Current treatment of Menière’s disease

Introduction
Menière’s disease is a fascinating condition. I have had a particular interest in it for several years. However, after reading many articles and attending numerous lectures, I have come to the conclusion that not much progress has been made in the treatment of Menière’s disease since Torok’s 1977 review and a further review by Ruckenstein et al in 1991. Working with my colleague and friend, Herman Hamersma, who has been managing patients with Menière’s disease since 1960 and who has arguably the most experience in the management of this disorder in South Africa, I have come to realise that progress is slow. Nothing is more true today than the words of Professor Quix of Utrecht: “Je behandel Menière’s met je smoel” (You treat Menière’s disease with your mouth). What he was saying was that stress and psychology play an enormous role in this disease; so listening and talking to the patient may well be the best treatment of all!

The concept of Menière’s disease
Menière’s disease is a disease of unknown aetiology. The classic triad of vertigo, hearing loss and tinnitus (in addition to a sensation of fullness in the ear) indicates the inner ear as the target organ. It was this connotation between these symptoms and the inner ear that earned Prosper Menière the honour of having a disease named after him in 1861. However, it has become clear that there are several disorders that can mimic the symptoms of Menière’s disease to produce a Menière syndrome. Congenital, vascular, traumatic, syphilitic and viral causes can be directly correlated with the symptoms.

More recent publications and research indicate that auto-immune inner ear disease (AIED) may play a role, especially in bilateral cases. The most promising explanation for Menière’s disease however, is that it is caused by the Herpes Simplex Virus (HSV) type 1 and that it forms part of a Polianglionitis of cranial nerves which occurs in episodes. (Polianglionitis Episodica or PGE). Although HSV type 1 infestation is very common, it must be remembered that more than 70 strains have been isolated with only a few strains implicated in the cranial neuropathies. Bell’s palsy and vestibular neuronitis are other conditions believed to be caused by HSV type 1. It is estimated that Menière’s disease affects about 0.2% of the population. A slight female to male preponderance (1.3:1) has been reported. The age group 40 – 60 years is mostly affected. It is very rare in children. The question often asked is what the chances are of the second ear developing symptoms. Figures of between 2% and 78% have been quoted in different articles. In my experience, I have found it to be less than 15%. In any event, the incidence is seen to increase over time but seems unlikely if the second ear is not involved within the first 5 years.

Treatment of Menière’s disease remains controversial
For many years it was believed that endolymphatic hydrops or an increase in endolymphatic pressure was the pathologic basis of Menière’s disease. But this is definitely not true in all cases as it is also present in 6% of normal subjects at autopsy. Gacek has found that the histological finding of hydrops may be due to fibrosis within the cochlea and vestibule. Others believe that Menière’s disease is due to vasospasm. I believe that as technology, imaging and functional scanning become more advanced, the question of what goes on in the inner ear will be answered.
In my practice, I use the criteria as defined by the Committee of Hearing and Equilibrium of the American Academy of Otolaryngology, Head and Neck Surgery (Table I) to diagnose the condition. It must be emphasised that not all symptoms may be present from the onset, and that cochlear and vestibular symptoms may appear in isolation. A vestibular and cochlear type of the disease may well exist.

Before embarking on any form of treatment, it is of importance to note that the natural history of Menière’s disease is characterised by exacerbations and remissions, which are totally unpredictable. It is nearly impossible to anticipate the outcome for an individual, based on his or her history and test results, and even on data from the general population.

The treatment of Menière’s disease remains controversial and always evokes debate. Success rates in treatment are typically always quoted as being between 60 – 80%, making it difficult to distinguish this from placebo treatment. This must be taken into consideration when reading articles and adopting new treatment methods. Any result better than this should be treated with circumspection. When looking at meta-analysis and embarking on evidence-based medicine, it is difficult to interpret results if standardised diagnostic criteria and outcome measures have not been used. To complicate matters even further, new data suggest that quality of life questionnaires incorporating the social and mental well-being of patients should be used in assessing outcome after treatment.

