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Horizon scanning report

The Meniett™ device for the treatment of Ménière's disease

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Executive Summary

Ménière's disease is a chronic, idiopathic disorder of the inner ear, characterised by spontaneous attacks of vertigo, fluctuating hearing loss, tinnitus and a feeling of aural fullness. The underlying pathologic basis of Ménière's disease is the distortion of the membranous labyrinth, characterised by endolymphatic hydrops. The Victorian Ménière's Disease Resource and Information Centre estimates that Ménière's disease affects one in every thousand Australians.

No "gold standard" for the treatment for Ménière's disease currently exists. A number of treatment alternatives are available that include non-invasive and conservative treatments such as dietary control, symptom control with antimetic agents, administration of vasodilators or medical ablation. If conservative treatment fails, surgical treatment may be considered and may include procedures that are either non-destructive or destructive to auditory function.

Medtronic Australasia Pty Ltd provide the Meniett™ device, which is a portable, patient administered device, capable of delivering low frequency and low-pressure pulses to the middle ear via an implanted ventilation (grommet) tube. Positive pressure changes in the inner ear compartment may result in a decrease in endolymphatic fluid volume, ameliorating the symptoms of Ménière's disease.

It appears that the Meniett™ device is effective in reducing patient symptoms such as the number of vertigo episodes, with five studies reporting a significant reduction in the frequency of attacks compared to placebo ($p=0.048$) (level II intervention evidence) and compared to baseline data in before and after studies ($p = 0.001$) (level IV intervention evidence). It should be noted, however, that despite the significant reduction of vertigo episodes for the patient group as a whole, one study reported a number of patients (12/67, 18 per cent) who experienced *more* vertigo episodes during follow-up when compared to baseline (level II intervention evidence). In addition, one study reported a clinically significant improvement in the number of vertigo episodes before and after insertion of the ventilation tube alone ($p = 0.001$) as well as before and after treatment with the Meniett™ device ($p = 0.001$) (level IV intervention evidence). In this study there was no significant difference between the effect of ventilation tube alone and the combined effect of ventilation tube in conjunction with treatment with the Meniett™.

Results varied widely on the effect of the Meniett™ device on hearing levels or electrocochleographic readings. Some studies reported statistically significant differences between treatment and placebo groups for electrocochleographic readings and hearing, whereas other studies reported no difference (level II intervention evidence). Similar heterogenous results were reported for the poorer quality before and after studies.

In studies that reported adverse events associated with the use of the Meniett™ device, middle ear infections were common (13.5 per cent of patients) as was the replacement of the ventilation tube over time, which is an expected side effect with long-term implantation of ventilation tubes.

The Meniett™ device is currently available as a Schedule 5 product and can be accessed through otolaryngologists. The device costs approximately A\$5,000 and for patients with the appropriate private health insurance a full rebate is payable. Insertion of a ventilation tube in the middle ear is necessary for the Meniett™ to function, and this procedure is currently funded on the Medicare Benefits Schedule.

Meniett™ appears to benefit most, but not all patients in terms of reducing the number of vertigo episodes, however it is difficult to ascertain if Meniett™ has a positive effect on the fluctuating hearing levels of Ménière's patients. Treatment with Meniett is non-destructive to hearing and has the advantage of preserving cochlear function, which may allow the patient to consider further treatment options in the future. Treatment with Meniett™ may have to be continued in the long term for continued symptom alleviation, however long-term use of the device may be associated with adverse events such as infection and the need for regular replacement of the tube.

Diffusion of the Meniett™ device is occurring rapidly in both the private and public health care sector of Australia, however it is not utilised uniformly throughout the public health sector. There is high level evidence on the effectiveness of Meniett™ for the management of the symptoms of Ménière's disease. However there is a lack of evidence on the effectiveness of the Meniett™ device on the hearing of patients affected by this disease. In addition, there is a lack of cost-effectiveness data concerning the use of the Meniett™ device to treat Ménière's. From the evidence presented in this report it is unlikely that the Meniett™ device would have any consequences on the Australian public health care system.

Introduction

The National Horizon Scanning Unit, Department of Public Health, University of Adelaide, on behalf of the Medical Services Advisory Committee (MSAC), has undertaken an Horizon Scanning Report to provide advice to the Health Policy Advisory Committee on Technology (Health PACT) on the state of play of the introduction and use of the Meniett™ alternating ear pressure device (Horizon Scanning Register number: 000109).

Medtronic Australasia Pty Ltd provide the Meniett™ device which delivers low frequency and low pressure pulses to the middle ear with the aim of providing symptomatic relief for patients with Ménière's disease. The Meniett™ device was approved for use by the United States Food and Drug Administration in 2000 and has approval from the Australian Registered Therapeutic Goods Administration (ARTG number 99185). It is offered through otolaryngologists in private practice and is currently in limited use in Australia. The Meniett™ device is a Schedule 5, Appendix C (prosthesis rebate group) product.

This Horizon Scanning Report is intended for the use of health planners and policy makers. It provides an assessment of the current state of development of the Meniett™ device, its present use, the potential future application of the technology, and its likely impact on the Australian and New Zealand health care systems.

This Horizon Scanning Report is a preliminary statement of the safety, effectiveness, cost-effectiveness and ethical considerations associated with the Meniett™ alternating ear pressure device.

Background

Description of the technology

The procedure

The association between changes in ambient pressure and inner ear function was first noted in the mid-1970s. Patients with acute Ménière's symptoms who were treated within a pressure chamber displayed improvements in symptoms when a relative over pressure was created within the middle ear space. It was hypothesised that a positive pressure change in the inner ear compartment may lead to an increased exchange of inner ear fluids, leading to a decrease in the endolymphatic fluid volume. An early placebo-controlled, randomised controlled trial (level II intervention evidence) conducted by Densert et al (1997) delivered low pressure pulses via a transtympanic ventilation tube inserted into the middle ear space via an opening in the tympanic membrane (or eardrum). Changes in the

four measures of the transtympanic electrocochleography (TT EcoG) were statistically significant when the treatment group was compared to the placebo group. In addition there was a significant difference between the before and after TT EcoG measurements in the treatment group, but no difference was noted before and after in the placebo group, demonstrating an improvement in electrophysical parameters in the treatment group. However, there was no concomitant improvement in the physical symptoms of Ménière's in either the treatment or placebo group (Densert et al 1997). Further studies postulated that the amplitude and frequency of the pressure pulses delivered to the middle ear space should be adjusted according to the total volume of the middle ear. This led to the development of the Meniett™ device (Densert et al 2000).

The Meniett™ is a small, non-invasive, portable, patient administered device for the treatment of Ménière's disease. The Meniett™ is an electronically controlled membrane pump, which generates low frequency, low amplitude pressure pulses. The device consists of an earpiece, pump house, electronic micro-controller hardware and software (Figure 1). Patients are required to have a tympanostomy tube (grommet) inserted under local anaesthetic into the middle ear space of the affected ear. A tube connects the earpiece to the pump house. Once the earpiece is placed into the ear thus sealing off the external ear canal, pressure pulses are generated and delivered to the middle ear via the tympanostomy tube. A built-in sensor can detect if there is an inadequate seal between the Meniett™ earpiece and the external ear canal, and treatment will be terminated. Once the earpiece is correctly seated in the ear canal, treatment can be recommenced (FDA 1999; Medtronic XOMED 2004).

