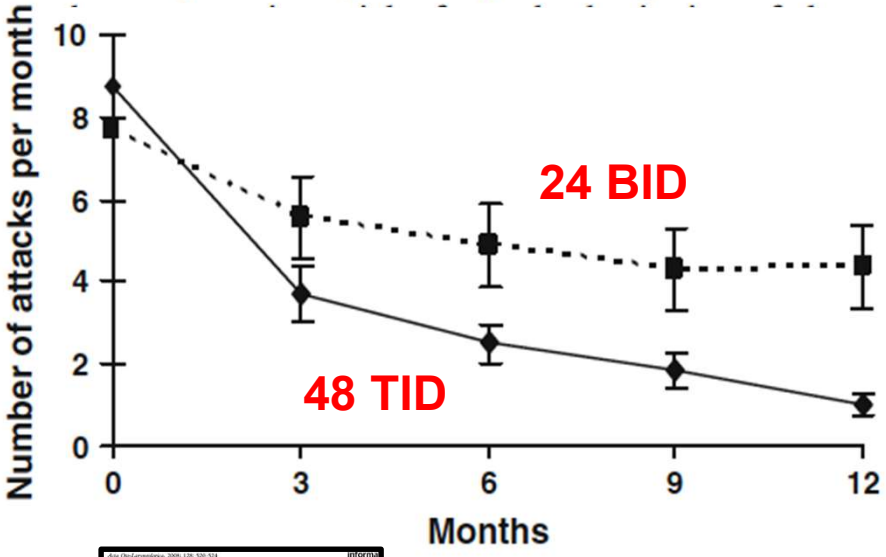
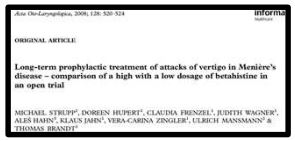
BETAHISTINE

- There have been remarkable studies about its efficacy on reducing the vertigo attacks with beneficial effects in MD
- Some studies report a dose dependent effect probably by increasing the blood flow in the stria vascularis
- The increase of inner ear blood flow reduces the increased endolymphatic pressure by achieving a balance in production and re-absorption of endolymph

The patients included in the study received either a low dosage of betahistine-dihydrochloride, i.e. 16 or 24 mg tid or a higher dosage of 48 mg tid. The full





ORIGINAL ARTICLE

Long-term prophylactic treatment of attacks of vertigo in Menière's disease – comparison of a high with a low dosage of betahistine in an open trial

Observation of treatment in 112 patients showed that high dosage of betahistine is significantly superior to 3 °— 24 mg/day, particularly with long-term administration (12 months)

within the inner ear [15–17]. It is conceivable that increased blood flow reduces the increased endolymphatic pressure in the inner ear by achieving a balance between production and re-absorption of endolymph. These studies also showed that the effect of betahistine was concentration-dependent: the higher the concentration, the higher the increase of inner ear blood flow. This correlates with the dose dependence found in our trial.

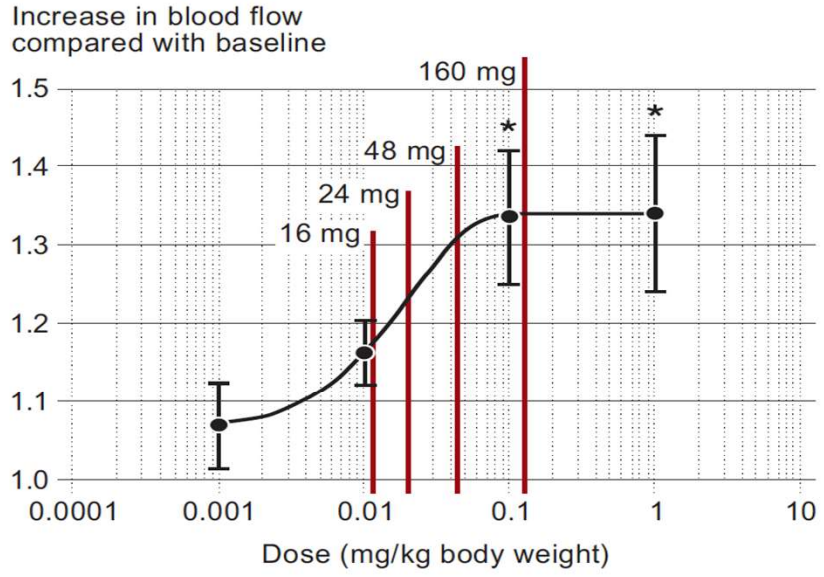
BETAHISTINE

- The increase of inner ear blood flow reduces the increased endolymphatic pressure by achieving a balance in production and re-absorption of endolymph

Recent animal experiments seem to indicate that the mechanism of action of betahistine and its metabolites is improved blood flow in the inner ear.

Aminoethylpyridine and hydroxyethylpyridine are, like betahistine, able to increase cochlear blood flow significantly. The effect of aminoethylpyridine was greatest. Pyridylacetic acid had no effect on cochlear microcirculation.

FIGURE 2



The relationship between cochlear blood flow and betahistine hydrochloride dosage in an animal experiment (non-linear regression curve; mean ± SD; * $p < 0.05$) and the calculated corresponding oral single doses (modified from [35]). The sigmoidal dose–effect curve correlates with the higher doses of up to 160 mg betahistine (red line) used clinically to prevent Menière's disease

CONSENSUS

sull'utilizzo della betaistina nella malattia di Ménière

Eur Arch Otorhinolaryngol (2011) 268:1237–1240
DOI 10.1007/s00405-011-1647-2

Franziska Lezius · Christine Adrion · Ulrich Mansmann · Klaus Jahn · Michael Strupp

SHORT COMMUNICATION

11 patients . All suffered from severe MD and had a high number of attacks per month. They had been treated with betahistine dihydrochloride in increasing dosages for more than 12 months, but had not responded sufficiently to the accepted high dosage of 48 mg tid, i.e., 144 mg per day. Therefore, approximately every 3 months the dosage was further increased.

In conclusion, very high-dosage and long-term treatment with betahistine dihydrochloride seems to be an effective treatment option for patients with severely progressing MD. It also has a good safety profile. However, further studies are needed for confirmation.

High-dosage betahistine dihydrochloride between 288 and 480 mg/day in patients with severe Menière's disease: a case series

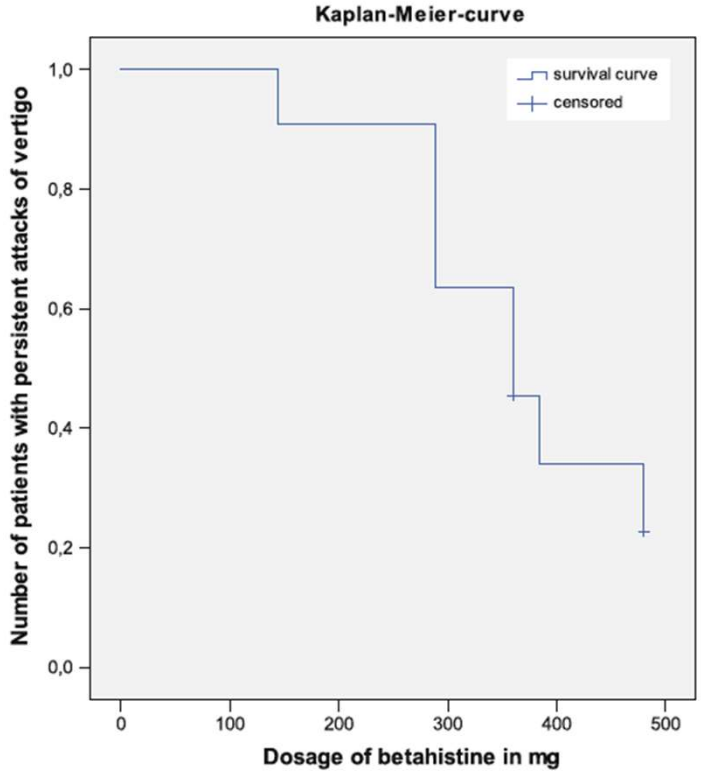


Fig. 1 Proportion of patients with persistent attacks of vertigo

BETAHISTINE

- **BEMED study (2016)**
  - The Authors reported that in a study of 221 patients in Germany, patients on placebo had **LESS** attacks/month than patients on either low dose betahistine (48 mg/day) or high dose betahistine (124 mg/day). This would argue that betahistine is ineffective for Meniere's disease. There were however some secondary measures such as attacks of rotatory or positional vertigo that improved slightly in the high-dose group. This would support the conjecture that betahistine is a placebo.

- **The Munich Experience (Strupp 2019)**
  - Given its rapid metabolism by intestinal and hepatic MAO-B enzyme, Betahistine could be used increasing progressively (on the basis of the beneficial effect) the dosage up to 480 mg/die in patients who do not respond to lower dosage, in the same way as the therapeutic approach in epilepsy using Tegretol

  - A combination of Betahistine with MAO-inhibitor (selegiline) reduced the dosage needed to avoid further attacks.


EXPERT OPINION ON PHARMACOTHERAPY
https://doi.org/10.1080/14656566.2019.1610386

Taylor & Francis

REVIEW

Advances in pharmacotherapy of vestibular and ocular motor disorders

Andreas Zwergal, Michael Strupp and Thomas Brandt

Department of Neurology, University Hospital LMU, Munich, Germany; German Center for Vertigo and Balance Disorders, DSGZ, LMU Munich, Munich, Germany; Clinical Neurosciences, LMU Munich, Munich, Germany

Thus, there is not sufficient evidence for any of the proposed treatments for the management of MD to be considered effective, and although several studies have been conducted, the results are inconclusive and inconsistent

- In order to define adequate **best practice criteria in MD therapy**, we started a rigorous and systematic analysis of the literature, identifying all the studies on betahistine in MD
- **The CC on betahistine in MD involved firstly a group of 78 Italian experts on vestibular disorders, who were asked a series of questions specifically prepared by 13 opinion leaders. A second CC involved a panel of 80 European experts from 10 different countries**
- To increase consensus, **the Delphi method** was used. The Delphi method is an iterative investigation method, which through several stages of evaluation aims to reach the most comprehensive opinion, shared in a single statement.
- This technique is used to obtain responses to a problem from a panel of independent experts in two or three rounds. After each round, an administrator provides a summary of the experts' answers and their rationale. The process ends when the experts' answers vary only slightly between rounds.

