EQKRAA, which is found in 90% of patients with RA in the HLA-DR1/DR4 molecules, and the ESRRAL sequence found in the *Proteus* haemolysin molecule.[2] The frequency of HLA-DR1/DR4 in the UK is around 35%, so about every third person in the UK has these genes.

Subsequently we suggested that RA could be a form of 'reactive arthritis' following *Proteus* urinary tract infection and this explains why women are more likely to develop RA than men. In a survey of 1,375 RA patients from 14 different countries, it was shown that RA patients have specific antibodies to *Proteus* when compared to blood donors,[3] and furthermore that isolation of urinary *Proteus* bacteria in RA patients correlates with antibodies to *Proteus* in serum.[4]

These antibodies are specific, since Japanese RA patients have antibodies to *Proteus* but not to *Klebsiella* whilst Japanese patients with ankylosing spondylitis (AS) have antibodies to *Klebsiella* but not to *Proteus* – thus each microbe is a specificity control for the other disease. Similar results have been obtained with Dutch patients.

The RA sera are cytotoxic for sheep red cells coated with EQRRAA or ESRRAL peptides, whilst AS sera are cytotoxic for sheep red cells coated with HLA-B27 peptide sequences.[5] This strongly suggests that RA sera are damaging to joint tissues and that *Proteus* infection of the upper urinary tract is the most probable cause of RA, in the same way that *Klebsiella* infection of the colon is the cause of AS.

At the borderline between the known and the unknown there will always be debate and CME readers should be aware of this problem.

References

1 Ebringer A, Ptaszynska T, Corbett M, Wilson C *et al*. Antibodies to *Proteus* in rheumatoid arthritis. *Lancet* 1985;**ii**:305–7.
2 Wilson C, Ebringer A, Ahmadi K, Wrigglesworth J *et al*. Shared amino acid sequences between major histocompatibility complex class II glycoproteins, type XI collagen and *Proteus mirabilis* in rheumatoid arthritis. *Ann Rheum Dis* 1995;**54**:216–20.
3 Ebringer A, Wilson C, Tiwana H. Is rheumatoid arthritis a form of reactive arthritis? *J Rheumatol* 2000;**27**:559–63.
4 Wilson C, Thakore A, Isenberg D, Ebringer A *et al*. Correlation between anti-*Proteus* antibodies and isolation rates of *P. mirabilis* in rheumatoid arthritis. *Rheumatol Int* 1997;**16**:187–9.
5 Wilson C, Rashid T, Tiwana H, Beyan H *et al*. Cytotoxicity responses to peptide antigens in rheumatoid arthritis and ankylosing spondylitis. *J Rheumatol* 2003;**30**:972–8.

ALAN EBRINGER
Professor of Immunology, King's College London; Honorary Consultant Rheumatologist UCL School of Medicine, Middlesex Hospital

Diagnosis and management of vertigo

Editor – Halmagyi's very useful review of vertigo (*Clin Med* March/April 2005 pp 159–65) did nevertheless contain some contentious points.

Figure 1 in his article shows a repositioning manoeuvre for benign paroxysmal positioning vertigo (BPPV). Small black particles are seen to drop down inside the posterior semicircular canal. As these otoconia 'fall away from the cupula they create a negative fluid pressure that pulls on the cupula', producing vertigo. What is the evidence for this force? If, say, stones are dropped inside a beaker of water, is there downward pressure on the water surface, increasing the incurvation of the surface film and so decreasing the volume of the water? Common sense and schoolboy physics suggest to me that BPPV is far more plausibly caused by trapped air bubbles moving around inside the bony labyrinth.[1] So what is the flaw in this simple idea?

He suggests that in transient vertebrobasilar ischaemia, unilateral auditory symptoms suggest an aural problem, but 'by contrast, sudden, temporary bilateral hearing loss does suggest brainstem ischaemia', referencing the authoritative team of Lee, Yi and Baloh.[2] This case was of a diabetic woman who, two days previously, had two episodes of transient vertigo with hearing loss in the left ear, which, being unilateral, Halmagyi would characterise as an aural rather than a brainstem problem. Her audiograms with their predominant reversible low-tone loss strike a chord with me, as when I worked with Professor R Hinchcliffe he offered to pay me £10 for every low-tone sensorineural loss I found that was not of cochlear origin. I never did collect any money! Any doubt as to cochlear origin was removed by finding normal stapedial reflex thresholds, and Lee *et al* found the 'prominence of hearing symptoms … best explained by the selective vulnerability of the cochlea to ischaemia'.