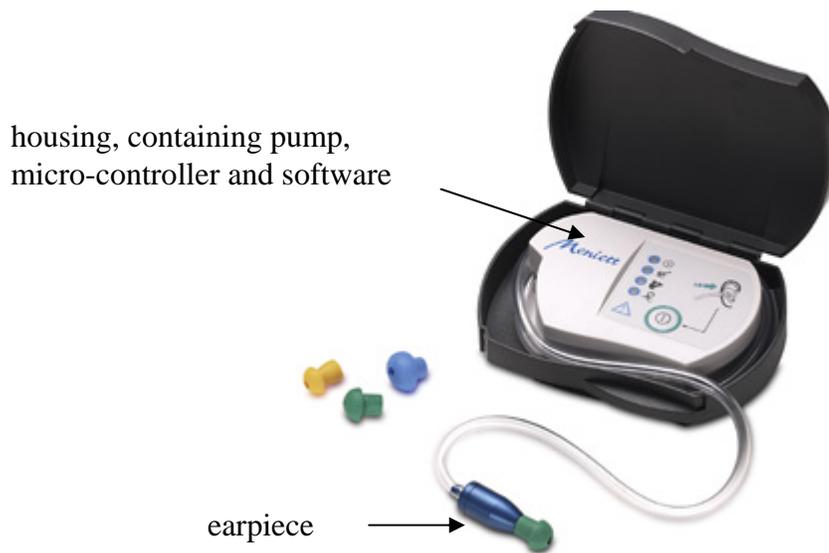


Figure 1 The Meniett™ device (Printed with permission: Medtronic XOMED 2004)

Treatment is performed when the patient is symptomatic and experiencing episodes of vertigo. After prescription and training by a physician, patients can

continue to treat themselves in the home environment. It is recommended that patients treat themselves for five minutes, three times per day, ie in the morning, midday and evening. Each five-minute treatment period consists of three cycles: one minute of pressure pulses followed by a 40 second pause. It is recommended that treatment should be maintained for 5-6 weeks or until remission of symptoms. The mechanism of action of the Meniett™ device is unclear but it is thought that the pressure pulses force the excess endolymphatic fluid back into the endolymphatic sac. As endolymphatic fluid is produced continually, the patient is required to repeat treatment with Meniett™ on a daily basis (FDA 1999; Medtronic XOMED 2004).

Intended purpose

The Meniett™ device is indicated for use in patients with symptomatic Ménière's disease. Ménière's disease is a chronic, idiopathic disorder of the inner ear, characterised by spontaneous attacks of vertigo, fluctuating hearing loss, tinnitus and a feeling of aural fullness. The basic anatomy of the inner ear is depicted in Figure 2. The underlying pathologic basis of Ménière's disease is the distortion of the membranous labyrinth, characterised by endolymphatic hydrops. Endolymph resides in the inner ear and unlike all other extracellular fluids has high levels of potassium but low levels of sodium and calcium, and is held at a positive potential (mV). All of these factors make endolymph uniquely important for the normal functioning of the cochlear. Small changes in any of these factors or disturbances in the inner ear fluid pressure may result in loss of hearing sensitivity or produce the symptoms of vertigo and nausea (Salt 2003). Ménière's disease results from either the over-production of endolymph, or the failure of endolymph to be absorbed, resulting in a distortion of the endolymphatic sac. In addition, many patients with Ménière's disease have abnormal levels of circulating complement and immune complexes, which is thought to play a role in the pathogenesis of the disease (Thai-Van et al 2001; Minor et al 2004). Other aetiological factors may be: anatomical (abnormalities of the temporal bone in the ear); genetic (a familial predisposition); viral (associations with herpes simplex I and II, Epstein-Barr and cytomegalovirus); vascular (associations of symptoms of Ménière's disease and migraine); metabolic (lack of sodium potassium ATPase activity) and psychological (associations with obsessional traits, psychosomatic personalities and neuroses) (Saeed 1998).

There are three distinct stages of Ménière's disease. During Stage I the predominant symptom is episodic vertigo, associated with nausea and vomiting. Attacks may last from 20 minutes to several hours. Between attacks, hearing returns to normal and examination of patients in remission invariably shows normal results. Patients in Stage II of disease progression experience severe attacks of vertigo accompanied by fluctuating hearing loss, usually affecting the lower pitches. In Stage III of the disease, hearing loss ceases to fluctuate and progressively worsens, attacks of vertigo diminish and may cease altogether, although patients may experience unsteadiness, especially in the dark (Saeed 1998; Gibson 2001). Diagnosis may be made on the history of the patient alone,

or by utilising a glycerol hydration test and electrocochleography. Patients with Ménière's disease demonstrate an improvement in hearing low frequency sounds in response to an oral dose of glycerol and a characteristic waveform in hydrops during electrocochleography (Saeed 1998).

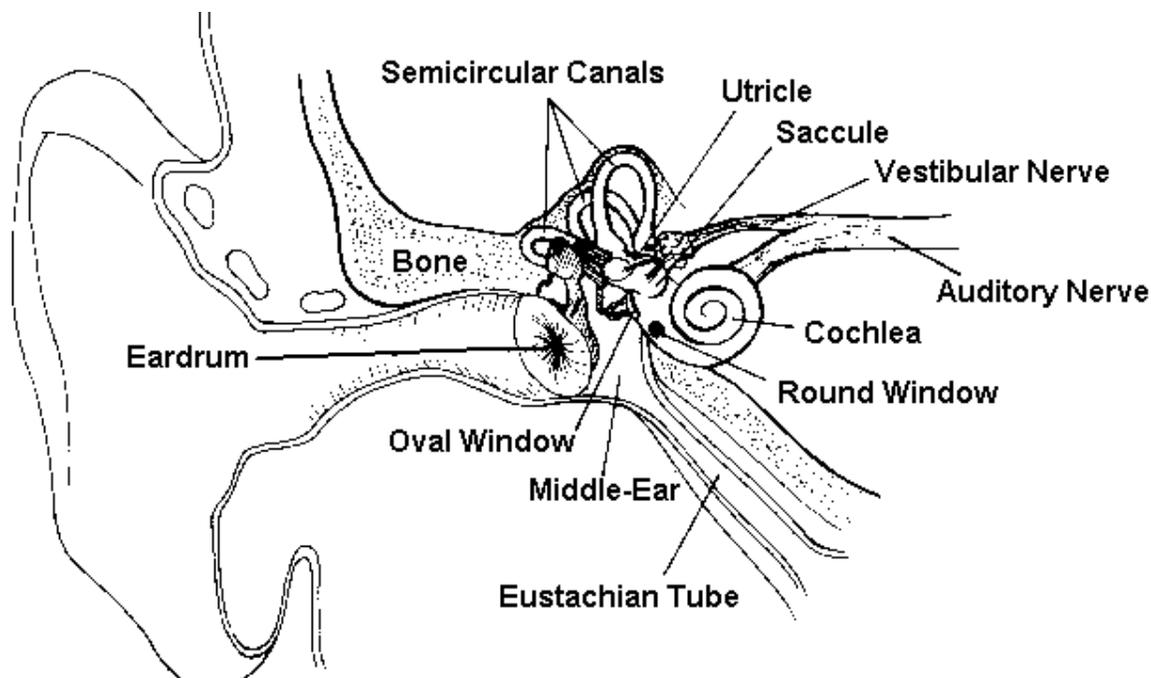


Figure 2 Anatomy of the inner ear (Vestibular Disorders Association 2004, printed with permission)

The anatomy of the normal inner ear is shown in Figure 2. In the normal inner ear (Figure 3A), the endolymphatic sac (A) maintains fluid at a constant level, the balance (B) and hearing (C) canals collect sensory information and the hearing and balance nerves (D) send this information to the brain. In the abnormal inner ear (Figure 3B), increased fluid in the endolymphatic sac (A) leads to swelling and pressure, the balance canal (B) also swells leading to a distortion of information, swelling blocks or distorts sound information in the hearing canal (C) resulting in distorted information being sent from the hearing and balance nerves (D) to the brain (Medtronic XOMED 2004).