Research Article

Good Clinical Approach: Delphi Consensus for the Use of Betahistine in Menière's Disease

Augusto Pietro Casani,[1] Elena Navari,[1] Giorgio Guidetti,[2] and Michel Lacour[3]

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[2] *Vertigo Center PCM, Modena, Italy*
[3] *Université Aix-Marseille University/CNRS, UMR 7260, Fédération de Recherche 3C, Centre de St Charles, Marseille, France*

Correspondence should be addressed to Augusto Pietro Casani; a.casani@med.unipi.it

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Academic Editor: Leonard P. Rybak

Meniere's Disease

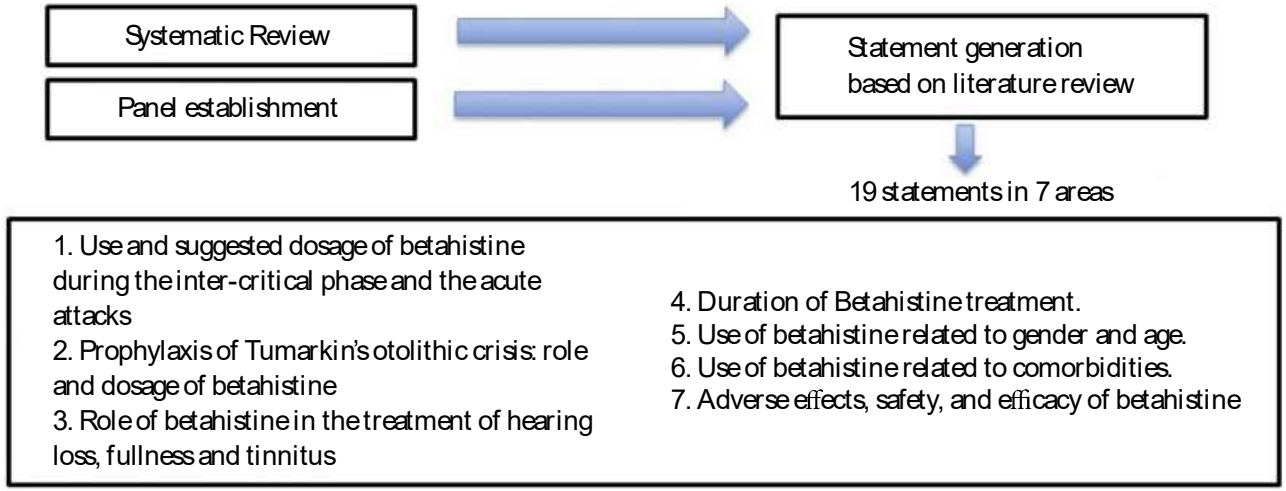


Figure 1: Process used to select and achieve consensus for statements about betahistine in Menière's Disease.

Table 1: Results of the Consensus Conference on the use and dosage of betahistine during the intercritical phase of MD. 1 = absolutely disagree, 2 = disagree, 3 = agree, 4 = more than agree, and 5 = absolutely agree. Consensus was reached when the sum of items 1 and 2 or 3, 4, and 5 reached 66%. Asterisk explanations: □ ***Negative consensus***, □□ ***No consensus***, and □□□ ***Positive consensus***.

	1	2	3	4	5
In the inter-critical phase therapy, referred to the vertigo in the Menière's disease, do you think that betahistine:					
1. Is useful	8%	5%	41%	23%	23%
	13%			**87%** □□□	
2. Is useful only when associated to other therapies	8%	66%	12%	12%	2%
	74% □			**26%**	
3. It's the first-choice drug	3%	26%	19%	26%	26%
	29%			**71%** □□□	
4. Shows poor efficacy	49%	45%	2%	4%	0%

19. In order to evaluate betahistine efficacy, I use:

The last statement analysed was ***"In order to evaluate Betahistine efficacy, I use:"***; Herman Kingma presented some slides on the available tools for efficacy evaluation, highlighting the importance of safety and effectiveness and the related issues of the lack of evidence, of the fragmentation of registries and of the underrepresentation of different study groups. The following discussion and new vote showed these results:

	1 strongly disagree	2 disagree	3 agree	4 more than agree	5 strongly agree
Number, intensity and duration of attacks in the last 6 months	0%		100%		
Auditive symptoms	55%		45%		
Audiometric tests	60%		40%		
Laboratory vestibular examinations	48%		52%		
Bed-side vestibular examinations	24%		76%		
Questionnaires for tinnitus	74%		26%		
Questionnaires on QoL	13%		87%		
Psychometric Questionnaires	55%		45%		
Other	72%		28%		

Meniere's Disease

If you use Betahistine for prophylaxis what is the dosage that you use:					
1. I do not use	45%	36%	6%	3%	10%
	81%			**19%**	
2. I use in the range from 8 to 32 mg/day	21%	64%	9%	3%	3%
	85%			**15%**	
3. I use in the range from 32 to 48 mg/day	3%	0%	41%	29%	17%
	3%			**97%**	
4. I use higher than 48 mg/day	4%	31%	50%	6%	9%
	35%			**65%**	
5. Vary in the course of time	3%	19%	54%	8%	16%
	22%			**78%**	
For how long do you think it is useful to extend treatment in case of more than 10 attacks in the last six months:					
53. At least 3 months	9%	25%	40%	5%	21%
	34%			**66%**	
54. At least 6 months	0%	11%	50%	25%	14%
	11%			**89%**	
55. At least 6 months, extendable to 1 year depending on the patient's condition	5%	5%	50%	7%	33%
	10%			**90%**	
56. More than one year	0%	38%	44%	11%	7%
	38%			**62%**	

In case of comorbid migraine:

	EUROPE					ITALY				
	1	2	3	4	5	1	2	3	4	5
61. I do not use betahistine	*6*	*12*	*9*	*2*	*1*	*9*	*21*	*7*	*1*	*2*
	60%		**40%**			**75%**		**25%**		
62. I use an association of betahistine plus an anti-migraine drug	*0*	*7*	*13*	*4*	*6*	*1*	*2*	*20*	*10*	*7*
	23%		**77%**			**8%**		**93%**		
63. I use only betahistine	*9*	*19*	*2*	*0*	*0*	*9*	*27*	*4*	*0*	*0*
	93%		**7%**			**90%**		**10%**		

In case of comorbid anxiety and/or depression:

	EUROPE					ITALY				
	1	2	3	4	5	1	2	3	4	5
64. I do not use betahistine	*11*	*7*	*2*	*0*	*0*	*12*	*19*	*4*	*3*	*2*
	90%		**10%**			**78%**		**23%**		
65. I use an association of betahistine plus an anxiolytic and/or antidepressant drug	*1*	*1*	*13*	*7*	*8*	*2*	*11*	*21*	*9*	*7*
	7%		**93%**			**26%**		**74%**		
66. I use only betahistine	*11*	*13*	*4*	*1*	*1*	*15*	*22*	*3*	*0*	*0*
	80%		**20%**			**93%**		**8%**		

17. You think that the adverse effects of betahistine are:

	1 strongly disagree	2 disagree	3 agree	4 more than agree	5 strongly agree
Less than 10%	9%		91%		
From 10 to 20%	86%		14%		
More than 20%	96%		4%		

Gastric disorders	10%	90%

Conclusion

European Vertigo Consensus Conference

Following the results of the European Vertigo Delphi Questionnaire and the discussion during the Rome Consensus Conference, the participants reached the following results:

99%

Betahistine is the **first choice drug** in the intercritical phase therapy for the vertigo in the Meniere's disease (99%)

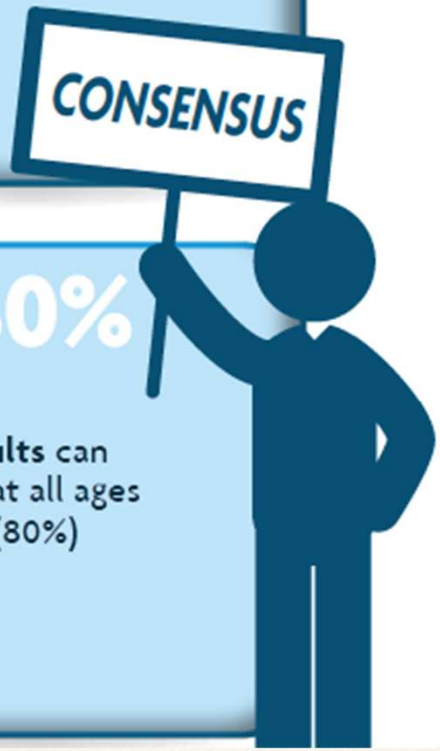
76%

Betahistine have a **positive effect** in the treatment of auditive symptoms in the initial phase of the disease (76%)

74%

Dosage of Betahistine in prophylaxis should range from 32 to 48 mg/day (74%) or it can vary in the course of time (76%)

76%



96%

In case of **1-3 attacks** in the last six months, treatment with betahistine can last up to 3 months (88%) and it can be extended to six months depending on the patient's condition (96%)

88%

79%

Treatment with Betahistine should be at least of 6 months extendable to 1 year depending on the patient's condition in case of 4-10 attacks in the last six months (79%) or in case of more than 10 attacks (90%)

90%

80%

The **best results** can be obtained at all ages indifferently (80%)

86%

In case of **comorbidity**, Betahistine is used in association with an anti-migraine drug (86%) in case of migraine and in association with an anxiolytic and/or antidepressant drug (93%) in case of anxiety and/or depression

93%

91%

Adverse effects of Betahistine are less than 10% (91%); more common side-effects are gastric disorders (90%)

90%

100%

Number, **intensity and duration** of attacks, bed-side vestibular examinations, questionnaire on QoL are the best way to evaluate betahistine efficacy (100%)

The parameters for a Good Clinical Research to evaluate Betahistine's efficacy are:

- Number of attacks for 6 months (100% of positive consensus)
- Intensity or severity of attacks (Vertigo score) (98%)
- Quality of life questionnaires (96%)
- Frequency of attacks (1 year)(95%)
- Questionnaire DHI (93%)
- Intensity of attacks in last 6 months (79%)
- Questionnaire on social impact of Meniere disease (79%)
- Days of work / number of days being disabled (76%)

- **The consensus of experts consulted on betahistine, in light of their clinical practice and daily management of patients with MD, shows a constant use of the drug during the intercritical phase, especially in monotherapy.**

- **Betahistine is considered to be safe, suitable for all age groups, and associated with a low incidence of side effects (mainly gastrointestinal symptoms).**

- **These statements, based exclusively on the clinical experience of the participants to the consensus conference, seems to be confirmed by a very recent Cochrane review suggesting a positive effects of betahistine in reducing vertigo symptoms without any significant side effects**

Cochrane Library

Cochrane Database of Systematic Reviews

Conclusion

Low quality evidence suggests that patients suffering from vertigo from different causes may have some benefit from betahistine in terms of reduction in vertigo symptoms. Betahistine is generally well tolerated. Future research into the management of vertigo symptoms needs to use more rigorous methodology and include outcomes that matter to patients and their families.

Murdin L, Hussain K, Schilder AGM.
Betahistine for symptoms of vertigo.
Cochrane Database of Systematic Reviews 2016, Issue 6. Art. No.: CD010696.
DOI: 10.1002/14651858.CD010696.pub2.

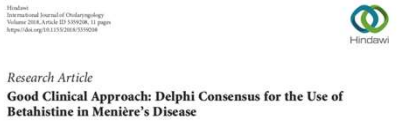
Betahistine for symptoms of vertigo (Review)

Murdin L, Hussain K, Schilder AGM

THE EXPERTS' CLINICAL PRACTICE AND PERSONAL EXPERIENCE WITH PATIENTS SUPPORT THE USE OF BETAHISTINE FOR MD TO REDUCE THE NUMBER AND SEVERITY OF VERTIGINOUS CRISES, PARTICULARLY DURING THE INTERCRITICAL PHASE OF THE DISEASE. BETAHISTINE DO NOT SHOW POSITIVE EFFECTS ON AUDITORY SYMPTOMS OF MD, BUT ITS USE SEEMS TO BE AT LOW RISK OF MAJOR SIDE EFFECTS. HOWEVER CLINICAL STUDIES BASED ON RIGOROUS METHODOLOGIES AND OUTCOME MEASURES ARE NEEDED TO CLEARLY EVALUATE THE ROLE OF BETAHISTINE IN THE TREATMENT OF MD.

