The Search for Idiopathic Intracranial Hypertension

An Investigation of Cerebral to Cochlear Pressure Transfer as a Direct Cause of Reversible and Irreversible Audiological Disorders

Sponsor ‘Defeating Deafness’, the Hearing Research Trust

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**Aim:** To investigate patients with known intracranial hypertension by studying the symptomatology and by using the TMD - Cerebral and Cochlear Fluid (CCFP) Pressure Analyser.

**Intracranial Hypertension:**
Intracranial hypertension, raised intracranial (cerebral) pressure, is frequently associated with an unknown pathology and can therefore be referred to as ‘ideopathic intracranial hypertension (IIH)’. In a number of countries including Britain, IIH has historically been referred to as ‘benign intracranial hypertension’ (BIH). It is accepted that BIH is a misnomer as the condition is often far from ‘benign’. The Americans preferred to refer to this condition as ‘pseudo Tumor cerebri’, a name which reflects the clinical presentation of the condition in some cases.

**Intracranial Hypertension is difficult and often impossible to diagnose by symptoms alone:**
- Headaches -- can be severe but often mild or not present at all
- Neurological symptoms -- not present or minor
- Papilleodema -- only present in less than 20% of cases and then only if you have reason to look!
- Chronic fatigue – currently too non-specific to be of diagnostic value

**Also:**
- The adult form is different from the paediatric form.

**Why do we need to find the patients with intracranial hypertension?**
- There is a significant cohort of mainly adult female patients with undiagnosed disorders associated with intracranial hypertension, and the main symptoms will include tinnitus, chronic fatigue or ‘brain fog’, and imbalance.
- Only exceptionally rarely are these patients cross referred from, for example, ENT to Neurology.
- Paediatric ideopathic intracranial hypertension appears to be equally prevalent in girls and boys and is arguably even more difficult to diagnose since the ‘tell-tell’ audiovestibular symptoms are rarely present.
- Such undiagnosed chronic disorders have a cost implications for health care since effective management is not possible.
- There is a significant quality of life issue for patients.
- If correctly diagnosed, it is usually treatable.
- Associations appear to exist between intracranial hypertension, Menière’s Disease and possibly endolymphatic hydrops.
Outcomes of the Current Research

Probably the most important finding of the current research is the discovery of abnormally large intra-aural cardiovascular and respiratory pressure waves of intracranial origin which exist for patients of all ages with ideopathic intracranial hypertension (IIH). Other work includes:

- An IIH symptom profile to allow appropriate cross referral of possible IIH patients from ENT to Neurology
- A normative trail of 60 females between the age of 20 and 50 years.
- The investigation of 15 children and 58 adults patients with various neurological disorders.
- Assessing the value of the Southampton non-invasive ‘Cerebral and Cochlear Fluid Pressure (CCFP) Analyser in the management of paediatric and adult patients with IIH.
- Confirming that low frequency tinnitus is the most well defined symptom of adult IIH.
- Confirming that the adult symptomatology of IIH is different from the paediatric form.
- Demonstrating that patients with neurological disorders are missed in the ENT clinic – two ENT patients with Benign Intracranial Hypertension (BIH) and one patient with Chiari Type 1 Malformation were found and several other suspect cases await a final diagnosis.
- Showing the reversible nature of tinnitus, imbalance and hearing loss once IIH has been correctly diagnosed.
- Demonstrating that untreated IIH can result in permanent cochlear damage in a group of patients tested with recurrent perilymphatic fistulae.
- Supporting the planned instigation of special clinics at the Queens Medical School with the Institute of Hearing Research, Nottingham, and the National Hospital for Neurosurgery and Neurological Diseases, Queens Square London.
- Formulating 7 theorem to explain interactions that occur between intracranial and inner ear fluids and the middle ear (Appendix D).
- Postulating that the characteristic low frequency tinnitus found with IIH is caused by fluid turbulence with the cochlear aqueduct.
- Raising the possibility that certain neurological conditions such as IIH, cerebral vascular disorders, Chiari I Malformation, and aqueductal stenosis, not only mimic the symptoms of Menière’s Disease, but in some cases cause endolymphatic hydrops due to disturbances of the intracranial-labyrinthine fluid dynamics. If this is indeed the case, then it seems likely that the newly discovered aberrant intra-aural/intracranial pressure waves are manifestations of these fluid disturbances. The possibility that endolymphatic hydrops is induced in such a manner, needs to be thoroughly researched in case controlled studies using electrocochleography and any other measures of hydrops.
Preface:-

Aim

Intracranial Hypertension
Intracranial Hypertension is difficult and often impossible to diagnose by symptoms alone:-

Why do we need to find the patients with intracranial hypertension?