Patients who are not suitable candidates for treatment with the Meniett™ device include those with the following conditions: perilymph fistula, vestibular Ménière's disease, retrocochlear damage such as acoustic neuroma and low-pressure hydrocephalus (Medtronic XOMED 2004).

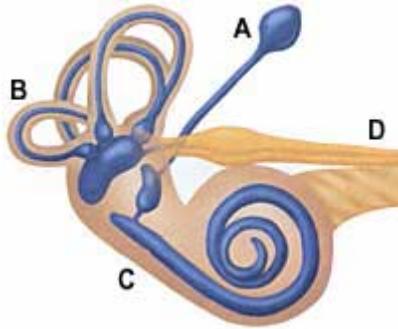


Figure 3A The normal inner ear
(Medtronic XOMED 2004, printed with permission)

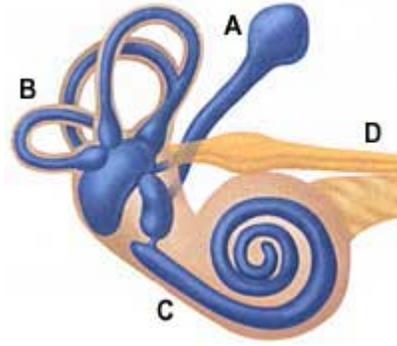


Figure 3B The abnormal inner ear

Clinical need and burden of disease

It is difficult to estimate the number of people suffering from Ménière's disease, as there have been no published studies estimating the prevalence or incidence of Ménière's disease in Australia or New Zealand. Incidence rates published overseas vary considerably from 157 per 100,000 in the United Kingdom, 46 per 100,000 in Sweden, 7.5 per 100,000 in France and 15 per 100,000 in the United States. These studies were conducted without consensus diagnostic criteria, which may account for the large variation (Minor et al 2004). A recent study by Kotimaki et al, based on the uniform diagnostic criteria developed by the American Academy of Otolaryngology – Head and Neck Surgery Committee on Hearing and Equilibrium estimated a prevalence of 43 per 100,000 and an average annual incidence of 4.3 per 100,000 in Finland (Kotimaki et al 1999). The Victorian Ménière's Resource and Information Centre estimates that Ménière's disease affects approximately one in every thousand Australians (Ménière's Support Group of Victoria 2004). Peak incidence occurs in the 40 to 60 year age group and it is slightly more common in females than males (1.3:1) (Minor et al 2004).

The number of Australian public hospital separations for patients with Ménière's disease in 2001-02 was 885 with an average length of stay of 3.0 patient days.¹ During this same period there were 1,974 separations for other disorders of vestibular function with an average length of stay of 3.3 patient days (AIHW 2004). These separations are likely to be for procedures such as endolymphatic sac surgery, translabyrinthine vestibular neurectomy or retrolabyrinthine vestibular or cochlear nerve section (Medical Benefits Schedule item numbers 41590, 41593 and 41596 respectively). In addition, the Health Insurance Commission reported 82 procedures in private hospitals during the same period, for these MBS item numbers, giving a total number of 967 procedures (HIC 2004).

¹ Total population in Australia was 18,972,350 as at August 2001. Source: Australian Bureau of Statistics.

There were 113 public hospital separations in New Zealand during the 2001-2002 period. Of these cases, 29 were day separations and the remaining 84 events had an average length of stay of 3.8 patient days.²

The number of patients who have surgical procedures may represent the 10 per cent of patients in whom conservative medical therapy is unsuccessful (Minor et al 2004).

Stage of development

The Meniett™ device has been available for private purchase in Australia for 2½ years. To date, approximately 150 units have been sold throughout Australia. Many of these purchases have occurred through the recommendation of the treating physician, although some have been patient motivated (personal communication, Medtronic).

Treatment Alternatives

Existing comparators

There are a number of medical and surgical therapies, which aim to reduce or ameliorate the symptoms of Ménière's disease, however there is no proven cure currently available. No gold standard exists for the treatment of Ménière's disease and most treatment regimens are tailored to the individual patient and their symptoms. Optimal treatment would be aimed at preventing vertigo, ameliorating tinnitus and reversing hearing loss. However, the majority of treatments are aimed principally at reducing vertigo, and have no effect on the prevention of long-term hearing impairment (Minor et al 2004; Saeed 1998).

Conservative measures aimed at preventing vertigo include dietary manipulation, pharmacological treatment and ablative treatment. Vertigo persists in approximately ten per cent of patients despite medical treatment. Surgical procedures are then indicated (Minor et al 2004).

Conservative medical treatments

A low sodium diet combined with the use of diuretics has been advocated for patients with Ménière's disease since the early 1930s (Minor et al 2004; Saeed 1998; Thai-Van et al 2001). The basis for this therapy is historical as there are no clinical data or controlled studies to provide support for the theory. As a low-sodium diet has little effect on plasma sodium levels, it is thought that this approach may improve symptoms by increasing aldosterone secretion, which in

² Source: From New Zealand Ministry of Health. Total population in New Zealand was 4,058,921 as at June 16 2004. Source: Statistics New Zealand.

turn may affect ion transportation in the ear, altering regulation of the endolymph (Thai-Van et al 2001).

Vasodilators, such as histamines, may be used prophylactically on the basis that Ménière's disease is associated with ischaemia of the stria vascularis. Betahistine is reported to increase cochlear blood flow and is currently the preferred anti-vertiginous drug. Several controlled clinical studies on patients administered betahistine have demonstrated short-term improvements in vertigo, hearing loss and tinnitus. Betahistine may be used as short-term treatment for acute attacks or for long-term maintenance (Thai-Van et al 2001; Saeed 1998).

Benzodiazepines are frequently used to treat acute attacks of Ménière's because of their sedative effect on the vestibulo-brain stem axis. Benzodiazepines bind to a specific site on the GABA (gamma-amino butyric acid) receptor, mediating inhibition of the vestibular response. Benzodiazepines are contraindicated in patients with chronic obstructive pulmonary disease and long-term use is not recommended as they may cause dependence, sedation and impaired memory (Thai-Van et al 2001; Saeed 1998).

Antiemetic agents, such as prochlorperazine and promethazine, are used to treat the symptoms of vertigo. All of these agents have sedative, anticholinergic and antiemetic properties, which may reduce stress and anxiety and impact on the symptoms of Ménière's (Saeed 1998).

Another alternative therapy for Ménière's disease is medical ablation. This occurs through the administration of vestibulotoxic agents, such as aminoglycosides, into the inner ear. Gentamicin is the most widely used agent for the selective ablation of the inner ear. Streptomycin may be used but cumulative doses carry a risk of cochlear toxicity and an increased incidence of ataxia and oscillopsia. In the past, aminoglycosides were delivered into the inner ear by transtympanic injection, and although effective, were associated with some damage to hearing. The development of transtympanic infusion pump microcatheters allow for greater control over dosing into the inner ear. Several studies have reported rates of elimination of vertigo of greater than 90 per cent with less impairment of vestibular or cochlear function (Kim & Toriumi 2003; Saeed 1998; Thai-Van et al 2001).