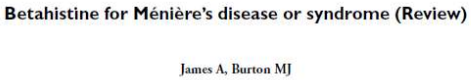
BETAHISTINE

- **European Consensus 2018**
  - According with the clinical experience this study supported betahistine's prescription for MD to reduce the number and severity of dizziness crises, particularly during the intercritical phase of the disease.


Research Article

Good Clinical Approach: Delphi Consensus for the Use of Betahistine in Menière's Disease

- **Cochrane Review**
  - Insufficient evidence to say if Betahistine has any effect on MD (2001)
  - Positive effect on reducing the symptoms with good tolerance even if larger studies with higher quality evidence are needed


Betahistine for Ménière's disease or syndrome (Review)

James A, Burton MJ

Despite the conflicting evidence Betahistine is very popular in Europe and Japan and has become the most used treatment for MD, in combination with diuretics and life-style changes as first-line treatment

THE COCHRANE COLLABORATION®

AUGUSTO PIETRO CASANI

DIPARTIMENTO DI PATOLOGIA MEDICA, CHIRURGICA, MOLECOLARE E AREA CRITICA

UNIVERSITÀ DEGLI STUDI DI PISA

Medical Treatment in MD

ACTA OTORHINOLARYNGOLOGICA ITALICA 2014;34:349-353

VESTIBOLOGY

Association of cinnarizine and betahistine in prophylactic therapy for Ménière's disease with and without migraine

L'associazione di betaistina e cinnarizina nella profilassi degli episodi vertiginosi nella Sindrome di Ménière con e senza comorbidità emicranica

R. TEGGI[1], O. GATTI[1], V. SYKOPETRITES[1], S. QUAGLIERI[2], M. BENAZZO[2], M. BUSSI[1]

[1] Division of ENT, San Raffaele Scientific Institute, Milan, Italy; [2] Division of ENT, IRCCS Policlinico San Matteo Foundation, University of Pavia, Italy

- **MIGRAINE**
  - Several studies have shown an higher incidence of migraine in MD patients compared to the normal population
  - Besides avoidance of common migraine triggers and use of dietary supplements (magnesium, riboflavin) a migraine prophylaxis is recommended

Table I. Number of vertigo spells, headaches and PTA average (db HL) in 6 months of monotherapy and 6 months of combined therapy in the sample of MD patients with migraine (n = 29).

	Betahistine	Betahistine + cinnarizine	P value
Vertigo spells	9.4 ± 4.3	3.8 ± 3.4	p = 0.0001
Headaches	3 ± 1.9	1 ± 0.6	p = 0.0001
PTA mean value	45.7 ± 8	53.4 ± 7.8	p = 0.001

The use of steroids is based on the autoimmune and/or allergic hypothesis of MD

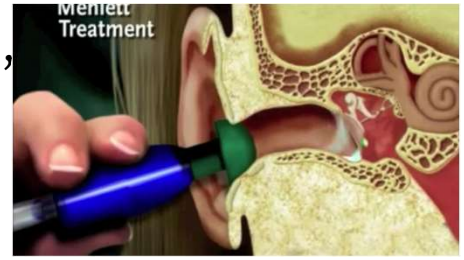
✓ Mechanism of action based on anti-inflammatory effect but probably aldo because of a positive effect on fluid homeostasis (receptors for steroid are present in inner ear)

✓ Diuretic + prednisone (0.35 mg/Kg/day x 18 weeks) better results than diuretic only in vertigo control (Morales, 2005)

✓ **Use of oral steroids is based on expert opinion as no clinical trials have been performed.**

Pressure Treatment in MD

- **VENTILATION TUBE**
  - Reduces the fluctuation in ME pressure that could produce EH; helpful to alleviate the symptom of aural pressure
- **MENIETT**
  - produces sequences of micro-pressure hypopressive pulses susceptible to act on the endolymphatic hydrops stimulating the longitudinal flow of endolymph
  - 3 applications/die for 5 min by V-T
  - Reduces the frequency of vertigo attacks (Thomsen 2005, Donhoffer e King 2008, f-up 4 ys)
  - Seems to stabilize the hearing loss (Barbara 2010)
  - **A recent Cochrane review concludes there is no evidence this therapy is effective**



- **Hyperbaric Oxygen Therapy**
  - Increase O2 in inner ear
  - Stimulates the longitudinal flow of endolymph
  - Improves microcirculation of inner ear

Original Article

Audiology 1996; 35:322–334

B. Fattori, G. De Iaco*, G. Vannucci, A. Casani, P. L. Ghilardi

E.N.T. Clinic University of Pisa, Italy
*Department of Hyperbaric Medicine, University of Pisa, Italy

Alternobaric and Hyperbaric Oxygen Therapy in the Immediate and Long-term Treatment of Menière's Disease

Medical Treatment in MD

SPI-1005 is an investigational drug that contains ebselen, a small molecule that is a new chemical entity, or NCE, under FDA classification. Ebselen is a selenorganic compound that mimics and induces glutathione peroxidase (GPx) activity and represents a novel class of anti-inflammatory. GPx activity is critical to several cell types and tissues in the inner ear, retina, brain, lung and kidney, and is often reduced during exposures to environmental insults. Loss of GPx activity has been shown to result in sensorineural hearing loss in multiple animal models. SPI-1005 is given orally and is being tested in several neurotologic indications including noise induced hearing loss and two types of ototoxicity (hearing loss, tinnitus, dizziness or vertigo): due to aminoglycoside antibiotics (such as tobramycin) and due to platinum-based chemotherapy.

anti-inflammatory and anti-neoplastic agent, SPI-1005 (**EBSELEN**).

Clinical evidence showed a marked reduction in hearing impairment in 55% of patients.

ebselen is thought to increase blood flow into the vestibulocochlear nerve, which causes a reduction in endolymphatic pressure, relieving the symptoms of MD.

By mimicking the actions of glutathione peroxidases, ebselen functions as a reducing agent that protects ophthalmic and otological structures from oxidative damage.

Dysregulation of the oxidative stress response is a hallmark of MD pathology.

Polymorphisms in genes such as glutathione peroxidase 1 (GPX1), paraoxonase 1 (PON1), and superoxide dismutase (SOD2) have been detected in people with a significantly heightened risk of developing MD and sudden sensorineural hearing loss.

An organoselenium compound, ebselen has additional classification as an anti-depressant and is also being investigated for efficacy in the treatment of bipolar disorder and reperfusion injury.

Diet and Medical Treatment in MD

The modern conception of Meniere's disease is that of unstable hearing and balance arising from a failure of inner ear homeostasis in a damaged or degenerating inner ear.
The actual causative process may no longer be in evidence, so treatments are palliative, seeking to pamper the **fragile inner ear** to minimize vestibular symptoms

Clinical Hints and Precipitating Factors in Patients Suffering from Meniere's Disease

Steven D. Rauch, MD

Treatments for Meniere's disease are very effective for management of vertigo. Diet and lifestyle measures achieve vertigo control in up to two-thirds of patients. Diuretic therapy helps achieve vertigo control in approximately two-thirds of those who fail the diet and lifestyle treatments. Only a small group of patients, 5% to 10% of the total, who continue to have intractable vertigo require invasive therapy.

Augusto Pietro Casani

Dipartimento di Patologia Medica, Chirurgica, Molecolare e Area Critica
Università degli Studi di Pisa

Ménière's Disease: Intratympanic Therapy

Meniérè's Disease

managed with medical theraphy in 2/3 of the cases

→ **Failure**

↓

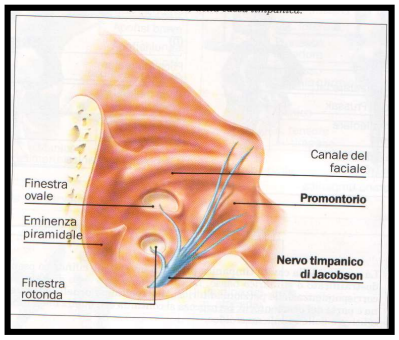
Surgical-Ablative approach

INTRATYMPANIC THERAPIES

→ **Aminoglycosides**

- **High Dose to Inner Ear**
- **Avoid SystemicToxicities**

- **Issue**
  - Permeability of RW
    - Anatomical Variations
    - Molecular Weight Substance
  - Distribution in Inner Ear
    - > in basal turn
  - Site of Lesion
    - > access in perilymph



- **Streptomycin**
  - **Schucknect 1957**
- **Gentamicin**
  - **Beck 1978;**
  - **Odkvist 1988;**
  - **Lange 1989**
  - **Nedzelsky 1992**
  - **Long Term Follow-up**
    - **Atlas & Parnes 2003**
    - **Harner et al 2001**
    - **Bodmer at al 2007**

Ménière's Disease: Intratympanic Therapy

- Dosing Regimen
  - Continuous Delivery
  - Multiple Daily Dosing
  - Weekly Dosing
  - Titration
  - Low- Dose

- Tendency to ↓ Dose e N° Injections
  - Cochlear damage is dose-related
  - No Complete ablation necessary
  - Low Dose Protocol
    - Good effectiveness
    - Lower risk (Hearing Loss, Residual Dizziness)

Intratympanic Gentamicin for Menière's Disease: a Meta-Analysis

Raanan Cohen-Kerem MD[1,2,*], Vitaly Kisilevsky MD[3], Thomas R. Einarson PhD[4], Eran Kozer MD[2], Gideon Koren MD[2], John A. Rutka MD, FRCSC[3]

Article first published online: 3 JAN 2009

DOI: 10.1097/01.mlg.0000149439.43478.24

Issue

The Laryngoscope

Volume 114, Issue 12, pages 2085–2091, December 2004

- 627 pts 15 paper
  - 93% Complete or Substantial Vertigo Control
  - No significant difference between various methods
  - > Vertigo Control when ablation is complete

Ménière's Disease: INTRATYMPANIC THERAPY

- 980 pts 27 paper
  - Complete Vertigo Control in 70-89%
  - Complete and Substantial Vertigo Control in > 90% pts
  - Titration offers > Vertigo Control
  - Low Dose < Vertigo Control

Otol Neurotol. 2004 Jul;25(4):544-52.

Intratympanic gentamicin therapy for Ménière's disease: a meta-analysis.

Chia SH, Gamst AC, Anderson JP, Harris JP.
Division of Otolaryngology, Head and Neck Surgery, Department of Surgery, School of Medicine, University of California at San Diego, USA.