The treatment philosophy
As long as a single aetiology for Menière’s disease evades us, numerous treatment options will always be advocated. In the majority of cases, treatment is directed towards vertigo, with insufficient focus on treatment for hearing loss and usually none in cases of tinnitus. Vertigo is generally accepted as the worst symptom but in older patients that have been suffering for a long time, hearing loss and even tinnitus may be a bigger problem. It is recognised now that the psychological impact of the disease on the patient is more often than not neglected. It is the severity and discomfort of the spells, the unpredictability of attacks and the fear of recurrence that accounts for anxiety, agoraphobia, depression, avoidance behaviours and other troubling mood states. This is perhaps the reason why one of the most famous sufferers of all times, Vincent van Gogh, cut off his ear. The question is often asked: what comes first, psychological dizziness or otologic anxiety? It should never be necessary to tell a patient that there is no treatment and that they should live with the disease.

The acute vertigo attack
Patients must be advised to lie down on a firm surface and stay as motionless as possible, which is precisely what they usually do during an attack anyway! They should also be told to keep their eyes open and fixed on a stationary object so that the visual system can help to suppress the vertigo. When movement is necessary it should be done as slowly as possible.

### Table I: Diagnostic scale for Menière’s disease of AAO-HNS

<table>
<thead>
<tr>
<th>Certain Menière’s disease</th>
<th>Definite Menière’s disease, plus histopathological confirmation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definite Menière’s disease</strong></td>
<td>Two or more episodes of vertigo of at least 20 min</td>
</tr>
<tr>
<td></td>
<td>Audiometrically documented hearing loss on at least one occasion</td>
</tr>
<tr>
<td></td>
<td>Tinnitus or aural fullness</td>
</tr>
<tr>
<td><strong>Probable Menière’s disease</strong></td>
<td>One definite episode of vertigo</td>
</tr>
<tr>
<td></td>
<td>Audiometrically documented hearing loss on at least one occasion</td>
</tr>
<tr>
<td></td>
<td>Tinnitus or aural fullness</td>
</tr>
<tr>
<td><strong>Possible Menière’s disease</strong></td>
<td>Episodic vertigo without documented hearing loss</td>
</tr>
<tr>
<td></td>
<td>Sensorineural hearing loss, fluctuating or fixed, with disequilibrium, but without definite episodes</td>
</tr>
</tbody>
</table>

In all scales, other causes must be excluded using any technical method (eg imaging, laboratory, etc).
I always encourage patients that, if at all possible, to see me during an attack or as soon as possible thereafter to document the physical findings. This may be important in confirming the disease and to establish the involved ear. This is not always easy to do based on the history alone because patients often have hazy recall of the exact symptoms. In case of the vestibular type of Menière’s, ear symptoms may be absent.

The cornerstone of treatment is directed towards reducing the vertigo, nausea and vomiting. A variety of drugs are available (Table II). Vestibular suppressants include anticholinergics, antihistamines and benzodiazepines and are mainly acetylcholine or histamine antagonists and GABA agonists. Antiemetics are more selective in action and are effective mainly due to their dopamine (D2) antagonistic properties. Some anti-emetics, however, have some muscarinic or antihistaminic (H1) effects that may assist in vestibular suppression. When vomiting is severe, intravenous fluid replacement and parenteral drug administration may become necessary.

Corticosteroids should be used for one week only. Steroids reduce inflammation and oedema, suppress the antigen-antibody-complement reaction in the inner ear due to viruses and other agents, help to suppress vertigo on vestibular nucleus level in the brainstem and facilitate central vestibular compensation. Prednisone, methylprednisolone and dexamethasone are good options.

If patients suffer from repeated attacks over a short period, a mild tranquiliser such as one of the longer acting benzodiazepines should be used.

Although not practised by all, antivirals in the form of valacyclovir or famciclovir can be added for one week.

Treatment between attacks
Many patients are sentenced to lifestyle adjustments on the basis of endolymphatic hydrops and vasospasm being the underlying pathogenesis of Menière’s disease. They are advised to restrict salt intake to between 1g and 2g per day and for those not willing to meticulously measure their salt intake, not to add salt or eat salty foods.

However, the idea of NaCl causing or aggravating fluid retention limited to the inner ear is noble but not proven. Research has shown that attacks of Menière cannot be provoked by infusing patients suffering with Menière’s disease with hypertonic salt solutions.