Surgical treatments

Surgical treatments of Ménière's disease are classified as either *non-destructive* procedures, which aim to act against the mechanism of hydrops and to conserve auditory function, or *destructive* procedures which may affect auditory function.

Non-destructive procedures:

Endolymphatic sac surgery involves decompression and drainage of the endolymphatic sac into the subarachnoid space or the mastoid cavity. Although this procedure is widely practised it is considered to be controversial and has been

termed placebo surgery, as the role that the sac plays in hydrops is unknown. Studies have reported complete resolution of vertigo in 50-75 per cent of cases following endolymphatic sac surgery, although recurrence is common in patients followed up for 10 years (Minor et al 2004; Saeed 1998; Thai-Van et al 2001).

Tympanostomy involves the insertion of a tympanostomy or ventilation tube through the tympanic membrane (eardrum) of the affected ear. Tympanostomy is viewed as a relatively minor operation, often performed in children for the relief of middle ear infections, and may be considered as a first surgical option in the treatment of Ménière's disease before more invasive surgery is considered (Saeed 1998; Thai-Van et al 2001; Minor et al 2004).

Vestibular nerve section may be performed with the aim of disassociating the affected labyrinth from the brain stem at the same time as preserving the patient's hearing by sectioning the vestibular nerve from the vestibular apparatus. This procedure carries a high level of risk due to the proximity of the facial nerve to the posterior cranial fossa. Despite being effective at controlling vertigo in 90-95 per cent of patients, the potential complications of this procedure include facial nerve paralysis and hearing loss. During the recovery period the brain adapts to the lack of vestibular input from the operated side and normal activity can be resumed (Thai-Van et al 2001; Saeed 1998).

Other non-destructive surgical options include sacculotomy, ultrasound treatment, cryosurgical treatment and cervical sympathectomy (Saeed 1998).

Destructive procedures:

When all other avenues have been exhausted, destructive surgical procedures may be considered for the treatment of Ménière's disease. Excision of the labyrinth is indicated for patients with poor or non-beneficial hearing. Surgical labyrinthectomy suppresses all information coming from the diseased labyrinth and sacrifices the cochlear apparatus, leading to total permanent deafness (Thai-Van et al 2001; Saeed 1998).

Other destructive surgical techniques include cochleosacculotomy, vestibulocochlear neurectomy and translabyrinthine vestibular neurectomy (Saeed 1998).

Selection of the surgical procedure is dependent on both the patient's and clinician's preferences. Although most clinicians will attempt to preserve any hearing, however poor (Saeed 1998).

Effectiveness

Five studies reported on the effectiveness of the Meniett™ device and one study reported on a precursor of Meniett™ (Densert et al 1997) for the treatment of Ménière's disease (Table 1).

The good quality study by Gates et al (2004) reported on the difference between patients treated with the Meniett™ device and a placebo group after a follow-up period of four months (level II intervention evidence). There was a significant decrease in the number of vertigo attacks ($p=0.048$) and the number of days lost from work due to sickness ($p=0.048$) between the Meniett™ and placebo groups after treatment. However, it should be noted that 12/67 (18%) of patients had an increased number of vertigo attacks during follow-up compared to baseline. There was no significant difference in hearing thresholds or electrocochleography between the two groups.

Another good quality study by Densert et al (1997) found that there was no improvement in any of the measured elements of electrocochleography after the implantation of the ventilation tube alone (level II intervention evidence). Significant improvements *were* reported for all elements of electrocochleography before and after the use of low-pressure pulses - in conjunction with the ventilation tube - in the treatment group. There was no significant difference before and after sham treatment in the placebo group. In addition, there was a statistically significant difference in the mean change between the treatment and placebo groups for all of the electrocochleographic elements measured. Although this study was of good quality, it was conducted on a small patient group ($n=39$) and follow-up was very short at two weeks. In addition this study only reported on electrocochleographic responses and not patient symptoms such as vertigo.

A further high level study by Ödkvist et al (2000) was of good quality, but follow-up was short (two weeks) (level II intervention evidence). A significant decrease in the number of vertigo episodes and a significant improvement in qualitative function (work, rest and social life) and electrocochleographic readings was reported for the treatment group compared to the placebo group, although no data were presented. The mean hearing improvement was at frequencies of 500, 1,000 and 2,000 Hz was 4dB, 5dB and 3dB, respectively. This improvement was statistically significant at only 500 ($p < 0.03$) and 1,000 Hz ($p < 0.01$).

The uncontrolled study by Barbara et al (2001) (level IV intervention evidence) reported a significant reduction in the number of vertigo episodes after the insertion of a ventilation tube alone ($p=0.001$) as well as after treatment with the Meniett™ device ($p < 0.001$). However the difference in the number of vertigo episodes associated with the ventilation tube alone compared to the ventilation tube plus treatment with Meniett™ was not statistically significant. The follow-up

period for this study was again short with only 20 days of ventilation tube alone followed by 20 days treatment with Meniett™.

Another uncontrolled study by Gates and Green (2002) had a longer follow-up period (mean 8 months) but was conducted on a small number of patients with intractable vertigo (n=10) (level IV intervention evidence). Complete control of vertigo was reported in 90 per cent of patients, with the remaining patient reporting a 50 per cent reduction in the frequency and severity of vertigo. Patients who ceased use of the Meniett™ device due to either blocked ventilation tubes or who did not use the device the prescribed number of times, experienced a recurrence of vertigo. Vertigo control took between one to three weeks, although one patient with an endolymphatic shunt did not experience remission of symptoms until four weeks. In addition, patients experienced a statistically significant 9dB improvement in hearing ($p=0.046$).

Table 1 Effectiveness of the Meniett™ device

Study	Intervention level of evidence	Study design	Study population	Outcomes
Precursor to Meniett™				
Densert et al (1997)	II	RCT	39 patients with a diagnosis of definite MD Meniett™ precursor n=21 Placebo n=18 Follow-up 2 weeks	<p>Electrocochleography</p> <p>SP/AP (%)^a Within group difference compared to baseline Treatment group $p < 0.0005$ Placebo group NS Difference in mean change between treatment vs placebo = $p < 0.0005$</p> <p>Width (ms)^a Within group difference compared to baseline Treatment group $p = 0.013$ Placebo group NS Difference in mean change between treatment vs placebo = $p < 0.025$</p> <p>1 kHz SP (-μV)^{ab} Within group difference compared to baseline Treatment group $p < 0.0005$ Placebo group NS Difference in mean change between treatment vs placebo = $p < 0.002$</p> <p>2 kHz SP (-μV)^{ab} Within group difference compared to baseline Treatment group $p < 0.0005$ Placebo group NS Difference in mean change between treatment vs placebo = $p < 0.0005$</p>

