Newer Theories on the Mechanism of Vertigo Attacks in Meniere’s Disease

Jeremy Hornibrook*
Department of Otolaryngology-Head and Neck Surgery, Christchurch Hospital, New Zealand

Perspective

Meniere’s disease is an inner ear disorder whose typical symptoms are vertigo attacks accompanied by fluctuating hearing, tinnitus and aural fullness in the affected ear. The disorder is named after a Frenchman Prosper Meniere who stated in a lecture to The Imperial Academy of Medicine “An auditory apparatus, until then perfectly healthy, can become, all of a sudden, the seat of functional troubles repeated cerebral accidents such as vertigo, giddiness, uncertain walking, spinning and falling nausea, vomiting, soon followed by profound deafness there is every reason to believe that the material lesion which is the cause of these functional troubles lies in the semicircular canals” [1]. In the 19th century common notions of the inner ear structures were that the cochlea was responsible mediating the nature and pitch of sound, the utricle and saccule for the perception of loudness, and the semicircular canals for transmission of bone-conducted sound and perception of sound direction [2]. Meniere was aware of the work of Marie Jean Pierre Flourens, who in 1824 lesioned pigeon semicircular canals inducing violent head and eye movements in the plane of the stimulated canal, implying a vestibular rather than a sound perception role [3]. PubMed cites 7,600 papers on Meniere’s disease over the last 153 years, but it remains enigmatic as to its fundamental cause and the mechanism of the vertigo attacks.

Nearly eighty years later advances in cadaver temporal bone histology allowed an internal view of inner ear disorders. In 1938 almost simultaneous publications by Yamakawa [4] of Japan and Hallpike and Cairns [5] of Great Britain noted that the characteristic feature of Meniere’s disease ears is an excess of cochlear endolymph which came to be called endolympathic hydrops. At the time endolymph was presumed to be produced in the cochlea and absorbed by the endolympathic sac by “longitudinal flow”.

Professor Harold Schuknecht at the Harvard Medical School established the largest and one of the few surviving human temporal bone laboratories. Experiments blocking the endolympathic duct or destroying the endolympathic sac in guinea pigs, cat and rabbits consistently result in endolympathic hydrops and degenerative changes in the organs of Corti and cochlear neurons, but never vertigo attacks. This led Schuknecht to state that “the most plausible explanation is that Meniere’s disease is caused by functional failure of the endolympathic sac” [6]. In Meniere’s ears he had frequently observed ruptures of Resissner’s membrane [7,8] and stated that “the episodes of vertigo and fluctuating hearing could be accounted for by the toxic effect of potassium on the sensory and neural structures which are normally bathed in endolymph” [6]. This did not explain why in non-human animal’s vertigo attacks do not occur, but rupture and potassium intoxication theory has been the predominant theory since 1963.

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Observations on nystagmus direction have been used to support or disprove the intoxication theory. On the assumption that the initial nystagmus is ipsilateral the potassium intoxication theory was supported by Dohlman on the basis that an initial ipsilateral direction of nystagmus during an attack would be consistent with increased potassium concentration surrounding afferent nerves [9].

McClure from the University of Western Ontario performed ENGs on 8 patients at differing times during Meniere’s attacks. In all cases the initial observed nystagmus was contralateral to the assumed Meniere’s ear, often reversing to ipsilateral, and in some cases alternating (in one case over seconds) over hours [10]. Others have observed the opposite pattern (initial ipsilateral) at
the onset of attacks [11,12]. McClure and colleagues also perfused the perilymphatic space in guineas with a high potassium solution producing an initial ipsilateral nystagmus followed by reversal in all animals. He rejected his patient observations as not supporting the potassium intoxication theory, but as supporting the alternative theory of raised endolymphatic pressure [13]. Tornndorf had argued that the aural symptoms in Meniere’s ears can be explained by raised endolymphatic pressure [14]. McClure speculated that such a sudden rise in endolymphatic pressure could result in mechanical distortion of the semicircular canal ampullae, which for the the horizontal canal would rotate the crest of the crista and turn the base of the cupula towards the utricle (utricofugal displacement), causing a contralateral nystagmus [13]. The limitations of conventional human and animal post-mortem histology and the differing observations of nystagmus during attacks have been advanced by other approaches.