	Class A %	Class A-B %	Hearing Loss ↑ %
Overall	76	90	25
Titration	81	96	24
Low Dose	67	87	24
Multiple Daily	76	91	35
Weekly	75	89	13
Continuous	71	89	24

MÉNIÈRE'S DISEASE: INTRATYMPANIC THERAPY

INTRATYMPANIC STEROIDS

Dexamethasone

Metilprednisolone

- I. T. > drugs levels than systemic delivery
- Anti-Inflammatory Effects
- Affect inner ear ion and fluid homeostasis
- Controls of aquaporin channel
- Ameliorate autoregolation of cochlear blood flow

PREVIOUS EXPERIENCES

- **POSITIVE**
  - Ito & Sakata, 1991
  - Shea & Ge, 1996
  - Sennaroglu et al 2001
  - Garduno et al 2005
  - Boleas-Aguirre et al 2008
  - Herraiz et al 2009
  - Beyea et al 2017
- **NEGATIVE**
  - Silverstein et al 1998
  - Barrs et al 2001
  - Barrs 2004
  - Hirvonen et al 2000
  - Dodson et al 2000
  - Lavigne te al 2016

Ménière's Disease: Intratympanic Therapy

- IT-Gentamicin
  - Control of vertigo attacks in > 90% pts
    - Low-dose 87% Titration 96%
  - Hearing Outcome
    - Low Dose 21% weekly dose 13.1%

Original Research—Otology and Neurotology

Intratympanic Treatment of Intractable Unilateral Ménière Disease: Gentamicin or Dexamethasone? A Randomized Controlled Trial

Augusto Pietro Casani, MD[1], Paolo Piaggi, MS[2], Niccolò Cerchiai, MD[1], Veronica Seccia, MD[1], Stefano Sellari Franceschini, MD[1], and Iacopo Dallan, MD[1]

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

Otolaryngology–Head and Neck Surgery 146(3) 430–437 © American Academy of Otolaryngology—Head and Neck Surgery Foundation 2012 Reprints and permission: sagepub.com/journalsPermissions.nav DOI: 10.1177/0194599811429432 http://otojournal.org

SAGE

  - Our Experience with Low-Dose Tecnique
    - Class A-B achieved in 93.5% pts
    - Hearing Loss in 12.5% pts
    - Post treatment disequilibrium in 10% (disappeared max in 1 month)
    - Increasing the interval between the dose ↓ risks of Hearing Loss
      - Salt et al 2008
      - Zhai et al 2010
    - Low Dose affect secretory dark cells ↓ endolymph overpressure

MÉNIÈRE'S DISEASE: INTRATYMPANIC THERAPY

- IT-Dexamethasone
  - Results in contrast with Favourable Outcomes of some reports
  - Vertigo Attacks
    - Class A-B achieved only in 70% pts (Natural history of MD)
  - Hearing Outcome
    - Preservation only in pts reporting Class A-B
    - No positive impact on MD with any changes in natural history
  - Dexamethasone vs Methylprednisolone (*burning sensation*)
    - Greater tolerability
    - Pharmacokinetics features
  - Poor Response due to
    - Low dosage (4 mg/ml)
    - No continous drug application
      - Pump system
      - Sustained delivery system
      - Phase 3 study ongoing with OTO-104

OTO-104 is a suspension of dexamethasone in buffered solution containing a glycol polymer, poloxamer 407. This thermoreversible poloxamer is a liquid vehicle that allows for injection into the middle ear and subsequently gels at body temperature, giving sustained delivery of glucocorticoid to the inner ear.

Ménière's Disease: Intratympanic Therapy

IT-Steroids

- Contra
  - Poor Vertigo Control
    - % similar to placebo
  - Dosing regimen should include multiple injections repeated at times of recurrence

- PROS
  - Pts who refuse ablative treatment
  - Bilateral MD
  - Autoimmune MD (?)
  - Well tolerated
  - Low Complications rates
    - Eardrum perforation
    - Otitis media

Intratympanic methylprednisolone versus gentamicin in patients with unilateral Ménière's disease: a randomised, double-blind, comparative effectiveness trial

www.thelancet.com Vol 388 December 3, 2016

Mitesh Patel, Kiran Agarwal*, Qadeer Arshad, Mohamed Hariri, Peter Rea, Barry M Seemungal, John F Golding, Jonny P Harcourt, Adolfo M Bronstein*

The study showed no significant difference between the methylprednisolone (two dose two weeks apart) and gentamicin for the control of vertigo, total number of injections, number of patients with relapsing vertigo or for the amount of pain from injection but better speech discrimination after methylprednisolone.

Ménière's Disease: INTRATYMPANIC THERAPY

What is the efficacy of gentamicin on the incidence of vertigo attacks and hearing in patients with Meniere's disease compared with steroids? A meta-analysis

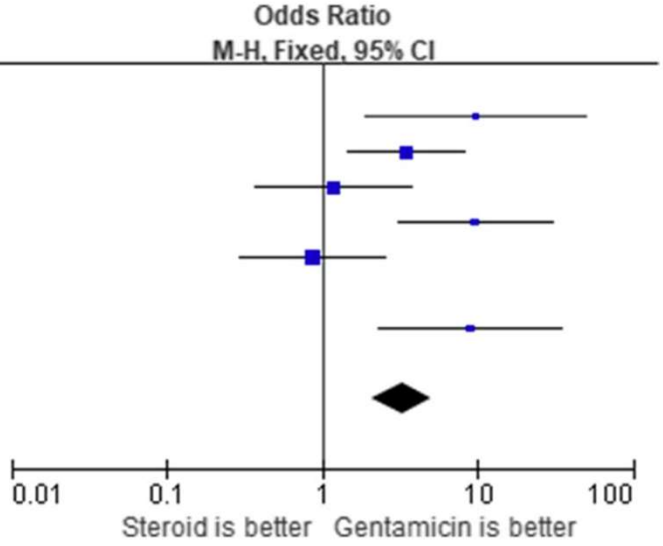
Minlin Jiang[1,2] · Zimu Zhang[1,2] · Chuanliang Zhao[2]

Received: 16 May 2020 / Revised: 17 June 2020 / Accepted: 18 June 2020

	Gentamicin		Steroid			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Akkuzu,B. 2016	22	24	6	9	0.0%	5.50 [0.74, 40.80]
Casani, A.P. 2012	30	32	17	28	5.0%	9.71 [1.92, 49.04]
Gabra, N. 2013	33	47	17	42	23.6%	3.47 [1.44, 8.34]
Guo, X. D. 2016	22	29	24	33	23.9%	1.18 [0.38, 3.70]
Naples, J. G. 2019	65	70	19	33	8.1%	9.58 [3.06, 30.01]
Patel, M. 2016	19	30	20	30	32.3%	0.86 [0.30, 2.50]
Sennaroglu,L. 2001	12	16	17	24	0.0%	1.24 [0.29, 5.18]
Wang, Q. L. 2017	32	35	19	35	7.2%	8.98 [2.31, 34.91]
Total (95% CI)		**243**		**201**	**100.0%**	**3.28 [2.12, 5.09]**
Total events	201		116			

Heterogeneity: Chi² = 16.38, df = 5 (P = 0.006); I² = 69%

Test for overall effect: Z = 5.31 (P < 0.00001)



Conclusions ITG is superior to ITS in reducing the number of vertigo attacks in the treatment of MD ($P < 0.01$); the impact on hearing is more heterogeneous in the studies. Overall, there was no clear difference between ITG and ITS on hearing improvement and on hearing loss.

MÉNIÈRE'S DISEASE: INTRATYMPANIC THERAPY

Journal of Neurology
https://doi.org/10.1007/s00415-020-10320-9

REVIEW

Effects of intratympanic gentamicin and intratympanic glucocorticoids in Ménière's disease: a network meta-analysis

Weiming Hao[1,3] · Huiqian Yu[1,3] · Huawei Li[1,2,3,4]

Received: 11 September 2020 / Revised: 8 November 2020 / Accepted: 15 November 2020

Intratympanic gentamicin and glucocorticoids both showed beneficial effects compared with placebo treatment in vertigo management of Ménière's disease. Intratympanic glucocorticoids therapy was associated with significantly less risk of hearing loss than gentamicin.

Ménière's Disease: INTRATYMPANIC THERAPY

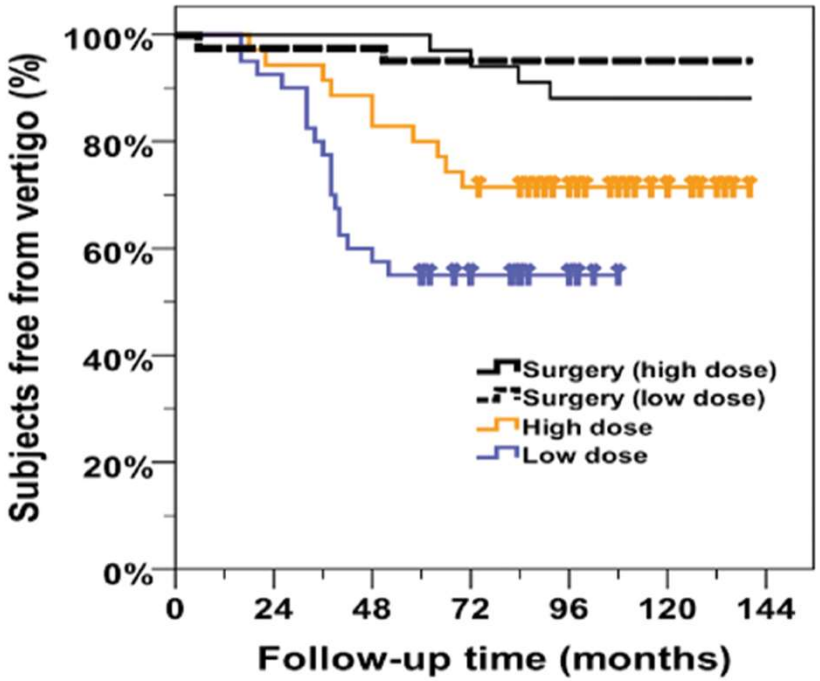


Figure 5. Kaplan-Meier curves for patients in the 2 groups (high and low dose) in relation to the time when they remained free from vertigo. The time of event was the date of visit where the patient underwent an additional round of intratympanic gentamicin treatment (for patients who needed a further treatment cycle). In the lowermost curves every "step" indicates the need for an additional round of treatment. The uppermost curves indicate survival for the 2 groups of patients (failure means the need for destructive surgery). Censored values (Y) indicate the last known visit for patients free from vertigo.