Other suggestions are for patients to include high potassium-containing food like bananas and orange juice in their diets while those advocating vasospasm as the cause suggest that caffeine and nicotine be avoided. The avoidance of alcohol seems logical but advising the patient to empty his or her wine cellar is pointless – unless it’s to the benefit of the doctor! Stress is an unavoidable everyday phenomenon and I can see no point in telling a patient to reduce stress without showing him or her how this should be done. Ruckenstein et al in 1991 concluded after a large review of available and current treatments that there is still no large, well-controlled study to show that any treatment is better than no treatment at all. Not much has changed since then. If these simple measures outlined above do help, why are we still treating so many patients with medication? Do I believe that these measures help? – NO! Do I still advocate them? – YES!

Diuretics
Diuretics seem a logical option if salt restriction alone does not control symptoms due to endolymphatic hydrops. It was demonstrated in a double-blind crossover study that 51% of patients on hydrochlorothiazide/triamterene experienced control of their vertigo compared to <10% on placebo. However, diuretics do not prevent hearing deterioration and may aggravate chronic tinnitus. Other diuretics that have been used are furosemide, amiloride (K+ sparing) and based upon the presence of carbonic anhydrase in the dark cells and the stria vascularis, acetazolamide. The side-effects of these drugs should be taken into account when deciding to use them in treatment.

Vasodilators
Betahistine dihydrochloride, a histamine derivate, has been used extensively for many years in the treatment of vertigo due to Menière’s disease. It has been shown to improve the microcirculation of the inner ear. It is also believed to act on the vestibular nuclei in the brainstem where it facilitates vestibular compensation after nerve section via an antagonistic effect on histamine H3 receptors and partial agonistic effect on histamine H1 receptors. There is still some debate regarding the optimal dose and currently 16mg three times a day or 24mg twice a day may be used.
Although no study has documented any improvement in hearing, it is still a drug that with its minimal side-effect profile, should be tried for the vertigo. Depending on the frequency of the attacks, a 3–6 month trial period is usually long enough to determine efficacy. Nicotinic acid before meals is also used by some. The end point of treatment is a good flush and to obtain this any dose between 50mg and 400mg may be needed.

**Stereoids**

For patients who suffer from frequent attacks, steroids can be considered. The instillation of steroids into the middle ear through the tympanic membrane offers three advantages:

- Less side-effects than systemic administration
- Does not damage the hearing
- Results in a higher concentration in the inner ear, if compared to the other administration routes

This form of treatment is often used in an only hearing ear.

**Aminoglycoside therapy**

It was in 1957 that Harold Schuknecht, one of the fathers of otology, introduced the use of aminoglycosides in the treatment of Ménière’s disease. Based on the fact that aminoglycosides are otoxic, they are utilised in creating a functional labyrinthectomy. Aminoglycosides are known to differ in the relative toxicity towards the inner ear and also in their different vestibulo- and oto-toxic potential. The rationale behind treatment with aminoglycoside nowadays is to create a selective inhibition of the dark cells producing the endolymph and not to damage the vestibular receptor cells. A staged inhibition is what is required, not a chemical labyrinthectomy.

Gentamicin and intramuscular streptomycin sulphate are most commonly used. Streptomycin produces bilateral effects and can therefore be used for bilateral Ménière’s disease.

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### Table II: Treatment of acute vertigo and nausea in adults

<table>
<thead>
<tr>
<th>NAME</th>
<th>DOSAGE</th>
<th>USE</th>
<th>SIDE-EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anticholinergic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glycopyrrolate</td>
<td>1-2mg q12h po</td>
<td>vs ms ae</td>
<td>Anticholinergic side-effects</td>
</tr>
<tr>
<td><strong>Antihistamines</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclizine</td>
<td>50mg q8h po or 100mg q8h im</td>
<td>VS MS</td>
<td>Sedation, moderate anticholinergic</td>
</tr>
<tr>
<td>Cinnarizine</td>
<td>25mg q8h po</td>
<td>VS MS</td>
<td>Sedation</td>
</tr>
<tr>
<td>Promethazine</td>
<td>25 -50mg q4-6h po or q4-6h im or q4-6h sup</td>
<td>VS MS AE</td>
<td>Sedation</td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>5-10mg q6-12h po or q4-6h im or q4-6h iv</td>
<td>VS</td>
<td>Seadtion, tolerance, addiction</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>1-2mg q8-12h po</td>
<td>VS</td>
<td>Sedation, tolerance, addiction</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>0,5mg q8h po</td>
<td>VS</td>
<td>Sedation, tolerance, addiction</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>0,5mg q8h po</td>
<td>VS</td>
<td>Sedation, tolerance, addiction</td>
</tr>
<tr>
<td><strong>Butyrophenone</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Droperidol</td>
<td>2,5 – 5mg q12h im</td>
<td>VS AE</td>
<td>Sedation, respiratory depression, extra-pyramidal reaction</td>
</tr>
<tr>
<td><strong>Phenothiazine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>5-10mg q4-6h po or q6h im or 25mg q12h sup</td>
<td>AE</td>
<td>Extrapyramidal reaction</td>
</tr>
<tr>
<td><strong>Serotonin Antagonists</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ondansetron</td>
<td>8mg q12h po or 8-32mg iv slowly</td>
<td>AE</td>
<td>Headache</td>
</tr>
</tbody>
</table>

