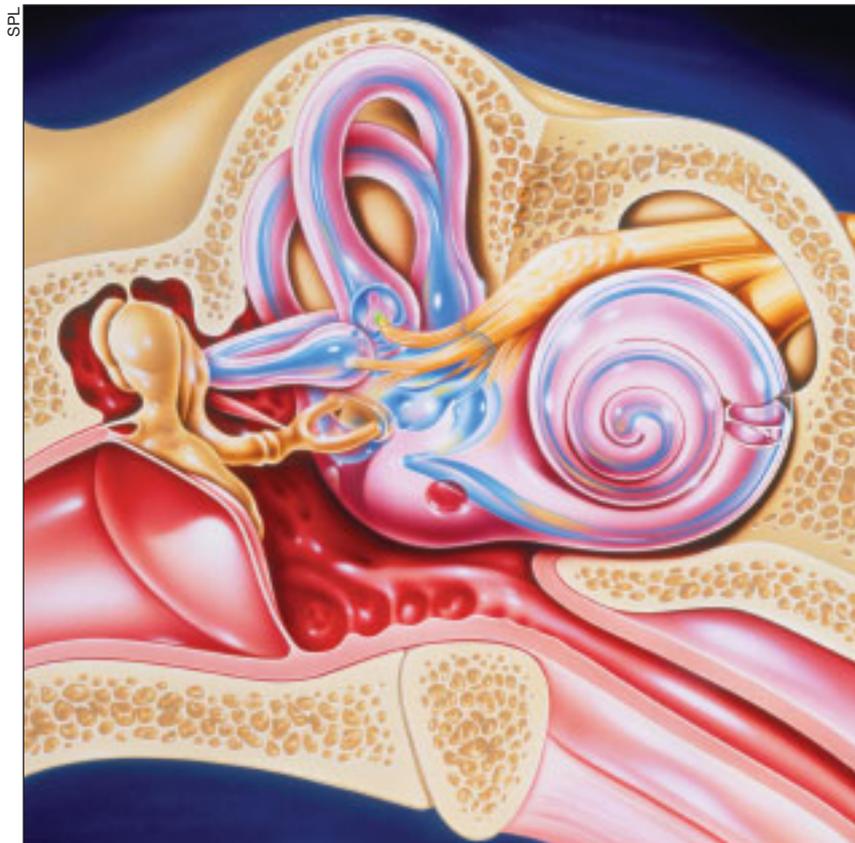


# What role for betahistine in the treatment of Ménière's disease?

John Phillips BSc, FRCS and Peter Prinsley BMedSci, FRCS



**Figure 1.** Ménière's disease is commonly treated with betahistine, which is proposed to cause vasodilatation in ischaemic areas of the stria vascularis and dark cells

The authors discuss the diagnostic criteria for Ménière's disease and the evidence base and cost implications for initiating betahistine, a potentially life-long treatment.

**B**etahistine dihydrochloride is an oral preparation of a histamine precursor marketed in Europe as a specific treatment for Ménière's disease. Its proposed mode of action is to cause vasodilatation in ischaemic areas of the stria vascularis and dark cells – the areas implicated in the pathogenesis of Ménière's disease.

There are a number of flaws in the proposed pharmacological treatment of Ménière's disease. One proposed mechanism for the pathophysiology for Ménière's dis-

ease is endolymphatic hydrops. However, any drug that increases blood flow to the organs responsible for producing endolymph should theoretically worsen hydrops.<sup>1,2</sup> Secondly, it seems to be a contradiction to treat patients with a histamine for a disease that is also relieved by systemic antihistamines.<sup>3</sup>

A systematic evaluation of the clinical role of betahistine for the treatment of Ménière's disease has been undertaken.<sup>4</sup> Only one grade B study and four grade C

studies were found, none of which produced convincing evidence for its use.

## Diagnosis

A definitive diagnosis of Ménière's according to the American Academy of Otolaryngology Head and Neck Surgery guidelines requires audiometrically documented hearing loss on at least one occasion and exclusion of other causes.<sup>5</sup> Such patients would require imaging of the acoustic

nerve to exclude an intracranial tumour.<sup>6</sup>

Other conditions may mimic the symptoms of Ménière's disease, such as migraine-associated vertigo, and require an alternative treatment strategy.<sup>7,8</sup> 'Atypical Ménière's disease' encompasses many variants of the classically described triad of symptoms; the underlying pathophysiology, however, is even less well understood. Betahistine has been anecdotally recommended for these entities despite their questionable existence as variants of true Ménière's.