A pioneer of electrocochleography, Professor William Gibson at the University of Sydney, performed transtympanic EcochG recordings in Meniere’s ears and normal ears with a tone burst stimulus [15]. In Meniere’s ears a 1 kHz tone burst produces a measurable large negative summating potential (SP), reflecting basilar membrane distortion from endolymphatic hydrops. From hundreds of recordings 87 patients could be identified as having an attack during the test, 1 to 24 hours before the attack and up to 72 hours after. All had an abnormally enlarged SP which was greatest 1 to 24 hours prior, dramatically decreasing during the attack, then increasing over the next 72 hours. This implies that prior to the attack hydrops increases, suddenly decreases during the attack and then increases over 72 hours, and that the Action Potential (AP) measuring cochlear nerve function, which might be expected to be reduced or lost from a rupture, is preserved. McNeill and colleagues from the University of Sydney [16] allowed Meniere’s patients to test their own hearing daily with a programmable hearing aid. In 6 who measured their hearing during an attack 5 had no change in hearing before, during and after the attack, and 1 had a probable change in threshold prior to but not during the attack. These observations make a rupture and potassium intoxication unlikely.

In a guinea pig model Daniel Brown and colleagues from the University of Sydney [17,18] injected 3 to 4 microlitres of artificial endolymph into the scala media and measured vestibular-evoked short latency potentials which are assumed to be from utricular neurons.

Recovery of cochlear function was often followed by a transient increase or decrease in utricular sensitivity (similarly if injected directly into the utricle) suggesting that there may be a sudden opening of the utricle-saccular duct to alleviate hydrostatic pressure, resulting in a change of utricular function due to an increase in its volume. Micro CT on these ears did not show ruptures.

Vestibular evoked potentials (VEMPs) have been studied as to their ability to diagnose hydrops in the vestibule. In static studies on ears between attacks there appears to be no single reliable VEMP measure [19]. Manzari and colleagues from the MSA ENT Academy at Cassino, in a dynamic VEMP study on 15 patients during an attack, found a significant increase in the n10 of the contralateral ocular VEMP (oVEMP) and a significant decrease in the ipsilateral cervical VEMP (cVEMP) [20]. This implies a decrease in saccular function followed by an increase in utricular function, consistent with a surge of endolymph towards the utricle. Although often not appreciated, isolated otolith stimulation or paralysis can elicit nystagmus and vertigo [21-23].

In combination these findings and other evidence have been the basis of the “drainage theory” by Gibson and Arenberg [24,25]. Experiments by Salt and colleagues from Washington University St Louis [26] have challenged normal “longitudinal flow” of endolymph by injecting chemical markers into guinea pig cochleas without volume disturbance. In normal volumes marker diffusion was static (radial) and not longitudinal, suggesting that the latter occurs only if there is an abnormal volume, as in endolymphatic hydrops. The endolymphatic sac contains hydrophilic proteins [27]. The theory is that mild cochlear hydrops is cleared by normal radial flow, but if there is excessive hydrops longitudinal flow is initiated by endolymphatic sac. It may successfully clear it, but if the endolymphatic duct is blocked obstruction to flow results in an endolymph build-up in the sinus of the endolymphatic duct which refluxes through the utricular valve of baste into the ampullae of the semicircular canals, so that the vertigo and nystagmus are explained by their behavior. In an MRI Meniere’s inner study with intratympanic Gadolinium, Gurkov and colleagues from the University of Munich [28] found hydrops only in horizontal canals in 5 patients, suggesting it may be the predominant canal affected.

Conventional theories on the pathophysiology of Meniere is disease have included an anatomical variation in size or position of the endolymphatic sac and duct, viral infection or an autoimmune involvement of the sac and duct or a genetically determined abnormality of endolymph control. It is now well accepted that benign paroxysmal positional vertigo (BPPV) is caused by detached utricular otoconia [29]. It is seldom asked what the fate of saccular otoconia is? Using 3D cone beam CT on Meniere’s ears, Professor HideyYamane from the University of Osaka and colleagues [29-31] have used 3D cone beam CT to study fine inner structure. In Meniere’s ears compared with opposite and normal ears there appears consistent obstruction of the reuniting duct, saccular duct, endolymphatic sinus and proximal endolymphatic sac, suggesting these blockages could be due to detached saccular otoconia. Similarity of the spectrum of age of onset of BPPV and Meniere’s disease raises the possibility they might have the same fundamental cause [32].

In summary, there is strong evidence from non-histological studies that membrane ruptures leading to potassium intoxication of perilymph is not the cause of Meniere’s vertigo attacks. Other evidence supports a hydrostatic process in which radial flow is overwhelmed, with an obstructed the endolymphatic sac attempting to clear the hydrops. The variable nystagmus observed might be explained by (even an alternating) stimulation of the horizontal canal receptor and the utricle. Progress on confirming the mechanism of Meniere attacks and other inner ear disorders is likely to await advances in the resolution of CT inner ear imaging in humans.

References
5. Hallpike CS, Cairns H. Observations on the pathology of Meniere's