vs – mild vestibular suppressant  
MS – mild motion sickness  
MS – moderate motion sickness  
MS – strong motion sickness  
vs – moderate vestibular suppressant  
MS – mild motion sickness  
MS – moderate motion sickness  
MS – strong motion sickness  
vs – strong vestibular suppressant  
AE – mild anti-emetic  
AE – moderate anti-emetic  
AE – strong anti-emetic  

Otorhinolaryngology
Gentamicin is classically applied intratympanically, either through a myringotomy incision or a grommet. The gentamicin is then absorbed through the round window membrane. Impregnated micro wigs and micro catheters can also be used to deliver medication.

The problems with aminoglycosides and specifically the intratympanic methods are:

- There is no universally standardised administration method
- The pharmacokinetics after administration is unpredictable
- Attacks of vertigo often re-occur
- When hearing loss occurs it may be difficult to distinguish from the natural disease process.

In my practice, I use intratympanic gentamicin for older patients with established hearing loss at risk for a bigger surgical procedure. I have found it to reduce vertigo in 90% of cases at an expense of 15% hearing loss.

Auto Immune Inner Ear Disease (AIED)

Damage to the inner ear by either auto immune antibodies or immune cells is the underlying mechanism claimed by many to be the cause of Menière’s disease. This is rare and there is controversy regarding the precise incidence. It has been estimated that AIED is responsible for 6% of patients with Menière’s syndrome and 16% of patients with bilateral Menière’s disease. I believe that this is more a clinical diagnosis and would rather be confirmed by a response to steroids than any other fancy and expensive laboratory test. Positive auto immune markers neither confirm or exclude the inner ear as target and may only help to diagnose a systemic auto immune disorder. AIED is worth considering especially in middle aged female patients with bilateral progressive hearing loss with poor speech discrimination on testing. Vertigo may be present in 50% of cases. Steroids, cytotoxic agents (methotrexate) plasma phoresis, anti-TNF agents and cochlear implants have been considered in the treatment. In patients suspected of having AIED, I will use steroids to see if I can get a response. However, methotrexate is no longer accepted universally for maintenance due to side effects. The light at the end of the tunnel is that cochlear implantation is available for those patients whose hearing cannot be saved. The final word has not been spoken!

Polyganglionitis episodica

The implication of HSV type 1 in Bell’s palsy and vestibular neuritis has led to the concept of a viral polyganglionitis as the cause for Menière’s disease. Unfortunately a rise in anti-HSV type 1 antibodies does not always accompany the attack. There is considerable research underway into the role of the neurotropic viruses. The fact that the virus resides in the ganglion has two major implications:

- It is incurable (unless the ganglion is removed which is not really practical in the case of the spiral ganglion)
- It replicates and produces symptoms when stress impairs the natural immune response.

L-Lysine is an essential amino acid and can help to inhibit replication of the herpes virus if taken in high dosages (1000mg/day).

Corticosteroids are routinely used for acute attacks, but for longer periods, side-effects need to be considered. As mentioned, intratympanic administration is a good alternative to systemic administration.