In late Meniere's disease, Halmagyi describes the deaf ear that distorts and recruits ('There is no need to shout!'). This muddles two distinct loudness concepts.[3] Recruitment occurs in cochlear deafness wherein soft sounds are not heard, moderate sounds seem quieter and suprathreshold sounds are heard normally, and, as in the case above, acoustic reflex thresholds are unchanged. In contrast, audiosensitivity is where some intense sounds seem unusually loud. This is often an early symptom of Meniere's disease before any shift in pure tone thresholds. It is important to make this distinction or else the audiosensitive patient with normal audiogram will be sent to the neurology or psychiatry department rather than the ear, nose and throat department. Just as it is unhelpful to tell older patients with audiovestibular symptoms and vascular risk factors that they must have had a stroke, so it is to tell younger audiosensitive patients that they must have problems in the brain or, worse, in the mind, rather than having a simple, usually temporary, ear malfunction. Audiosensitivity and slight endolymphatic hydrops are common since they can result from cochlear hypotension from low blood pressure, weight loss, dehydration etc.[3]

References

1 Gordon AG. BPPV – Benign paroxysmal positional or bubble provoked positioning vertigo? *J Neurol Sci* 1992;**111**:229–30.
2 Lee H, Yi HA, Baloh RW. Sudden bilateral simultaneous deafness with vertigo as a sole manifestation of vertebrobasilar insufficiency. *J Neurol Neurosurg Psychiatry* 2003;**74**:539–41.
3 Gordon AG. 'Hyperacusis' and origins of lowered sound tolerance. *J Neuropsychiatry Clin Neurosci* 2000;**12**:117–9.

AG GORDON
Audiologist, London

In response

Editor – Dr Gordon makes three thought-provoking points.

Firstly, he says that semicircular canal

microbubbles cause benign paroxysmal positioning vertigo. That otoconial particles exist in the endolymphatic ducts of the semicircular canals is beyond doubt: Parnes has removed one.[1] Furthermore, the observed directions of positional nystagmus fit best with cupular activation by particles heavier, rather than lighter, than endolymph,[2] and there are at least two hydrodynamic models that show how such particles could, by a plunger effect, cause endolymph movement, cupular displacement and thereby positional vertigo and nystagmus.[3] The idea of microbubbles, presumably still beyond the resolution of 0.625 mm slice thickness spiral CT scanners, awaits verification.

The second point he makes is that deafness in brainstem stroke is cochlear. That bilateral deafness can occur with brainstem lesions is beyond doubt.[4] Nonetheless, even in patients with bilateral sudden simultaneous deafness in the setting of brainstem stroke, the deafness is usually cochlear, due presumably to bilateral anterior inferior cerebellar and consequently cochlear artery occlusion.[5] Nevertheless, the clinical observation that someone who suddenly loses hearing in one ear has a problem in the ear, and someone who suddenly loses hearing in both ears has a problem in the brain, is still correct.

His third point is that loudness discomfort in Meniere's disease and in normal subjects is not the same. Loudness discomfort in an ear with normal air-conduction thresholds might be due to superior canal dehiscence, a diagnosis that can be proven,[6] or to 'slight endolympathic hydrops', one that cannot. Loudness discomfort, over-recruitment, occurs in cochlear deafness with normal acoustic reflex thresholds (recruitment) although the acoustic reflex threshold itself is not a guide to the loudness discomfort level.[7] Nevertheless, the clinical observation that a unilateral recruiting deafness, unlike a chronic bilateral recruiting deafness, is probably relevant to the cause of recurrent vertigo, is still correct.

References

1 Welling DB, Parnes LS, O'Brien B, Bakaletz LO *et al*. Particulate matter in the posterior semicircular canal. *Laryngoscope* 1997;**107**:90–4.
2 Aw ST, Todd MJ, Aw GE, McGarvie LA, Halmagyi GM. Benign positional nystagmus: a study of its three-dimensional spatio-temporal characteristics. *Neurology* 2005;**64**:1897–905.
3 Squires TM, Weidman MS, Hain TC, Stone HA. A mathematical model for top-shelf vertigo: the role of sedimenting otoconia in BPPV. *J Biomech* 2004;**37**:1137–46.
4 Egan CA, Davies L, Halmagyi GM. Bilateral total deafness due to pontine haematoma. *J Neurol Neurosurg Psychiatry* 1996;**61**:628–31.
5 Lee H, Baloh RW. Sudden deafness in vertebrobasilar ischemia: clinical features, vascular topographical patterns and long-term outcome. *J Neurol Sci* 2005;**228**:99–104.
6 Minor LB, Carey JP, Cremer PD, Lustig LR *et al*. Dehiscence of bone overlying the superior canal as a cause of apparent conductive hearing loss. *Otol Neurotol* 2003;**24**:270–8.
7 Olsen SO, Rasmussen AN, Nielsen LH, Borgkvist BV. The acoustic reflex threshold: not predictive for loudness perception in normally-hearing listeners. *Audiology* 1999;**38**:303–7.

GM HALMAGYI
Neurology Department
Royal Prince Alfred Hospital
Sydney, Australia