Meniett™				
Gates et al (2004), United States	II	RCT	67 patients with a diagnosis of definite Ménière's disease Meniett™ n=34 Placebo n=33 Follow-up 4 months	<p>Proportion of vertigo attacks ^c Difference between treatment vs placebo <i>baseline</i> $p=0.77$, NS Difference between treatment vs placebo <i>after treatment</i> $p=0.048$ 12/67 (17.9%) patients experienced more vertigo days during follow-up compared to baseline</p> <p>Proportion of sick days ^c Difference between treatment vs placebo <i>baseline</i> $p=0.89$, NS Difference between treatment vs placebo <i>after treatment</i> $p=0.048$</p> <p>Hearing thresholds dB ^a (means of frequencies 0.25, 0.5 and 1 kHz) Difference between treatment vs placebo $p=0.058$, NS</p> <p>Electrocochleography Data not shown, no change in electrographic results</p>
Ödkvist et al (2000), Sweden	II	RCT	56 patients with a diagnosis of definite Ménière's disease Meniett™ n=31 Placebo n=25 Follow-up 2 weeks	<p>Vertigo episodes Treatment group: statistically significant reduction in frequency and intensity of vertigo, dizziness, aural pressure and tinnitus, (data not shown) Placebo group: no significant difference ($p>0.05$)</p> <p>Functionality (work, rest, driving, social life) Treatment group: statistically significant improvement, (data not shown) Placebo group: no significant difference ($p>0.05$)</p> <p>Hearing Treatment group: hearing significantly improved at 500 Hz ($p<0.03$) and 1,000 Hz ($p<0.01$) post-treatment Placebo group: no significant improvement in hearing</p> <p>Electrocochleographic recordings Treatment group: significant decrease in SP potentials at 1,000 and 2,000 Hz post-treatment (data not shown) Placebo group: no significant difference ($p>0.05$)</p>

Barbara et al (2001), Italy	IV	Case series	24 patients with a diagnosis of definite MD Follow-up 40 days	Episodes of vertigo Difference in mean vertigo episodes before and after VT alone : Wilcoxon $z = -3.33, p=0.001$ Difference in mean vertigo episodes before and after Meniett™ : Wilcoxon $z = -3.63, p=0.000$ No difference between effect of VT alone and VT + Meniett™
Densert and Sass (2001), Sweden	IV	Case series	37 patients with a diagnosis of definite MD Follow-up 18 -24 months	Number of Vertigo episodes Stage 1 & 2 (n=9) Difference in mean vertigo episodes before and after Meniett™ : Wilcoxon $p=0.012$ Stage 3 (n=18) Difference in mean vertigo episodes before and after Meniett™ : Wilcoxon $p<0.0005$ Stage 4 (n=10) Difference in mean vertigo episodes before and after Meniett™ : Wilcoxon $p=0.008$ Hearing levels dB (means of frequencies 0.5, 1, 2, and 3 kHz) Stage 1 & 2 (n=9) Difference in mean vertigo episodes before and after Meniett™ : Wilcoxon NS Stage 3 (n=18) Difference in mean vertigo episodes before and after Meniett™ : Wilcoxon $p=0.002$ Stage 4 (n=10) Difference in mean vertigo episodes before and after Meniett™ : Wilcoxon NS Functionality Stage 1 & 2 (n=9) Difference in mean vertigo episodes before and after Meniett™ : Wilcoxon $p=0.011$ Stage 3 (n=18) Difference in mean vertigo episodes before and after Meniett™ : Wilcoxon $p<0.0005$ Stage 4 (n=10) Difference in mean vertigo episodes before and after Meniett™ : Wilcoxon $p=0.007$

Gates and Green, (2002), United States	IV	Case series	<p>10 patients with a diagnosis of definite MD</p> <p>Mean follow-up 8 months (range 3-11 months)</p>	<p>Vertigo (n=10)</p> <p>9/10 (90%) patients had complete control over vertigo</p> <p>1/10 (10%) patients described a 50% reduction in vertigo frequency and severity</p> <p>Hearing status (n=8)</p> <p>5/8 (62.5%) improved hearing</p> <p>1/8 (12.5%) no change in hearing</p> <p>2/8 (25%) slight worsening of hearing</p> <p>Overall there was a statistically significant 9-dB improvement in the PTA, $t = 2.42$, $p = 0.046$</p>
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MD = Ménière's disease, VT = ventilation tube, SP/AP: SP = summing potential component and AP = action potential, of the electrocochleographic recordings, PTA = pure tone average, NS = not significant, ^a values are mean (standard deviation), ^b burst evoked SP (summing potential) at 1 and 2 kHz, ^c values are median (25th – 75th percentile), p values determined by Mann Whitney U test

Safety

No safety outcomes were reported in the higher quality papers (level II intervention evidence). Two studies reported on complications associated with the use of the Meniett™ device (level IV intervention evidence) (Table 2). Neither of these studies had a control group, however both had long follow-up periods compared to the other studies included for assessment in this report. It would be expected that problems associated with the implantation of a ventilation tube would occur in the immediate post-operative stage (eg transient otorrhea) or over a longer period of time (eg infection, perforated tympanic membrane or replacement of ventilation tube).

The smaller case series by Gates and Green (2002) reported 2/10 (20%) patients required the replacement of the ventilation tube after 3 months and vertigo symptoms returned during this time. Other complications including a blood clot and otorrhea were considered minor. The study by Densert and Sass (2001) had the longest follow-up time (18 to 24 months) and reported that, on average, the ventilation tube was re-inserted twice per patient. In addition 5/37 (13.5%) patients experienced a middle ear infection, which was treated with antibiotics and required the replacement of the ventilation tube.

Although not direct evidence of the safety of the Meniett™ device, a meta-analysis by Kay et al (2001), describing the sequelae (level I intervention evidence) of the long-term implantation of ventilation tubes, is relevant (Kay et al 2001). Long-term tubes were associated with a higher incidence of otorrhea, perforation of the tympanic membrane and cholesteatoma. Otorrhea occurred 2.2 times more frequently in ears with long-term compared to short-term ventilation tubes (33% vs 15%) ($p < 0.001$). The risk of having otorrhea, requiring the replacement of the ventilation tube, increased 7.7 times with the presence of a long-term ventilation tube ($p < 0.001$). In addition cholesteatoma rates were 70 per cent higher with long-term ventilation tube insertion ($p = 0.041$).

Table 2 Complications association with Meniett™

Gates and Green, (2002), United States	IV	Case series	10 patients with a diagnosis of definite MD Mean follow-up 8 months (range 3-11 months)	1/10 (10%) delayed device use due to obstruction of VT by blood clot 2/10 (20%) developed otorrhea (discharge), symptoms cleared after topical therapy 2/10 (20%) required replacement of ventilation tube after 3 months
Densert and Sass (2001), Sweden	IV	Case series	37 patients with a diagnosis of definite MD Follow-up 18-24 months	5/37 (13.5%) patients experienced middle ear infections, treated with replacement VT and antibiotics 0/37 (0%) permanent perforations of tympanic membrane 0/37 (0%) prolonged discharge from middle ear Ventilation tubes were replaced on average twice per patient during the follow-up period

MD = Ménière's disease, VT = ventilation tube

Potential Cost Impact

Cost Analysis

There are currently no cost-effectiveness data available for the utilisation of the Meniett™ device.

Simple costings

The Meniett™ device is available under Schedule 5; Appendix C. Currently hospitals in Australia purchase the device from Medtronic for approximately A\$5,000 plus GST. Patients with private health insurance, or those covered by the Department of Veteran Affairs can claim a full rebate from their health insurance providers (personal communication, Medtronic). Before using the Meniett™ device, patients must first have a ventilation tube or grommet inserted into their middle ear. This procedure is available through the MBS (item number 41632) at a fee of \$202.65, however as the Meniett™ device is provided by specialist otolaryngologists this procedure may have to be performed in a private hospital, which may attract a further fee depending on the patient's private health cover status. It is recommended that patients are trained with the device by their treating clinician, which may incur either the cost of a specialist consultation in a public hospital (MBS item number 104, fee \$72.60) or the cost of a private consultation.

Ethical Considerations

Informed Consent

The Meniett™ device raises a number of difficult and complex ethical issues, which do not necessarily all point in the same direction if a decision needs to be made about the ethical acceptability of the device.