And then there is stress. Reduction of stress levels is perhaps the most important of all treatments offered. A mild tranquiliser like clobazam or alprazolam SR can be prescribed to help reducing stress and anxiety. It is safer to use longer acting benzodiazepines due to the lower dependency potential. I routinely do not use them for more than 3 months at a time. Lifestyle adjustments and coping skills are also important and as emphasised by Herman Hamersma: “The dishes need not be done immediately after a Sunday lunch – go and rest for a while before attending to the chores”. http://www.timeurgency.com

Pressure treatment

Whether manipulation of middle ear pressure really helps for Menière’s disease remains unanswered. Some animal studies have shown the presence of receptors around the round window that may be sensitive to pressure changes. This phenomenon may explain why some patients may benefit from the mere insertion of a grommet. The Meniett device delivers pulsed pressure to the middle and inner ear via a grommet. It is not known whether it pushes the excess endolymph through the endolymphatic valve or if it has an effect on the pressure receptors. Although it may be non-invasive, non-destructive and safe, I am not yet convinced that it is not just another expensive placebo!

Tinnitus

Doctor, but what about the noise in my ears? Undoubtedly the most dreaded question a patient can ask me.
A discussion of the management of tinnitus is not the objective of this article – luckily, because I do not have the answers. The chances of reducing the tinnitus of the Menière’s attack is always better than managing the chronic persistent form. There are just so many other causes for tinnitus and no drug is really indicated to cure it. Hearing aids usually help when hearing loss is present and noise makers when it is not. I wholeheartedly believe in Tinnitus Retraining Therapy (TRT) and usually dump this responsibility on my audiologist. Betahistine can be tried and alprazolam 0.5mg in a step up, step down regime. The dependence possibility of these drugs in patients with severe tinnitus may be compared to the irrelevancy of opioid dependency in cancer patients. A high degree of depression is related to tinnitus; tinnitus may drive patients crazy and cause them to eventually commit suicide.

Many other options for treatment exist. By all means try them, but avoid telling your patient that nothing can be done. However, you should discourage them from going on a crusade to find the perfect drug.

For chronic tinnitus I always quote 25-50% reduction for all the treatments and surgical options I offer. But again, this same result could probably be achieved with over the counter herbal remedies.

**Vestibular rehabilitation exercises**

The place of vestibular rehabilitation exercises is limited to patients with permanent reduction in vestibular function due to Menière’s disease and to those who have had ablative (destructive) surgery. In my opinion, no ablative surgery should ever be offered if a structured vestibular rehabilitation programme is not provided. This is like amputating a limb without supplying a prosthesis. In patients who experience normal balance between attacks, vestibular rehabilitation exercises play no role whatsoever.

Tai Chi and Yoga help to improve balance and may be advised but these are not as effective as structured adaptation and substitution-based vestibular exercise programmes.

**Others**

Homeopathy, acupuncture, lipoflavinoids, hyperbaric oxygen, Ca antagonists and histamine – no comment!

**Surgery**

A simplistic approach I have followed for a few years is to establish how much the vertigo bothers the patient and whether they are willing to undergo a surgical procedure. After a trial of medical treatment the patient will usually indicate when surgery is required. Except possibly in the case of Tumarkin’s disease (a special form of Menière’s disease where patients experience drop attacks) no clear cut criteria exist as to when surgery is indicated. Each and every patient’s case needs to be judged on its own merits. Whatever the case, no destructive or ablative surgery should ever be performed unless a proper means of diagnosis has been followed and unless a structured vestibular rehabilitation programme can be offered. When a neurectomy is performed or a vestibular end organ destroyed, it is permanent. This may become a problem when the patient gets older and develops other problems that may impair balance control. Apart from the placement of grommets, there are only three surgical procedures utilised for vertigo in Menière’s disease in the 21st century. They are divided in non-destructive (non-ablative) and destructive (ablative), referring to the effect on the vestibular end organ and nerve. The non-destructive procedure is the Endolymphatic Sac Decompression, and the destructive procedures are the Labyrinthectomy and Vestibular Neurectomy. All other, older procedures have now been wisely abandoned.

**Conclusion**

The best result is spontaneous remission.

The primary aim of the treatment must be to enhance a remission and to accomplish this, anti-stress management is essential.

Medical treatment against HSV-type 1 is prescribed, but needs improvement.

The side-effects of the disease require symptomatic treatment.

If the disability is severe and the quality of life impaired, surgical treatment should be considered. Surgery can be very successful.

**Recommended Reading**