Original Research—Otology and Neurotology

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

Otolaryngology–Head and Neck Surgery
2014, Vol. 150(5) 847–852

DOI: 10.1177/0194599813520398
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Intratympanic Gentamicin for Ménière's Disease: Short- and Long-term Follow-up of Two Regimens of Treatment

Augusto P. Casani, MD[1], Niccolò Cerchiai, MD[1], Elena Navari, MD[1], Iacopo Dallan, MD[1], Paolo Piaggi, PhD[2], and Stefano Sellari-Franceschini, MD[1]

MÉNIÈRE'S DISEASE: INTRATYMPANIC THERAPY

Original Research—Otology and Neurotology

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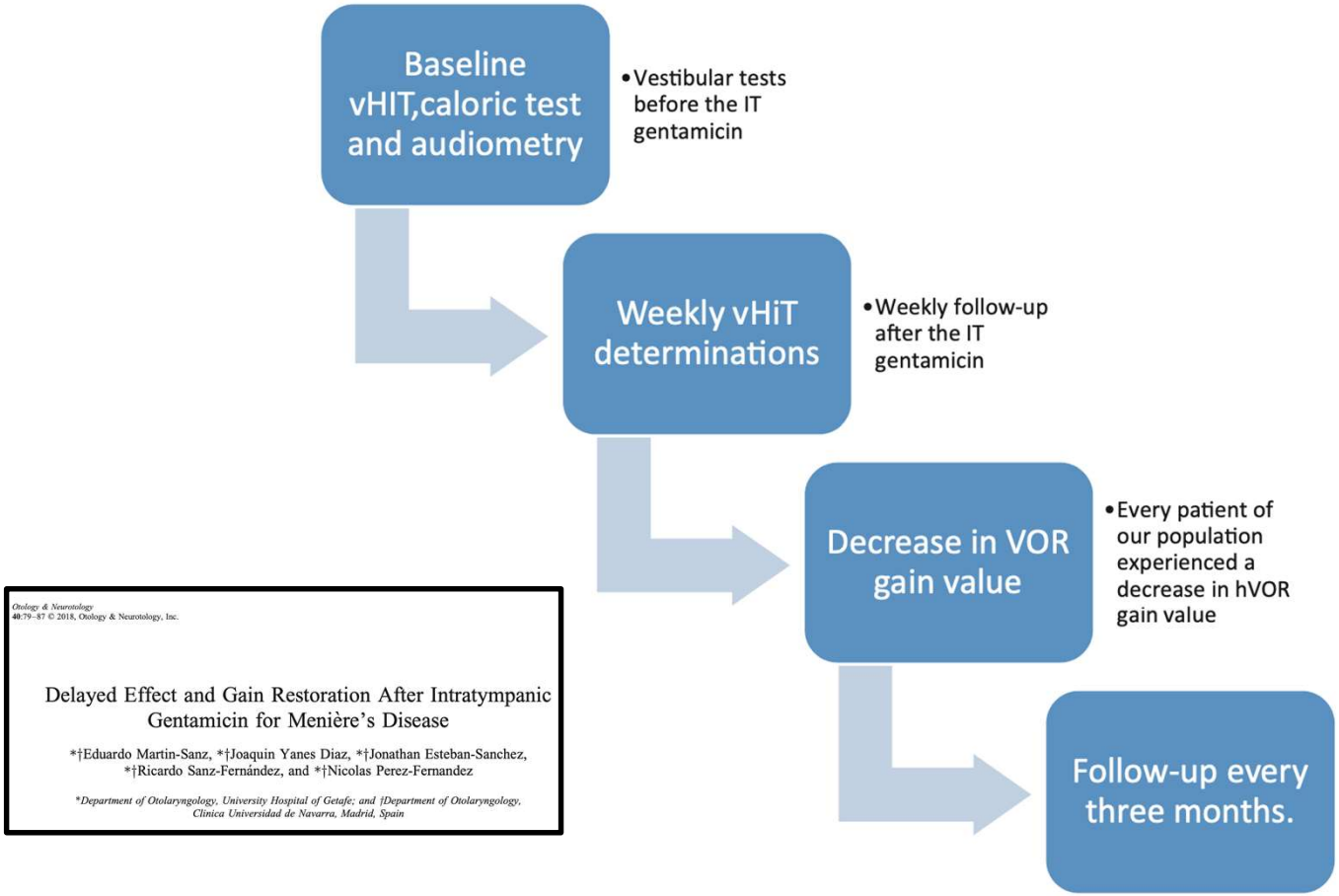
Augusto P. Casani, MD[1], Niccolò Cerchiai, MD[1], Elena Navari, MD[1], Iacopo Dallan, MD[1], Paolo Piaggi, PhD[2], and Stefano Sellari-Franceschini, MD[1]

CONCLUSIONS

- LD-ITG represents a good method of treatment of unilateral refractory MD, combining a low rate of side effects with an excellent capacity to provide a vertigo control
- The long-term follow-up showed that LD-ITG needed more frequently than the high dose protocol of repeated rounds of injections
- Patients treated with HD-ITG has less chance to need repeated rounds, but the efficacy of the retreatment seems to be not so high, requiring in almost 40% of the cases the need of more aggressive ablative surgical therapy.

- **All this lead to indicate that low dose ITG has to be proposed as "on demand" protocol, informing the patient about the possibility of repeated round of treatment until to achieve a complete vertigo control**
- Importantly, carriers of a mutation in the mitochondrial gene MTRNR1 develop complete deafness even after single injection of aminoglycoside and so patients need appropriate patient screening before the injection.

Ménière's Disease: INTRATYMPANIC THERAPY



Otology & Neurotology
40:79–87 © 2018, Otology & Neurotology, Inc.

Delayed Effect and Gain Restoration After Intratympanic Gentamicin for Menière's Disease

*†Eduardo Martin-Sanz, *†Joaquin Yanes Diaz, *†Jonathan Esteban-Sanchez, *†Ricardo Sanz-Fernández, and *†Nicolas Perez-Fernandez

*Department of Otolaryngology, University Hospital of Getafe; and †Department of Otolaryngology, Clinica Universidad de Navarra, Madrid, Spain

FIG. 1. Flowchart of our protocol; hVOR indicates horizontal VOR; IT, intraympanic; vHIT, video Head Impulse Test. Audiometry and vHIT tests were performed at each follow-up assessment in addition to a neuro-otologic examination.

Ménière's Disease: INTRATYMPANIC THERAPY

- Based on controlled trials, the best evidence for positive effects on the frequency of attacks is available for the intratympanic instillation of gentamicin.
- Another advantage of ITG is that small doses can result in a partial vestibular ablation, which reduces the severity of vertigo enough for the patient to be able to await the «burn out stage» without causing a significant disturbance of the balance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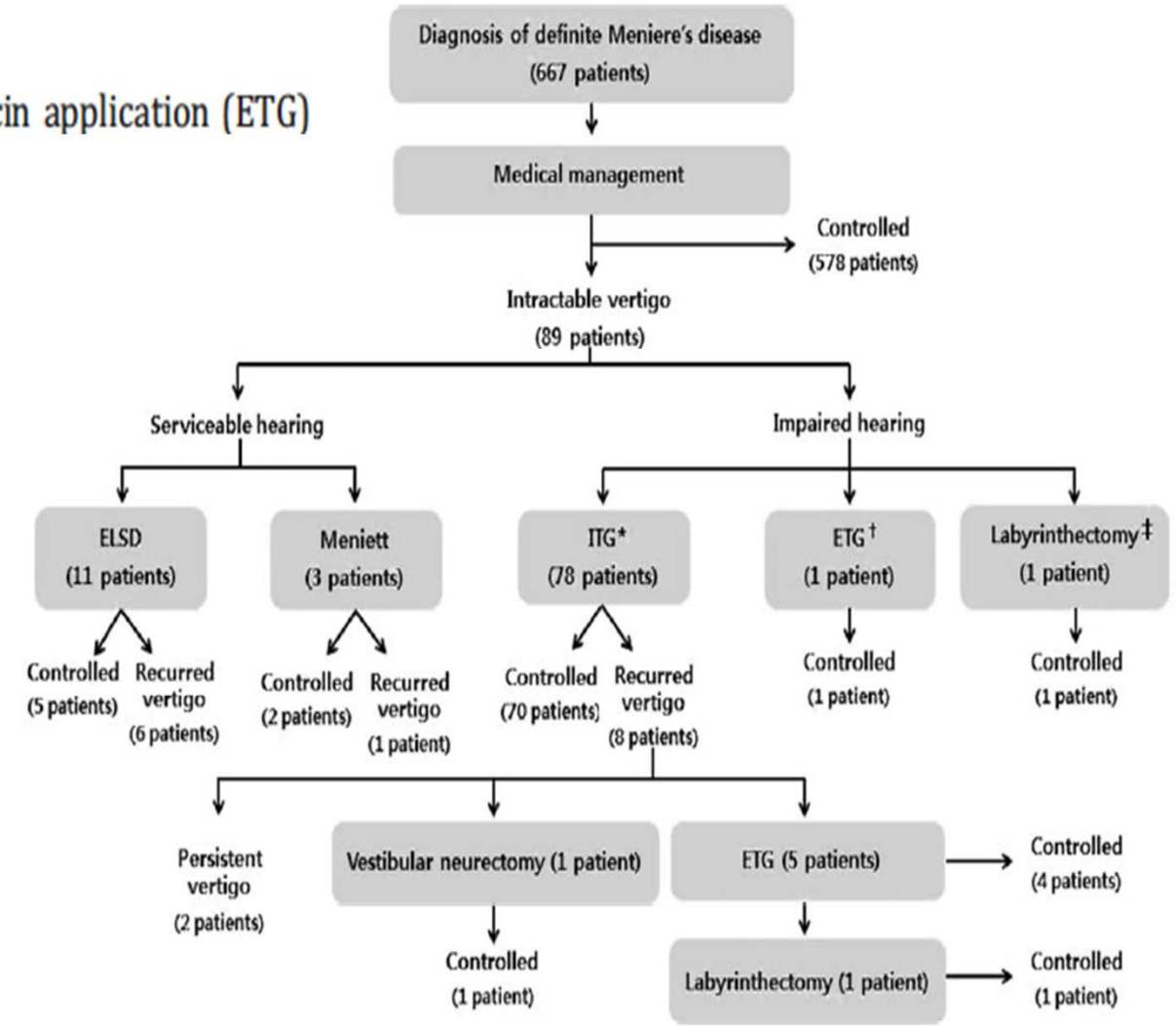
The Laryngoscope

Management of Intractable Ménière's Disease After Intratympanic Injection of Gentamicin

Yoon Chan Rah, MD; Jae Joon Han, MD; Jaehong Park, MD; Byung Yoon Choi, MD, PhD; Ja-Won Koo, MD, PhD

exploratory tympanotomy and gentamicin application (ETG)



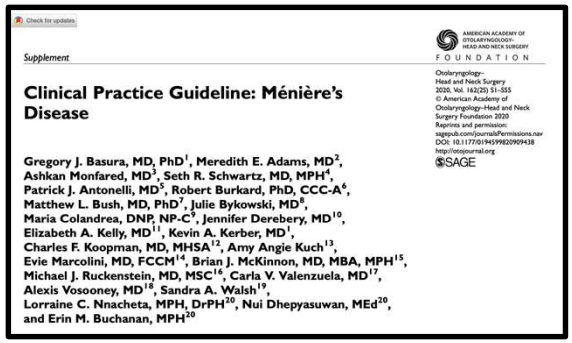
CONCLUSION

ITG showed favorable vertigo control (89.5%) and hearing preservation rate (91.6%). However, 10 (10.5%) cases still suffered from intractable episodic vertigo, and six of them were revealed to have failed to achieve sufficient attenuation of vestibular function even after multiple ITGs. For those who have failed ITG, ETG can be considered (success rate in this study: 71.4%). Labyrinthectomy or vestibular neurectomy can be chosen for those who failed to achieve vertigo control even after ETG.