First, the lack of clear and unequivocal evidence of effectiveness places particular obligations on clinicians when providing patients with information about the Meniett™ device and seeking their consent to treatment. Clinicians have an ethical obligation to inform patients that treatment with the Meniett™ device is controversial and that there is insufficient evidence to assess its effectiveness in treating Ménière's disease. Even if they do this, the fact that a clinician offers the treatment is likely to have a profound impact on patients' likelihood of consenting to use the device.

Second, the existence of a vocal consumer and patient support group can complicate decisions about the implementation of new technologies when those technologies are controversial or lack solid evidence of effectiveness. For example, there has been a robust ethical debate about the use of experimental treatments for patients with AIDS. On the one hand, the principle of beneficence obliges clinicians to provide treatments, which are likely to benefit patients, and allows some discretion in the case of treatments that have not been proven effective. On the other, consumer groups have argued that the principle of respect for patient autonomy obliges us to allow patients to make their own decisions about whether they will use treatments which are experimental or controversial. At the very least, we have an ethical obligation to seek and take into account the views of consumer and patients support groups.

Access Issues

Finally, there are broader access and equity issues. This technology is currently offered as a Schedule 5, Appendix C (prosthesis rebate group) product and is available from specialist otolaryngologists. Thus it is already available to one group in the population (those who can afford to pay) and not to others. Thus, a decision *not* to make the device available in the public sector perpetuates inequity.

Patients with access to private health insurance can claim the cost of the Meniett™ device as a full rebate (rebate code MC 256) from all private health insurers. In addition, the Department of Veteran Affairs has a rebate scheme for the Meniett™ device, allowing eligible patients to access the device at no cost. Medtronic XOMED has a short-term loan scheme for patients without private health insurance, where the device is made available to patients for three months. If the device is found to be effective, patients may negotiate a payment plan with Medtronic XOMED (personal communication, Medtronic XOMED).

In addition, because the device is available only through specialist otolaryngologists, who primarily operate in larger metropolitan areas, it is unlikely that this product would be available in rural or remote areas of Australia due to the lack of treating specialists in these areas.

Training and Accreditation

Training

Patients are required to undergo initial training in the use of the Meniett™ device by their physicians. Training for physicians is provided by Medtronic XOMED.

Clinical Guidelines

In Australia there are currently no clinical practice guidelines established for the treatment of Ménière's disease. The American Academy of Otolaryngology – Head and Neck Surgery have produced guidelines for the diagnosis and the evaluation of therapy of Ménière's disease. Due to a lack of clinical data clearly establishing the effectiveness of one treatment over another, therapy recommendations are based on the empirical observations of clinicians and therefore there are no established guidelines for the treatment of patients with Ménière's, whatever the stage (Thai-Van et al 2001; Thorp et al 2003).

Limitations of the Assessment

Methodological issues and the relevance or currency of information provided over time are paramount in any assessment carried out in the early life of a technology.

Horizon Scanning forms an integral component of Health Technology Assessment. However, it is a specialised and quite distinct activity conducted for an entirely different purpose. The rapid evolution of technological advances can in some cases overtake the speed at which trials or other reviews are conducted. In many cases, by the time a study or review has been completed, the technology may have evolved to a higher level leaving the technology under investigation obsolete and replaced.

An Horizon Scanning Report maintains a predictive or speculative focus, often based on low level evidence, and is aimed at informing policy and decision makers. It is not a definitive assessment of the safety, effectiveness, ethical considerations and cost effectiveness of a technology.

In the context of a rapidly evolving technology, an Horizon Scanning Report is a 'state of play' assessment that presents a trade-off between the value of early, uncertain information, versus the value of certain, but late information that may be of limited relevance to policy and decision makers.

This report provides an assessment of the current state of development of the Meniett™ device for the treatment of Ménière's disease, its present and potential

use in the Australian public health system, and future implications for the use of this technology.

Search Strategy used for the Report

The medical literature (Table 4) was searched utilising the search terms outlined in Table 3 to identify relevant studies and reviews, until December 2004. In addition, major international health assessment databases were searched.

Availability and Level of Evidence

Five studies were included in this report to assess the safety, effectiveness and cost-effectiveness of the Meniett™ device for the treatment of Ménière's disease. In addition, one study by Densert et al (1997), which utilised a precursor of the Meniett™ device was also included for assessment. Profiles of these studies are provided in Appendix B. In total, three level II and three level IV (intervention level of evidence) studies were included for assessment of effectiveness (Table 1). Of these six studies, two reported on safety outcomes of patients fitted with the ventilation tubes necessary for the functioning of the Meniett™ device (level IV intervention evidence) (Table 2). Gates and Green (2002) and Gates et al (2004) received funding from Medtronic Xomed to conduct their studies.

Table 3 Search terms utilised

Search terms
EmTree Headings Meniere Disease, Inner Ear Disease, Vestibular Disorder, Hearing Disorder
Text words Meniere*, Meniere dis*, inner ear dis*, hearing loss, vertigo, tinnitus, Meniett, Meniett Device
Limits English

Table 4 Literature sources utilised in assessment

Source	Location
<i>Electronic databases</i>	
AustHealth	University library
Australian Medical Index	University library
Australian Public Affairs Information Service (APAIS) - Health	University library
Cinahl	University library
Cochrane Library – including, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials (CENTRAL), the Health Technology Assessment Database, the NHS Economic Evaluation Database	University library
Current Contents	University library
Embase	Personal subscription
Pre-Medline and Medline	University library
ProceedingsFirst	University library
PsycInfo	University library
Web of Science – Science Citation Index Expanded	University library
<i>Internet</i>	
Current Controlled Trials metaRegister	http://controlled-trials.com/
Health Technology Assessment international	http://www.htai.org
International Network for Agencies for Health Technology Assessment	http://www.inahta.org/
Medicines and Healthcare products Regulatory Agency (UK).	http://www.medical-devices.gov.uk/
National Library of Medicine Health Services/Technology Assessment Text	http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat
National Library of Medicine Locator Plus database	http://locatorplus.gov
New York Academy of Medicine Grey Literature Report	http://www.nyam.org/library/grey.shtml
Trip database	http://www.tripdatabase.com
U.K. National Research Register	http://www.update-software.com/National/
US Food and Drug Administration, Center for Devices and Radiological Health.	http://www.fda.gov/cdrh/databases.html
Websites of Specialty Organisations	
Vestibular Disorders Association (VEDA)	http://www.vestibular.org/index.html
Ménière's Resource and Information Centre	http://www.menieres.org.au/
Australian and New Zealand Head and Neck Society	http://www.anzhns.org/
American Academy of Otolaryngology-Head and Neck Surgery	http://www.entnet.org/index2.cfm

Sources of Further Information

No further sources of information have been identified.

Conclusions

It is difficult to ascertain the number of people currently suffering from Ménière's disease in Australia. The Victorian Ménière's Disease Resource and Information Centre estimates that Ménière's disease affects one in every thousand Australians.

No "gold standard" for the treatment for Ménière's disease currently exists. A number of treatment alternatives are available that include non-invasive and conservative treatments such as dietary control, administration of vasodilators or medical ablation. If conservative treatment fails, surgical treatment may be considered and may include procedures that are non-destructive or destructive to auditory function.

The Meniett™ is a portable, patient administered device, which delivers low frequency and low-pressure pulses to the middle ear via an implanted ventilation (grommet) tube. It is thought that a positive pressure change in the inner ear compartment may lead to an increased exchange of inner ear fluids. This would result in a decrease in endolymphatic fluid volume, ameliorating symptoms of Ménière's disease such as vertigo and nausea.