Outcomes of the Current Research

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Section 1

Introduction

The current research provides the clinical tools necessary for non-surgical diagnosis of ideopathic intracranial hypertension (IIH) and related neurological disorders. Diagnosis of this condition is by combining non-invasive intracranial and cochlear pressure measurements made by the CCFP (TMD) Analyser with a detailed assessment of the neurological and in particular the audiovestibular symptomatology. During this research it became evident that IIH could not be considered in isolation from other neurological conditions with similar yet subtly different presentations. In total 58 adult and 15 paediatric patients were investigated in the study with a variety of disorders including:

- Ideopathic Intracranial Hypertension (IIH) diagnosed as Benign Intracranial Hypertension (BIH)
- Cerebral vascular disorders
- Late acquired/diagnosed hydrocephalus
- Chiari-Arnold type I malformation
- Aqueductal Stenois
- Sagittal sinus thrombosis
- Recurrent perilymphatic fistulae

The methods developed during the research are now assisting the diagnosis and management of paediatric and adult patients. For example as a direct consequence of our research, a Type I Chiari malformation (cerebella tonsillar herniation) has been confirmed in a 22 year old female. This patient was originally referred to us from ENT with a Menière’s like condition. We also tested two young female patients who had been under ENT management for several years and had undergone ENT surgery before papilleodema was found in a perchance visit to the optician. The presence of intracranial hypertension (BIH) was confirmed in both cases (Marchbanks, 1999). We are still awaiting definitive diagnosis for a number of patients, including several who have a combination of audiovestibular symptoms with intractable headaches, and in whom aberrant intra-aural pressure waves have been found.

Two groups of patients of special interest were those with recurrent perilymphatic fistulae which have been identified by Dr. Weider, of the Dartmouth Medical School, USA. These patients have recurrent perilymphatic fistulae, tinnitus and dizziness due to confirmed raised intracranial pressure (BIH). They are clear examples that irreversible cochlear damage can occur with intracranial hypertension. The second group are those with Ménière’s like symptoms as caused by Chiari I malformations and are being researched by Drs. Kula and Milhorat of the Departments of Neurosurgery and Neurology, State University of New York Health Center at Brooklyn -- the proposition is that cerebella tonsillar herniations alter the intracranial-cochlear fluid dynamics in such a manner as to cause endolymphatic hydrops. Time was spent in both US clinics and a group of 15 patients were tested. Both clinics plan to continue their respective research with our test methods.

The above research findings are discussed in the remainder of this report, and are the subject of a number of papers given/published and in preparation.
Section 2

The Diagnosis of Ideopathic Intracranial Hypertension (IIH)

2.1 The CCFP (TMD) Analyser

A control group of 60 normally hearing females between the age of 20 and 50 were investigated. These subjects answered the same medical history and symptom questionnaire as the patients. The normals also underwent the same acoustic impedance audiometry and tympanometry test protocols. Tests with the CCFP (TMD) Analyser included assessment of the cochlear/intracranial pressure, whether intracranial to cochlear pressure communication existed and measurement of background intra-aural noise which is usually of cardiovascular and respiratory origins. In agreement with previous research, the TMD technique provides an effective non-surgical method for estimating the absolute intracranial pressure and is a particularly sensitive method for monitoring long-term cochlear/intracranial pressure changes in children and most adults. During the research the TMD technique reduced the need for repeated lumbar puncture measurements, notably in the paediatric group.

Two areas of uncertainty seem to exist when using the TMD technique for pressure assessment with some adults. Both instances appear to be associated with pulsating intracranial pressure. More data with the assistance of the Newcastle clinical trial is being collected to test the following postulates. In the first case and contrary to what is expected, 5 to 10% of adults appear to show a decrease in cochlear fluid pressure on moving from sitting to the supine position. Based on observations, it is postulated that this ‘unexpected’ pressure reduction is as a result of a large change in the amplitude of the intracranial cardiovascular pressure wave, sitting compared with supine. In the second instance, there appears to be a higher than expected number of ‘false-negatives’ when using the TMD to estimate absolute intracranial pressure in the ear with low frequency or pulsatile tinnitus — comparisons being made with direct measurements of cerebrospinal fluid pressure by lumbar puncture. In this instance it is postulated that a high level of intracranial cardiovascular activity generate a measurable change perilymphatic fluid pressure. If true, these postulates provide evidence that intracranial pressure waves can generate differential pressures between the intracranial fluid, perilymph and endolymph. Such a discovery could conceivably provide a pathophysiological process for some occurrences of endolymphatic hydrops (section 5.2).