Menière's Disease: Therapeutic Options

Table 4. Summary of Guideline Key Action Statements.

Statement	Action	Strength
Statement 7. Symptomatic management of vertigo	Clinicians should offer a limited course of vestibular suppressants to patients with Ménière's disease for management of vertigo only during Ménière's disease attacks.	Recommendation
Statement 8. Symptom reduction and prevention	Clinicians should educate patients with Ménière's disease on dietary and lifestyle modifications that may reduce or prevent symptoms.	Recommendation
Statement 9. Oral pharmacotherapy for maintenance	Clinicians may offer diuretics and/or betahistine for maintenance therapy to reduce symptoms or prevent Ménière's disease attacks.	Option
Statement 10. Positive pressure therapy	Clinicians should not prescribe positive pressure therapy for patients with Ménière's disease.	Recommendation against
Statement 11. Intratympanic steroid therapy	Clinicians may offer, or refer to a clinician who can offer, intratympanic steroids to patients with active Ménière's disease not responsive to noninvasive treatment.	Option
Statement 12. Intratympanic gentamicin therapy	Clinicians should offer, or refer to a clinician who can offer, intratympanic gentamicin to patients with active Ménière's disease not responsive to nonablative therapy.	Recommendation
Statement 13. Surgical ablative therapy	Clinicians may offer, or refer to a clinician who may offer, labyrinthectomy in patients with active Ménière's disease who have failed less definitive therapy and have nonusable hearing.	Recommendation
Statement 14a. Role of vestibular therapy for chronic imbalance	Clinicians should offer vestibular rehabilitation/physical therapy for Ménière's disease patients with chronic imbalance.	Recommendation
Statement 14b. Role of vestibular therapy for acute vertigo	Clinicians should not recommend vestibular rehabilitation/physical therapy for managing acute vertigo attacks in patients with Ménière's disease.	Recommendation against
Statement 15. Counseling for amplification and hearing assistive technology	Clinicians should counsel patients, or refer to a clinician who can counsel patients, with Ménière's disease and hearing loss on the use of amplification and hearing assistive technology.	Recommendation
Statement 16. Patient outcomes	Clinicians should document resolution, improvement, or worsening of vertigo, tinnitus, and hearing loss and any change in quality of life in patients with Ménière's disease after treatment.	Recommendation



Supplement

Clinical Practice Guideline: Ménière's Disease

Gregory J. Basura, MD, PhD[1], Meredith E. Adams, MD[2], Ashkan Monfared, MD[3], Seth R. Schwartz, MD, MPH[4], Patrick J. Antonelli, MD[5], Robert Burkard, PhD, CCC-A[6], Matthew L. Bush, MD, PhD[7], Julie Bykowski, MD[8], Maria Colandrea, DNP, NP-C[9], Jennifer Derebery, MD[10], Elizabeth A. Kelly, MD[11], Kevin A. Kerber, MD[1], Charles F. Koopman, MD, MHSA[12], Amy Angie Kuch[13], Evie Marcolini, MD, FCCM[14], Brian J. McKinnon, MD, MBA, MPH[15], Michael J. Ruckenstein, MD, MSC[16], Carla V. Valenzuela, MD[17], Alexis Vosooney, MD[18], Sandra A. Walsh[19], Lorraine C. Nnacheta, MPH, DrPH[20], Nui Dhepyasuwan, MEd[20], and Erin M. Buchanan, MPH[20]

Surgical Management of Menière's Disease

- A recent literature review confirm the decline of surgical treatment of MD in favor of IT injections
- Endolymphatic Sac Surgery (ESS) was introduced by Portmann in 1927
- Now is considered as a placebo surgery (Danish study, Cochrane review)

TABLE 2. *Summary of relationship among sac procedure, hydrops, and relief from vertigo*

Approach to sac	No. cases	Hydrops	Relief from vertigo
Not exposed	5	5	4
Exposed, lumen not entered	8	8	4
Lumen entered	2	2	0

Histopathology After Endolymphatic Sac Surgery for Ménière's Syndrome

*Jong Woo Chung, †Jose Fayad, †Fred Linthicum, ‡Akira Ishiyama, and *Saumil N. Merchant

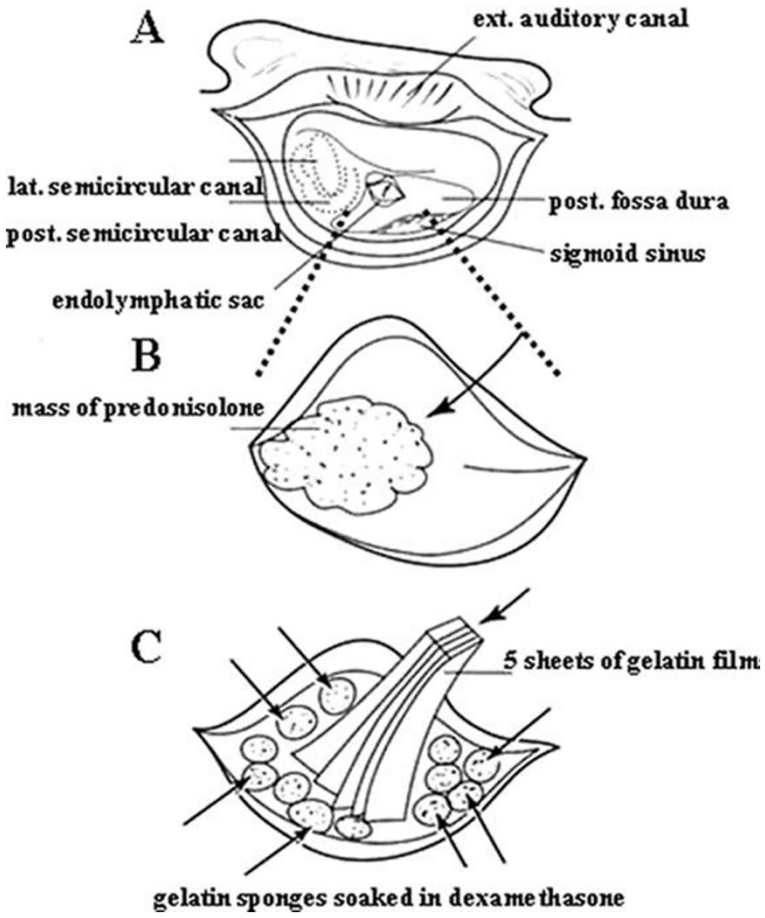
*Massachusetts Eye and Ear and Infirmary, Harvard Medical School, Boston, Massachusetts; †House Ear Institute; and ‡University of California, Los Angeles, Los Angeles, California, U.S.A.

- The surgery failed to expose the sac in 5 cases; 4 of the 5 had relief from vertigo.
- The sac was exposed, but the shunt failed to reach the lumen of the sac in 8 cases; 4 of the 8 had relief from vertigo.
- The shunt was successfully placed within the lumen of the sac in 2 cases; both cases failed to experience relief from vertigo.
- Endolymphatic hydrops was present in all 15 cases.

- **Endolymphatic sac surgery does not relieve hydrops in patients with Ménière's syndrome.**

Surgical Management of Menière's Disease

Kitahara [38] proposed the injection of dexamethasone into the sac. As the endolymphatic sac is the only location for immune reactions in the temporal bone the hypothesis by Kitahara makes sense. In a retrospective study, Wick et al. suggested that endolymphatic sac shunt procedures may benefit from steroid instillation at the time of shunt placement [39].



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Surgical Management of Menière's Disease

- In a recent study good results are reported using a technique of endolymphatic duct was blocked
- It is possible that ES itself secretes endolymph or a hormone that enhances hydrops and precipitates the attacks of vertigo

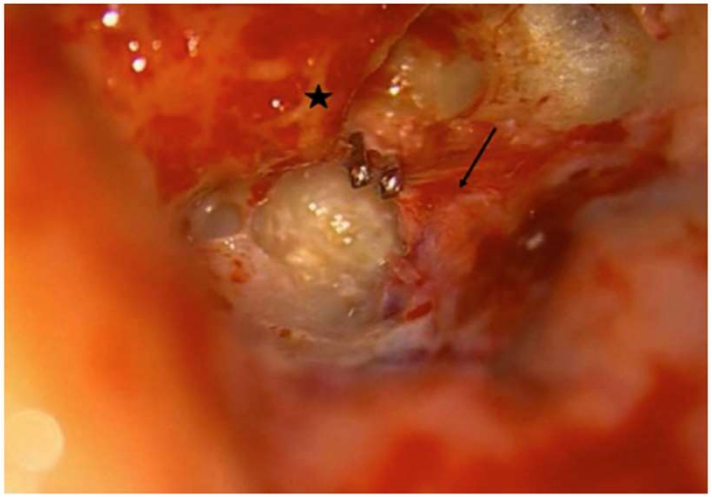

Figure 1 Right ear mastoidectomy and endolymphatic sac dissection (arrow) showing the two titanium clips blocking the endolymphatic duct behind the posterior semicircular canal (star). (Color version of figure is available online.)

Surgical Management of Menière's Disease

- Among the surgical techniques for MD, the only 2 methods that have gained high evidence in cases of intractable vertigo attacks are:

- LABYRINTECTOMY
  - It is the oldest surgical method to treat MD, today limited to older patients (residual dizziness and vestibular rehab)
  - Indicated in patients with poor hearing, with good contralateral vestibular function
  - Associated with cochlear implant to restore hearing at the same time
- VESTIBULAR NEURECTOMY
  - Tends to be more favorable regarding hearing outcomes
  - Most efficient technique for Tumarkin's crisis

Acta Neurochir (2017) 159:123–130
DOI 10.1007/s00701-016-2996-9

CLINICAL ARTICLE - NEUROSURGICAL TECHNIQUES

Translabyrinthine vestibular neurectomy and simultaneous cochlear implant for Ménière's disease

Pietro Canzi[1] · Marco Manfrin[1] · Marco Perotti[2] · Federico Aprile[1] · Silvia Quaglieri[1] · Elisabetta Rebecchi[1] · Giulia Locatelli[1] · Marco Benazzo[1]

Menière's Disease: Therapeutic Options

- investigate current treatment practices and self-reported effectiveness in MD.
- lost days of work per month due to disease

The Journal of International Advanced Otology
J Int Adv Otol 2019; 15(1): 112-7 • DOI: 10.5152/iao.2019.5758

Original Article

Patient Perceptions of Effectiveness in Treatments for Menière's Disease: a National Survey in Italy

Bryan Ward, Vincent Wettstein, John Golding, Giulia Corallo, Daniele Nuti, Franco Trabalzini, Marco Mandalà