Of the studies included in this assessment, three were good quality studies describing patients randomised to treatment with the Meniett™, or a precursor to this device, compared to a placebo group (level II intervention evidence) and three were uncontrolled case series (level IV intervention evidence). Three studies had very short follow-up periods (14 to 40 days) and as one study reported control of vertigo took 1 to 3 weeks, short-term studies may not be sufficient to evaluate the effect of Meniett™ on patients fully. One good quality study (Ödkvist et al 2000) was poorly reported with no data presented. An initial study reporting on the precursor to the Meniett™ device documented electrocochleographic readings but did not report on patient symptoms such as vertigo.

Two studies reported a statistically significant reduction from baseline of mean vertigo episodes for patients receiving treatment with the Meniett™ device compared to placebo (level II intervention evidence). However, only one of these studies reported data ($p=0.048$). It should be noted that in this study, despite a significant reduction of vertigo episodes for the patient group as a whole, a number of patients (12/67, 18 per cent) experienced *more* vertigo attacks during follow-up when compared to baseline.

Interestingly one short-term follow-up (40 days), before and after study reported a clinically significant reduction in the number of vertigo episodes after the insertion of the ventilation tube alone ($p = 0.001$) as well as after treatment with the Meniett™ device ($p < 0.001$) (level IV intervention evidence). In this study there was no significant difference between the effect of ventilation tube alone and the combined effect of ventilation tube in conjunction with treatment with the

Meniett™. One before and after study noted that symptoms of vertigo returned in patients who ceased using the Meniett™ (level IV intervention evidence).

Three high quality studies reported on either hearing levels or electrocochleographic readings after treatment with Meniett™ compared to placebo (level II intervention evidence). Results varied widely, depending on the hearing frequencies analysed. One study reported a statistically significant improvement in the difference of mean electrocochleographic readings in the Meniett™ treatment group compared to the placebo group ($p<0.001$). However, another study reported no significant difference. Similar results were reported for the before and after studies.

Adverse events associated with the use of the Meniett™ device, or more specifically the insertion of the ventilation tube, were reported in only two studies. Middle ear infections were common (13.5 per cent of patients) as was the replacement of the ventilation tube over time, which is an expected side effect with long-term implantation of ventilation tubes.

The Meniett™ device is currently available as a Schedule 5 product and patients may access the device when treated by specialist otolaryngologists. The device costs approximately A\$5,000. Insertion of a ventilation tube in the middle ear is necessary for the Meniett™ to function, and this procedure is available on the Medicare Benefits Schedule.

In summary, Meniett™ appears to benefit most, but not all patients in terms of reducing the number of vertigo episodes. It is difficult to ascertain if treatment with Meniett™ has a positive effect on the hearing levels of patients. It appears that treatment with Meniett™ would have to be continued in the long term for a sustained reduction in symptoms and as yet the longest follow-up study is 18 to 24 months. Long-term use of Meniett™ may be associated with adverse events associated with long-term implantation of tympanic tubes such as infection and the need for regular replacement of the tube.

Appendix A

Interim designation of levels of evidence*

Level	Intervention §	Diagnosis **	Prognosis	Aetiology †††	Screening
I *	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	An independent, blinded comparison with reference standard, among an appropriate population of consecutive patients, conducted at a similar point in time	A prospective cohort study ***	A prospective cohort study	A randomised controlled trial
III-1	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)	An independent, blinded comparison with reference standard, among non-consecutive patients or confined to a narrow population of study patients or reference standard conducted at a different point in time §§	All or none §§§	All or none §§§	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)
III-2	A comparative study with concurrent controls: Non-randomised, experimental trial † Cohort study Case-control study Interrupted time series with a control group	An independent, blinded comparison with an appropriate population of patients, but the same reference standard not applied to all study patients ††	Analysis of prognostic factors amongst untreated control patients in a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls: Non-randomised, experimental trial Cohort study Case-control study
III-3	A comparative study without concurrent controls: Historical control study Two or more single arm study †	Reference standard and test not independently applied or not blinded	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: Historical control study Two or more single arm study

	Interrupted time series without a parallel control group				
IV	Case series with either post-test or pre-test/post-test outcomes	Diagnostic case-control study ^{††}	Case series, or cohort study of patients at different stages of disease	A cross-sectional study	Case series

^{*} A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence.

[§] Definitions of these study designs are provided on pages 7-8, *NHMRC (2000). How to use the evidence: assessment and application of scientific evidence.*

[†] This also includes controlled before-and-after study studies, as well as indirect comparisons (i.e. utilise A vs B and B vs C, to determine A vs C).

[‡] Comparing single arm studies i.e. case series from two studies.

^{**} The dimensions of evidence apply only to studies of diagnostic accuracy. To assess the effectiveness of a diagnostic test there also needs to be a consideration of the impact of the test on patient management and health outcomes. See *MSAC (2004) Guidelines for the assessment of diagnostic technologies.*

^{§§} In cases where the reference standard results are likely to be unaffected by a difference in the time of testing (e.g. genetic testing), and this is the only factor indicating Level III-1 status, the study should be assigned a level II status.

^{††} Includes studies with differential verification and/or partial verification.

^{†††} A group of patients already known to have the disease compared with a separate group of normal/healthy people known to be free of the disease. In this situation patients with borderline or mild expressions of the disease, and conditions mimicking the disease are excluded, which can lead to exaggeration of both sensitivity and specificity. This is called spectrum bias because the spectrum of study participants will not be representative of patients seen in practice.

^{***} At study inception the cohort is either non-diseased or all at the same stage of the disease.

^{§§§} All or none of the people with the risk factor(s) experience the outcome. For example, no smallpox develops in the absence of the specific virus; and clear proof of the causal link has come from the disappearance of small pox after large-scale vaccination.

^{††††} If it is possible and/or ethical to determine a causal relationship using experimental evidence, then the "Intervention" hierarchy of evidence should be utilised. If it is only possible and/or ethical to determine a causal relationship using observational evidence (i.e. cannot allocate groups to a potential harmful exposure, such as nuclear radiation), then the "Aetiology" hierarchy of evidence should be utilised.

Note 1: Assessment of comparative harms/safety should occur according to the hierarchy presented for each of the research questions, with the proviso that this assessment occurs within the context of the topic being assessed. Some harms are rare and cannot feasibly be captured within randomised controlled trials; physical harms and psychological harms may need to be addressed by different study designs; harms from diagnostic testing include the likelihood of false positive and false negative results, harms from screening include the likelihood of false alarm and false reassurance results.

Note 2: When a level of evidence is attributed in the text of a document, it should also be framed according to its corresponding research question e.g. level II intervention evidence; level IV diagnostic evidence; level III-2 prognostic evidence etc.

Hierarchies adapted and modified from: NHMRC 1999; Bandolier 1999; Lijmer et al. 1999; Phillips et al. 2001

* This hierarchy of evidence is currently being trialled by the NHMRC

Appendix B

Profiles of the studies included for assessment for the safety and effectiveness of the Meniett™ device for the treatment of Ménière's disease.