2.2 The Symptomatology

A typical profile for IHH was devised and this is given in Appendix C. In agreement with other studies, our research confirms that the principle symptomatology of ideopathic intracranial hypertension (IIH) is:

- headache
- chronic fatigue and ‘brain fog’
- tinnitus
- visual obscurations
- dizziness
- sometimes a hearing loss

Our own findings concur with other researchers, in that low frequency and/or pulsatile tinnitus may be the single and most distinct indicator of IIH in the adult population. Other conditions such as cerebral vascular disorders will also cause tinnitus with similar characteristics, so that it is important to provide a diagnostic strategy whereby these conditions may be differentiated.
A symptom of IIH is chronic fatigue or ‘brain fog’ which presumably reduce the individuals ability to cope with the tinnitus and their perception of the effectiveness of clinical management. Diagnosing IIH as the underlying cause of tinnitus promises to significant improve the management of certain low frequency tinnitus that exists in combination with chronic fatigue. Successful identification of IIH should allow for effective treatment that in most cases result in total relief from the tinnitus, balance and symptoms of chronic fatigue as demonstrated in the present study.

None of the 15 children investigated in the present study (ages 4 to 16) reported characteristic tinnitus or balance problems and this compares with at least 60% of the adults who reported distinct tinnitus. Unless papilleodema can be found, this makes the diagnosis of IIH in children even more challenging in that only defining symptoms may be chronic fatigue with or without headaches.

2.3 Screening for ideopathic Intracranial Hypertension

It is evident that IIH remains largely undiagnosed. Even in our own small study of IIH, three cases had been missed by ENT and we await confirmation of diagnosis in a number of other cases (two patients with confirmed BIH and one patient with Chiari I malformation). In addition, 6 of the 10 patients tested from Dr. Weider’s group demonstrate recurrent perilymphatic fistula, tinnitus and dizziness, as a result of BIH. In these cases, intracranial hypertension was only confirmed because Dr. Weider had the foresight to perform lumbar punctures on these ENT patients.

Serious consideration should be given to a pilot screens of ENT, headache and chronic fatigue patient populations so as to identify the extent of undiagnosed IIH. Since tinnitus, possibly in combination with imbalance and hearing loss, are key symptoms, then the audiology practitioner needs to play a major role in identifying adult IIH. More informed screening for this condition in ENT should also be established.

Undiagnosed IIH within the population is clearly a ‘quality of life’ issue for the individual, particularly since it is associated with chronic fatigue and ‘brain fog’. It should also be of interest to the World Health Organisation (WHO) in that ‘quality of life’ is one of the metrics used to assess the impact, cost effectiveness and mix of health services that will optimise the health of the population.

The current ‘Defeating Deafness’ Research contributes towards our understanding of IHH by:-

- Providing clear guidelines for identifying IIH in the adult population in terms of a detailed screening questionnaire.
- Investigating the efficacy of an audiological technique (TMD) as a means for screening for IIH in adults and children.
- By providing comparative studies to assist with the differential diagnosis of IIH and cerebral vascular disorders which are also associated with pulsatile tinnitus.
- By identifying patient groups that show that cerebral to cochlear pressure transfer relates to both reversible and irreversible audiological disorders.
- By identifying a number of ENT patients in which Ménière’s -like symptoms were confirmed to be due to underlying neurological disorders.
- By highlighting that the audiological practitioner has the most appropriate experience for applying the TMD Technique and the ‘Defeating Deafness’ IIH Questionnaire when screening for IIH.
Section 3

Aberrant Intracranial Pressure Waves

In the current study, aberrant low frequency pressure waves of presumed intracranial origin were seen across the entire IIH (BIH) age range and in other patients with neurological disorders (now also independently reportedly seen with a BIH patient in the Newcastle clinical trial). Intra-aural pressure waves with abnormally large amplitude were seen in 68% of these patients and only in one of 50 of the normal controls. Interestingly a significant proportion of patients exhibited the aberrant pressure waves in the sitting position only (32%), and these would have been missed by conventional surgical intracranial pressure measurements and lumbar puncture which are undertaken in the supine position.