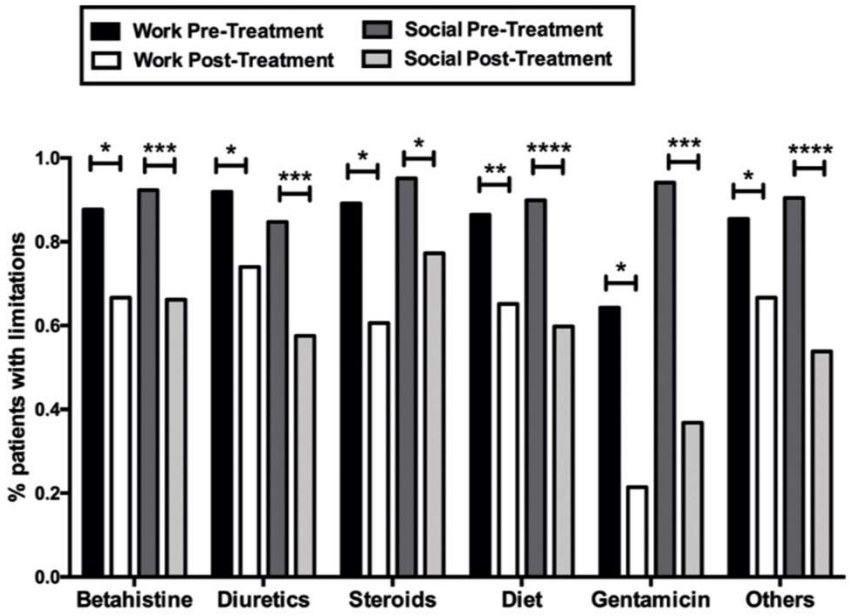

Figure 4. Proportion of respondents reporting limitations in working life and social activities before and after treatment, by treatment group. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

- High prevalence of functional disability that persists in many patients despite treatment.
- All therapies are associated with fewer reported mean vertigo episodes.
- The findings in the present study support a prominent **placebo effect** in treatments for MD
- **Compared with other treatments, chemical labyrinthectomy with ITG was associated with the greatest treatment effect.**

Menière's Disease: Therapeutic Options

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International consensus

International consensus (ICON) on treatment of Ménière's disease

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[e] Department of otolaryngology, head and neck surgery, university of Sidney, Australia
[f] Department of otolaryngology, Nara medical university, Japan
[g] Department of otolaryngology, Skull Base Surgery, CHU de Bordeaux, université de Bordeaux, 33000 Bordeaux, France

J. Nevoux et al. / European Annals of Otorhinolaryngology, Head and Neck diseases xxx (2017) xxx–xxx

ICON algorithm for treatment of Menière's disease

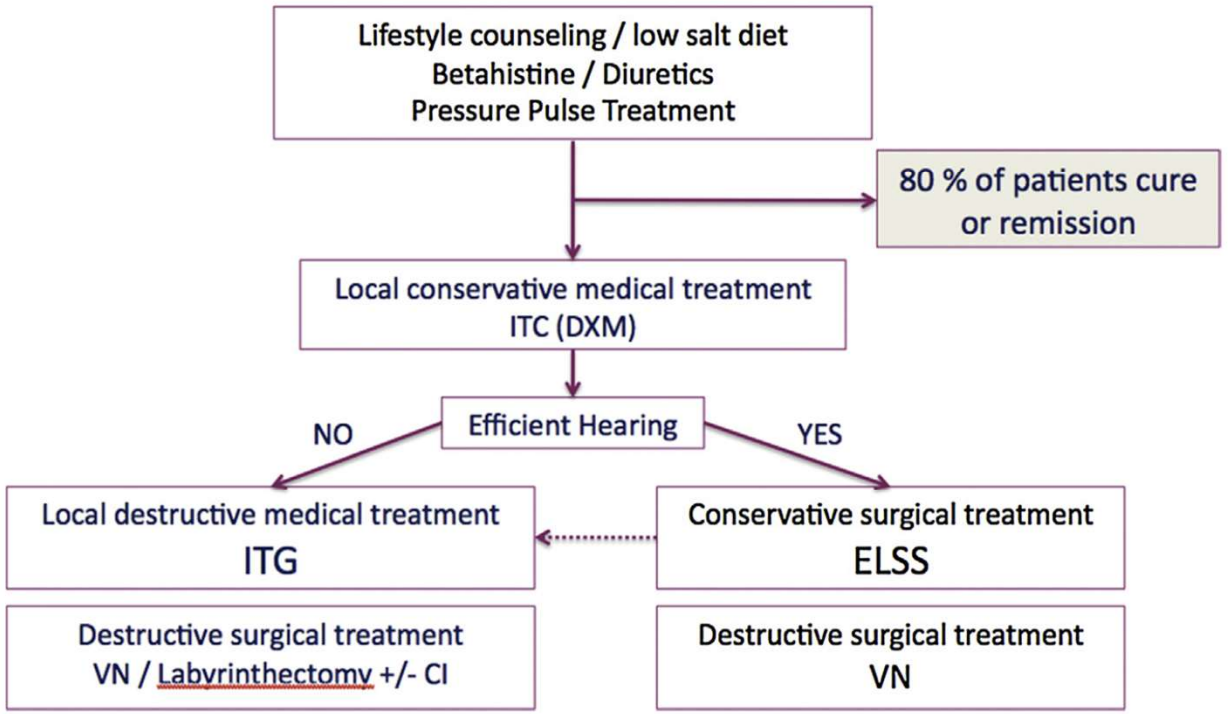

Fig. 1. Proposition of algorithm of treatment of Ménière's disease.

Curr Treat Options Neurol (2015) 17:14
DOI 10.1007/s11940-015-0341-x
Neurologic Ophthalmology and Otology (RK Shin and DR Gold, Section Editors)

Treatment of Menière's Disease

Jeffrey D. Sharon, MD*
Carolina Trevino, MD
Michael C. Schubert, PhD
John P. Carey, MD

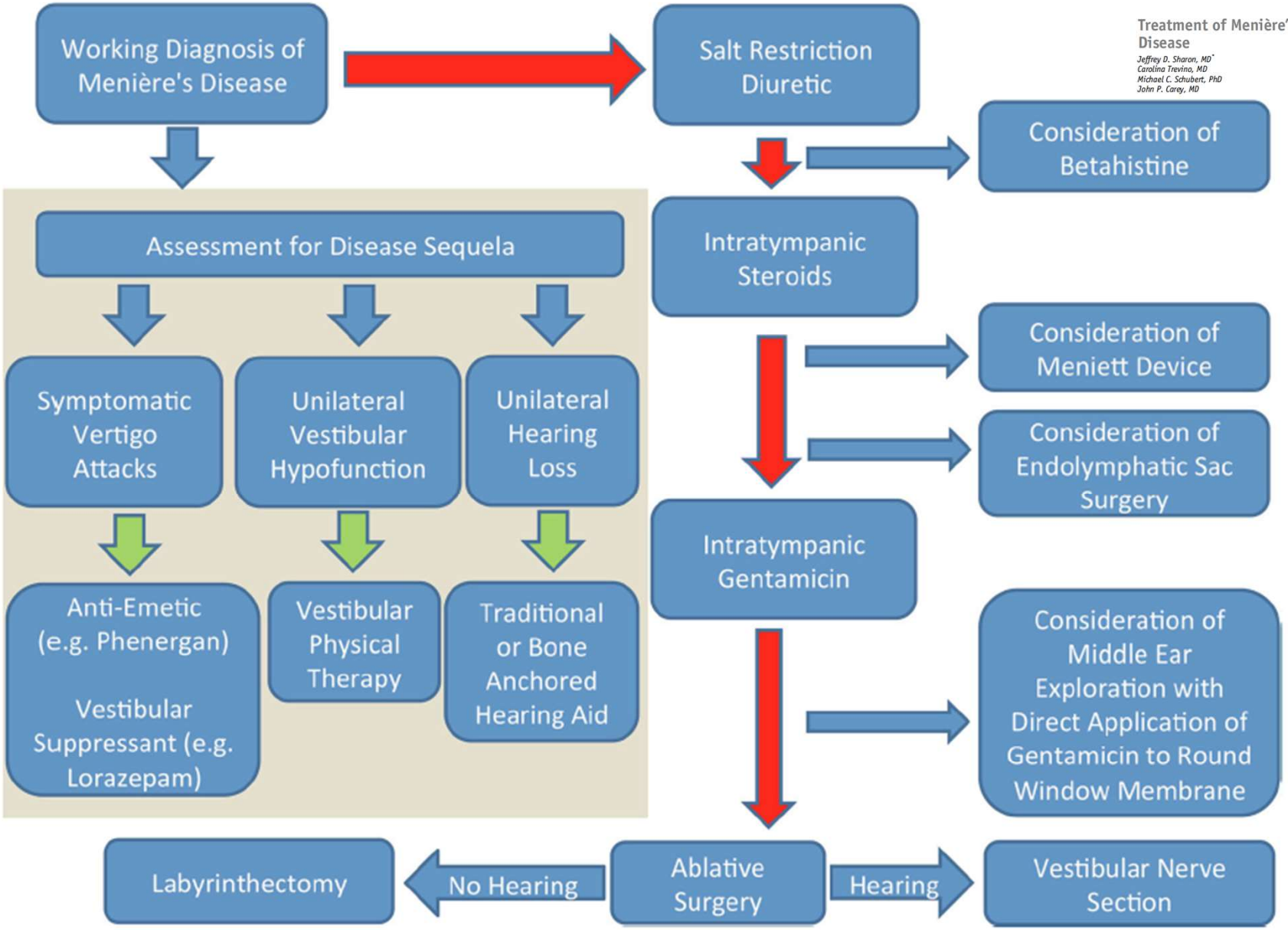

Fig. 1. Treatment algorithm for Menière's disease. *Blue arrows* refer to decisions that should be made in all patients; *red arrows* refer to disease progression. This algorithm was designed for treating unilateral disease.