### Prevalence

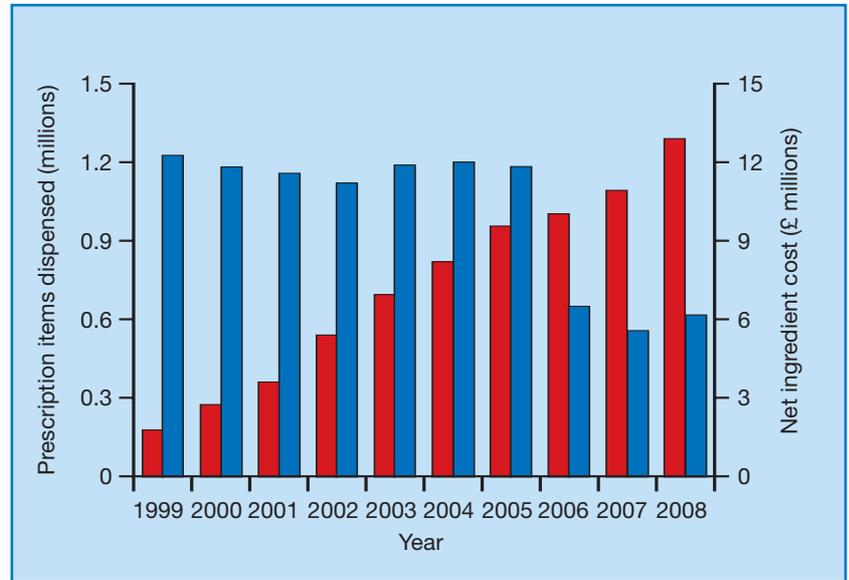
The actual prevalence of Ménière's disease in England is hard to define. One study examined the records of eight general practices in England during the year ending March 1952.<sup>9</sup> The authors were a little vague regarding their methods and the diagnostic criteria used, but their results suggested a prevalence of 157 per 100 000.

Another study in 1956 identified a prevalence of 56 per 100 000 when patients passing through a major otology centre in the UK were closely examined.<sup>10</sup>

Other estimates have been proposed, but the methodologies employed have led to ambiguous results. To date the most reliable data we have available regarding the prevalence of Ménière's disease in the UK are from 1956.

The difficulty in calculating the prevalence of Ménière's disease is that official diagnostic criteria are often overlooked and there is a tendency for many physicians to group all cases of recurrent vertigo into the category of Ménière's disease.

In the US Framingham study, 1.48 per cent of the population when questioned claimed to have a



**Figure 2.** Number of prescriptions and cost of betahistine prescribed in England, 1999-2008; source: PPA

history of Ménière's disease.<sup>12</sup> A Japanese study defined Ménière's as the combination of repeated attacks of true vertigo, fluctuating cochlear symptoms with vertigo, and exclusion of other diseases; the reported prevalence in this study was 16-17 per 100 000.<sup>13</sup>

### Betahistine prescription

Data provided by the Prescription Pricing Authority (PPA) reveal that 113 000 prescriptions for betahistine are currently being filled each month in England (see Figure 2).<sup>14</sup> The Office for National Statistics reports the population of England to be 50.4 million.<sup>15</sup>

Commonly a prescription would be repeated on a monthly basis, and using these figures the prevalence of betahistine usage in England would be 0.2 per cent of the population, or 200 per 100 000. This is clearly higher than the estimated prevalence of Ménière's in 1956 and much higher than studies that have used official diagnostic criteria.

It would be safe to say that a current prevalence of 56 per 100 000

in England would be an overestimate, as there is no evidence of a change in known aetiological factors and it would be more likely that some patients with recurrent vertigo in 1956 would nowadays be given an alternative diagnosis to Ménière's disease due to our improved understanding of other conditions that present with recurrent vertigo.

Even using this generous estimation of the current true prevalence of Ménière's disease, only 28 224 people would actually have this condition in England. Despite reservations over the clinical efficacy of betahistine, restricting its use to only patients with true Ménière's would save over £4 million per annum.

### Conflicting advice

Firm guidelines for the use of betahistine are hard to find, as even NHS websites provide conflicting advice. Evidence-based organisations – such as the James Lind Alliance, which incorporates the Database of Uncertainties about the Effects of Treatments (DUETs; [www.duets.nhs.uk](http://www.duets.nhs.uk)) – endorse the

findings of the above-mentioned Cochrane review.

Other NHS websites such as Clinical Knowledge Summaries ([www.cks.library.nhs.uk](http://www.cks.library.nhs.uk)) sanction the use of betahistine for prophylaxis, but neither cites any evidence nor provides any scientific justification.

In the preparation of this article both the National Institute for Health and Clinical Excellence (NICE) and the Medicines and Healthcare products Regulatory Agency (MHRA) were contacted regarding national prescribing policy. Neither of these organisations has been involved in the clarification of the therapeutic uses for betahistine.

Betahistine has few serious side-effects, but there are financial as well as ethical implications in prescribing a sometimes life-long drug regimen in the absence of a definitive diagnosis.

### Conclusion

Patients with symptoms of Ménière's disease are often challenging to manage; a variety of medical as well as surgical treatments may be available to them, and other more serious pathology may need to be considered.

The authors recommend that patients with symptoms of Ménière's disease are appropriately

managed by an otolaryngologist with an interest in Ménière's disease, and the initiation of a potentially life-long treatment with betahistine is given careful consideration.

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