Intervention level of evidence	Study	Location	Study design	Study population	Outcome assessed	Length of follow-up
IV	Barbara, M. Consagra, C. Monini, G. Harguindey, A. Vestri, A. Filipo, R. (2001)	Rome, Italy	Case series	24 patients with a diagnosis of definite MD, duration ranging from 1-20 years. Patients with symptoms ≤ 3 years = "young" patients (n=10), those with symptoms ≥ 3 years = "old" patients (n=14) Age range 30-64 years	Number of symptomatic episodes of vertigo Auditory symptoms	20 days VT alone 20 days VT plus Meniett™ device Follow-up = 40 days total
IV	Densert, B. and Sass, K. (2001)	Halmstad, Sweden	Case series	37 patients with a diagnosis of definite MD, hearing loss between 25-80 dB PTA and vertigo attacks with duration >20 minutes	Vertigo Hearing thresholds Functionality	Follow-up 18 -24 months
IV	Gates, G.A. and Green, J.D. (2002)	Washington, United States	Case series	10 patients with a diagnosis of definite MD	Vertigo Hearing Improvement in symptoms	Mean follow-up 8 months (range 3-11 months)
II	Gates, G.A. Green, J.D. Tucci, D.L. Telian, S.A. (2004)	Washington, United States	RCT	67 patients with a diagnosis of definite MD	Number of symptomatic episodes of vertigo Hearing Electro-cochleography	Follow-up 4 months

II	Ödkvist, L. Arlinger, S. Billermarck, E. Densert, B. Lindholm, S. WallQvist, J. (2000)	Linköping, Halmstad, Kalmar and Jönköping, Sweden	RCT	56 patients with a diagnosis of definite MD, randomised to treatment with Meniett™ (n=31) or placebo (n=25) Age range 20-65 years Hearing loss between 20- 65 dB	Number of symptomatic episodes of vertigo Hearing Electro- cochleography	Follow-up 2 weeks
Precursor to Meniett™ device						
II	Desert, B. Densert, O. Arlinger, S. Sass, K. Ödkvist, L. (1997)	Lund and Linköping, Sweden	RCT	39 patients with a diagnosis of definite MD, randomised to treatment with Meniett™ precursor (n=21) or placebo (n=18)	Electro- cochleography	Follow-up 2 weeks

MD = Ménière's disease, VT = ventilation tube, RCT = randomised controlled trial, dB = decibels, PTA = pure tone averages

References

- AIHW (2004). *AIHW National Hospital Morbidity Database* [Internet]. Australian Institute of Health and Welfare. Available from: <http://www.aihw.gov.au/cognos/cgi-bin/ppdscgi.exe?DC=Q&E=/AHS/principaldiagnosis0102> [Accessed 4th January 2005].
- Bandolier editorial (1999). *Diagnostic testing emerging from the gloom?* [Internet]. Bandolier. Available from: <http://www.jr2.ox.ac.uk/bandolier/band70/b70-5.html> [Accessed 2004].
- Barbara, M., Consagra, C. et al (2001). 'Local pressure protocol, including Meniett, in the treatment of Meniere's disease: Short-term results during the active stage', *Acta Oto-Laryngologica*, 121 (8), 939-944.
- Densert, B., Arlinger, S. & Odkvist, L. M. (2000). 'New technology to control symptoms in Meniere's disease', *Acta Oto-Laryngologica*, 120 (5), 672-674.
- Densert, B., Densert, O. et al (1997). 'Immediate effects of middle ear pressure changes on the electrocochleographic recordings in patients with Meniere's disease: a clinical placebo-controlled study', *American Journal of Otolaryngology*, 18 (6), 726-733.
- Densert, B. & Sass, K. (2001). 'Control of symptoms in patients with Meniere's disease using middle ear pressure applications: two years follow-up', *Acta Oto-Laryngologica*, 121 (5), 616-621.
- FDA (1999). *510(k) Summary* [Internet]. United States Food and Drug Administration. Available from: <http://www.fda.gov/cdrh/pdf/k991562.pdf> [Accessed 5th January 2005].
- Gates, G. A. & Green Jr., J. D. (2002). 'Intermittent pressure therapy of intractable Meniere's disease using the Meniett device: A preliminary report', *Laryngoscope*, 112 (8 I), 1489-1493.
- Gates, G. A., Green Jr., J. D. et al (2004). 'The effects of transtympanic micropressure treatment in people with unilateral Meniere's disease', *Archives of Otolaryngology - Head and Neck Surgery*, 130 (6), 718-725.
- Gibson, B. (2001). 'Meniere's Disease', *Current Therapeutics*, August, 46-49.
- HIC (2004). *HIC Statistical Reporting* [Internet]. Australian Government Health Insurance Commission. Available from: http://www.hic.gov.au/providers/health_statistics/statistical_reporting.htm [Accessed 4th January 2005].
- Kay, D. J., Nelson, M. & Rosenfeld, R. M. (2001). 'Meta-analysis of tympanostomy tube sequelae', *Otolaryngology and Head and Neck Surgery*, 124 (4), 374-380.
- Kim, D. W. & Toriumi, D. M. (2003). 'What's new in otolaryngology - Head and neck surgery', *Journal of the American College of Surgeons*, 197 (1), 97-114.
- Kotimaki, J., Sorri, M. et al (1999). 'Prevalence of Meniere disease in Finland', *Laryngoscope*, 109 (5), 748-753.

- Lijmer, J. G., Mol, B. W. et al (1999). 'Empirical evidence of design-related bias in studies of diagnostic tests.' *Journal of the American Medical Association*, 282 (11), 1061-1066.
- Medtronic XOMED (2004). *Meniett.com* [Internet]. Medtronic XOMED. Available from: <http://www.meniett.com/> [Accessed 4th January 2005].
- Ménière's Support Group of Victoria (2004). *The Ménière's Resource and Information Centre* [Internet]. Available from: <http://www.menieres.org.au> [Accessed 4th January 2005].
- Minor, L. B., Schessel, D. A. & Carey, J. P. (2004). 'Meniere's disease', *Current Opinion in Neurology*, 17 (1), 9-16.
- NHMRC (1999). *A guide to the development, implementation and evaluation of clinical practice guidelines*, National Health and Medical Research Council, Commonwealth of Australia, Canberra, ACT.
- Odkvist, L. M., Arlinger, S. et al (2000). 'Effects of middle ear pressure changes on clinical symptoms in patients with Meniere's disease - A clinical multicentre placebo-controlled study', *Acta Oto-Laryngologica, Supplement*, - (543), 99-101.
- Phillips, B., Ball, C. et al (2001). *Levels of Evidence and Grades of Recommendations* [Internet]. Centre for Evidence-Based Medicine, Oxford, UK. Available from: Available from: http://www.cebm.net/levels_of_evidence.asp [Accessed 28th January 2004 2004].
- Saeed, S. R. (1998). 'Fortnightly review. Diagnosis and treatment of Meniere's disease', *British Medical Journal*, 316 (7128), 368-372.
- Salt, A. N. (2003). *Cochlear fluids* [Internet]. Cochlear Fluids Research Laboratory, Department of Otolaryngology, Washington School of Medicine. Available from: <http://oto.wustl.edu/cochlea/> [Accessed 5th January 2005].
- Thai-Van, H., Bounaix, M. J. & Fraysse, B. (2001). 'Meniere's disease: pathophysiology and treatment', *Drugs*, 61 (8), 1089-1102.
- Thorp, M. A., Shehab, Z. P. et al (2003). 'The AAO-HNS Committee on Hearing and Equilibrium guidelines for the diagnosis and evaluation of therapy in Meniere's disease: have they been applied in the published literature of the last decade?' *Clinical Otolaryngology and Allied Sciences*, 28 (3), 173-176.
- Vestibular Disorders Association (2004). *Inner ear anatomy* [Internet]. Vestibular Disorders Association. Available from: <http://www.vestibular.org/index.html> [Accessed 11th January 2005].