These pressure waves have a number of characteristics that have been categorised into four distinct types as shown in figure 1. Type 1 shows extraordinarily large pressure waves that are synchronous with the heartbeat. In agreement with accepted cerebrospinal fluid (CSF) mechanics, these pressure waves are seen to increase in amplitude as the mechanical compliance of the CSF system reduces with increasing intracranial pressure, (Davson et al). Figures 2 and 3 show a clear relationship between the intra-aural cardiovascular pulse amplitude and the lumbar pressure in a 15 year old boy with BIH who underwent serial lumbar puncture measurements. Type 2 and 3 are intra-aural pressure waves that are associated with respiration and in type 3, the amplitude of the cardiovascular pulse varies with the phase of the respiration. The type 4 intra-aural pressure wave has been named the ‘M’ wave and is of unknown origin. It is an extraordinarily sharp and large pressure pulse that can be over ten times greater than the normal intra-aural pressure wave. It appears to be triggered by respiration, and then decays over a few seconds. One could speculate that it is due to a build-up of pressure and then a sudden release of pressure on forced opening of an intracranial fluid channel. This speculation is consistent with the confirmed aqueductal stenosis suffered by one patient exhibiting the ‘M” wave (second case an ENT patient yet to be diagnosed). Alternatively the possibility of the intracranial respiration pressure wave being modified by intermittent opening of the cochlear aqueduct need also to be considered.

Further investigation is required to determine whether in certain cases of BIH, the prognosis is more closely related to the peak amplitude of the pressure waves than abnormal baseline intracranial pressure. It is interesting to note that in a case control study of patients with IIH but without papilleodema, that Wang et al (1998) concludes that tinnitus is a better predictor of this condition than headaches. We postulate that this type of tinnitus is caused by the cardiovascular intracranial pressure waves (see section 4). Furthermore, Wang et al (1998) concludes that the presence of tinnitus was considered to be the strongest indicator that a poor outcome to treatment was likely.

Other researchers also report relationships between intracranial pressure and intra-aural pressure pulses. A German research group, Lang et al (2000), has proposed that certain characteristics of the intra-aural pressure pulse may allow non-invasive measurement of intracranial pressure and compliance to be made. In earlier work, Matsuyama et al (1994) and Doumoto et al (1994) in Japan, undertook simultaneous measurements of the intra-aural and intracranial (cisterna magna) cardiovascular pressure waves in cats and humans. This research was conducted to test and prove the hypothesis made by myself in 1987 that states that intracranial pressure will have a direct influence on labyrinthine pressure.
Type 1: Cardiovascular

Type 2: Respiratory

Type 3: Cardiovascular amplitude modulated with respiration phase

Type 4: 'M' waves – Triggered by respiration?

Figure 1: Categorisation of various intra-aural pressure waves
Figure 2: Example TMD recordings of cardiovascular pulse amplitude with varying lumbar puncture pressure (LP) – 15 year old male Benign Intracranial Hypertension patient.

Figure 3: Intra-aural cardiovascular (CV) pulse amplitude vs. lumbar puncture pressure (LP) – 15 year old male Benign Intracranial Hypertension patient.
There is a clear need to understand the types of intra-aural wave in terms of the underlying pathology. By this method, we will begin to understand whether a particular wave type will assist differential diagnosis and improve our knowledge of underlying pathophysiology. As a demonstration of the process of classification of the pressure waves, figure 4 tabulates are our preliminary findings for wave type, sitting and supine, versus etiology. There appears to be a predominance of BIH patients with type 1, cardiovascular intra-aural pressure waves, otherwise more data needs to be collected before clear patterns will be seen. Figure 5 considers the type of intra-aural pressure wave against the possible underlying pathophysiology.

We are at the beginning of a new and exciting area of research into these intra-aural pressure waves. There is clearly the need for more detailed and extensive patient studies along the lines outlined in this section.

<table>
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<tr>
<th>Etiology</th>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 1+2</th>
<th>Type 3</th>
<th>Type 4</th>
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<td>Sagittal sinus thrombosis</td>
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<td>Chiari I malformation</td>
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<td>2</td>
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<tr>
<td>Unknown etiology</td>
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<td>Post Lymes Disease</td>
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<td>0</td>
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<td>Occipital headache + tinnitus</td>
<td>1</td>
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</table>

**Figure 4:** Pressure Wave Type versus Etiology -- Preliminary Findings
Considering both ears, 18 abnormal intra-aural pressure waves were found in the sitting position (red/underlined numerals) compared with the supine position (black numerals)
### Type 1: Cardiovascular
- Raised intracranial pressure resulting in reduced intracranial compliance and a greater pressure pulse per given blood volume change.
- Associated with Benign Intracranial Hypertension – Pseudo Tumor Cerebri.
- Possibly associated with cerebral vascular disorders.