Menière's Disease: Therapeutic Options

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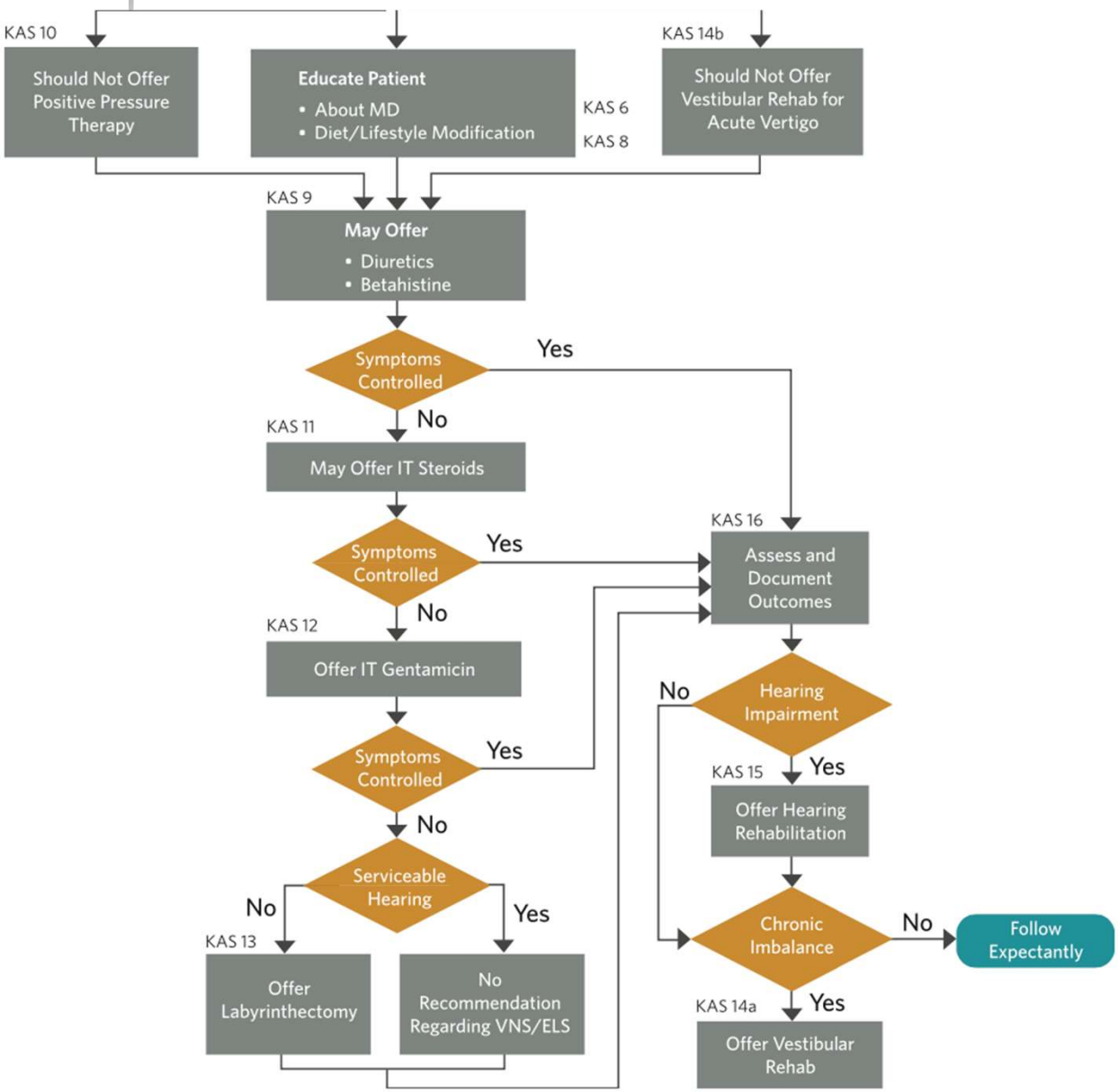
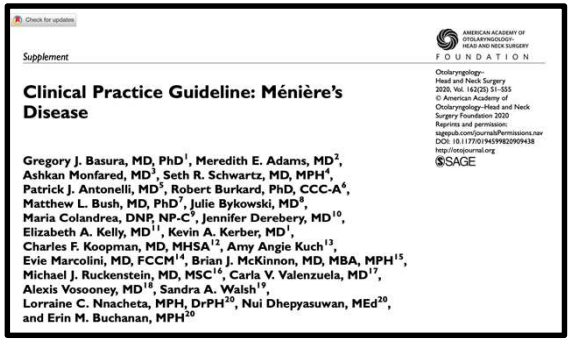
Menière's Disease: Therapeutic Options





Supplement

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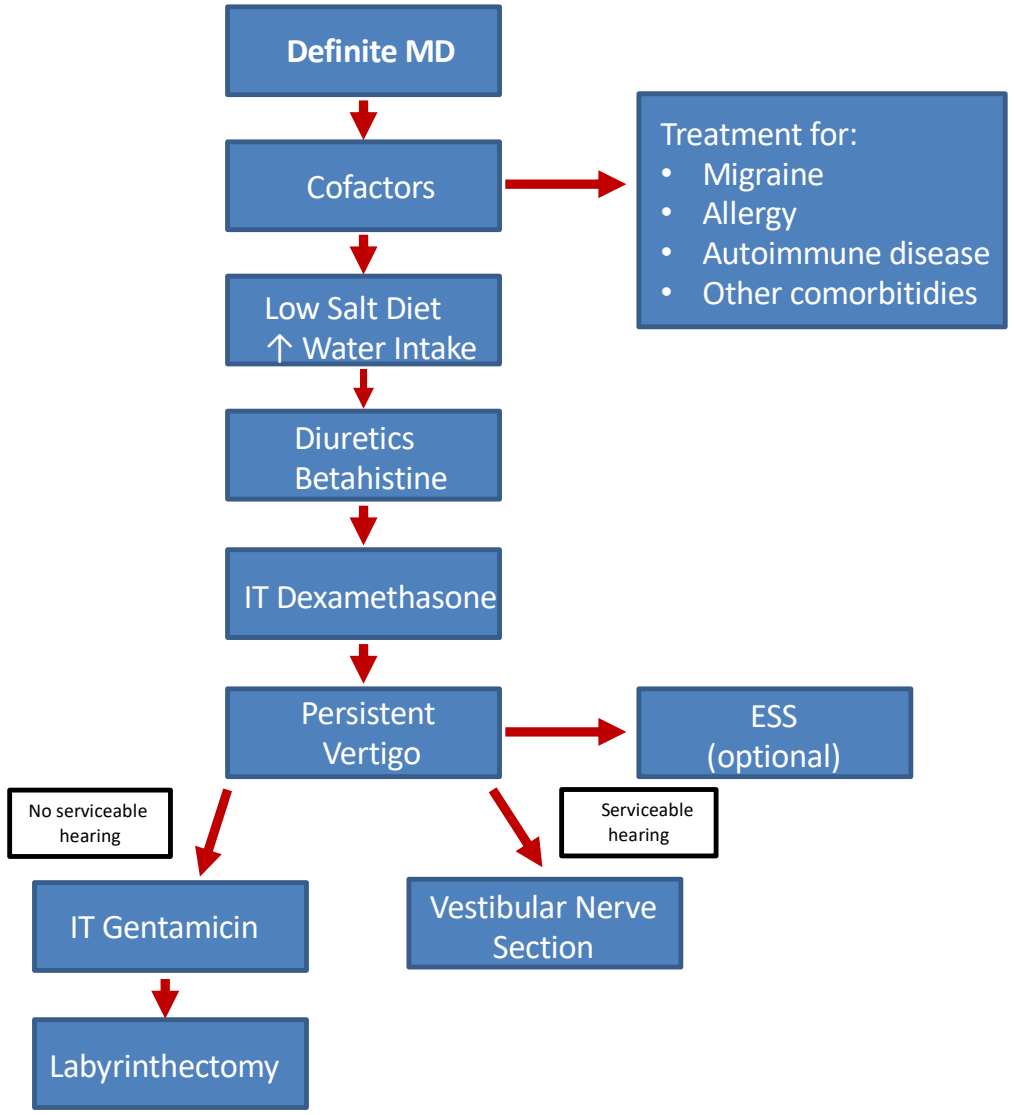
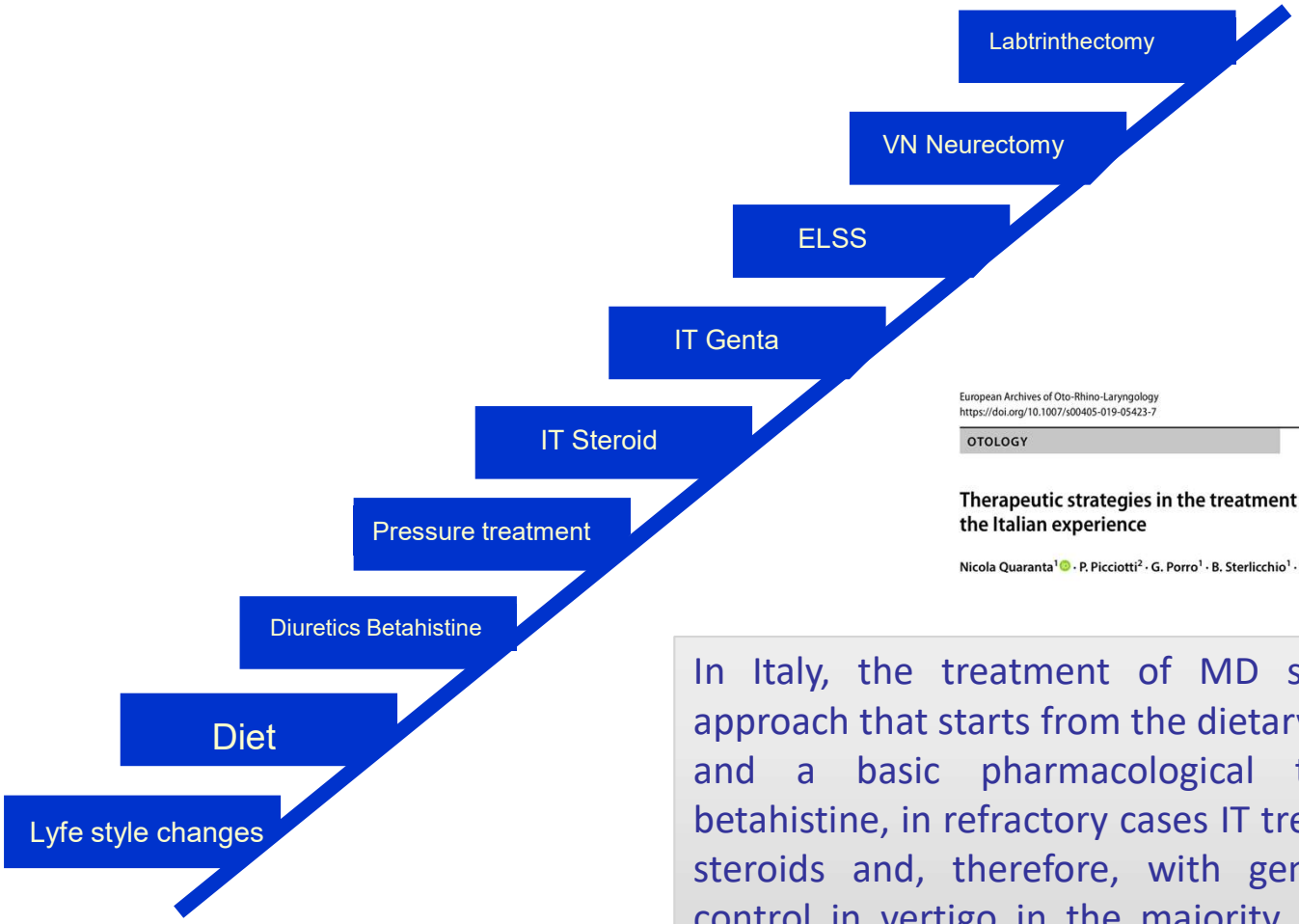
Menière's Disease: Therapeutic Options



Menière's Disease: Therapeutic Options

- Proposed Treatment ladder progressing up according to the clinical need

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OTOLOGY

Therapeutic strategies in the treatment of Menière's disease: the Italian experience

Nicola Quaranta[1] · P. Picciotti[2] · G. Porro[1] · B. Sterlicchio[1] · G. Danesi[3] · P. Petrone[4] · Giacinto Asprella Libonati[5]

In Italy, the treatment of MD stand on a gradual approach that starts from the dietary-behavioral changes and a basic pharmacological therapy based on betahistine, in refractory cases IT treatment initially with steroids and, therefore, with gentamicin allows the control in vertigo in the majority of cases. In case of failure of IT treatment, VNS is the surgery of choice.

Menière's Disease: Therapeutic Options

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