### Type 2: Respiratory
- Reduced intracranial compliance which may be independent of raised intracranial pressure (i.e. the pressure may be normal).
- Reduced cerebrospinal volume.
- Possibly associated with Chiari I Malformation and Benign Intracranial Hypertension – Pseudo Tumor Cerebri.
- Possibly associated with increased respiratory resistance, i.e. nasal obstruction.

### Type 3: Cardiovascular
- Raised intracranial pressure that results in reduced intracranial compliance which reduces further in phase with respiration, and therefore modulates the cardiovascular activity – this is classical intracranial hydrodynamics.
- Possibly associated with Benign Intracranial Hypertension – Pseudo Tumor Cerebri.
- Synchronous with and possibly triggered by respiration.
- Possibly pressure-respiration related opening of cochlear aqueduct.
- Possibly a build-up of intracranial pressure and then a sudden release on forced opening of an intracranial fluid channel.
- Found in one case of aqueductal stenosis and one case following unconfirmed viral meningitis.

### Type 4: ‘M’ waves – Triggered by respiration?

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**Figure 5:** Type of Intra-aural Pressure Wave and Possible Associations
Section 4

The Pathophysiology of Imbalance and Tinnitus found with Intracranial Hypertension

4.1 Infra-sound and Imbalance

Intra-aural pressure waves of cardiovascular origins can be recorded from most ears. This activity is transmitted to the intracranial fluid and the ear via the arteries and with a fundamental frequency of 1-2 Hz, which corresponds to heart rate of 60-120 beats per minute. The significance of intra-aural cardiovascular activity was reported by Andreasson et al in 1978 and was also researched by myself (Marchbanks, 1980; Marchbanks and Reid, 1990; Andreasson et al, 1978; Marchbanks, 1984). Interest in intra-aural cardiovascular activity arises from the fact that externally applied low frequency sound and infrasound produces nystagmus and sensations of falling forwards (Evans, 1976; Erlich and Lawson, 1980; Kacker and Hinchcliffe, 1970; Hill Britton, 1986; Parker et al, 1968). I have hypothesised that internally generated cardiovascular pressure waves (infrasound) may also be linked to some forms of peripheral balance problems, and low frequency or pulsatile tinnitus which is experience by patients with intracranial hypertension and other pressure problems (Marchbanks, 1996a, 1986b). Independently, Epley has also hypothesised that the intracranial cardiovascular pressure wave is transmitted through to the intralabyrinthine fluid and can stimulate the otolithic receptor (Epley, 1993).

Imbalance may also occur even if the intracranial cardiovascular pressure wave exists with an amplitude within normal limits. Hypothetically, this may be possible since the transmission of the intracranial-labyrinthine pressure wave will depend on the properties of the communication route(s), which in most cases is presumed to be the cochlear aqueduct. Since the properties of the cochlear aqueduct will not be identical bilaterally, then presumably in some cases significant differences in intralabyrinthine pressure waves will occur. In particular, large differences may occur under circumstances of increasing cardiovascular (respiratory) wave amplitude such as with changes in posture, physical exertion or under stressful conditions (Appendix D, theorem 2,3).

In a similar manner, cases of unusually wide cochlear aqueduct or vestibular aqueduct should be considered. Using the TMD technique, Ernst et (1995) found abnormal perilymphatic in patients where the internal auditory meatus allowed a free communication of the intracranial and intralabyrinthine fluids. These patients had a X-linked Progressive Mixed Deafness Syndrome and were chosen since they were at risk from perilymphatic gusher during stapes surgery. In these cases of wide intracranial-labyrinthine routes, then it can be expected that intracranial pressure waves will traverse with negligible attenuation of amplitude (Appendix D, theorem 2,4).

Finally, other anatomical factors which may need to be considered are highlighted by Minor et al (1998) in their article on ‘Sound- and/or pressure-induced vertigo due to bone dehiscence of the superior semicircular canal’. These authors report eight patients with vertigo, oscillopsia, and/or disequilibrium related to sound, changes in middle ear pressure, and/or changes in intracranial pressure. In some cases the patients can also experience chronic disequilibrium. The existence of dehiscence of the semicircular canal was confirmed with computer tomographic scans of the temporal bones and surgical plugging of the affected canal was shown to be beneficial in patients with disabling symptoms. It seems reasonable to consider that internally generated intracranial/aural pressure waves (infra-sound), can act in a similar manner to externally applied sounds and pressure changes. The prevalence of bone dehiscence of the superior semicircular canal in the general population is unknown. However, this condition should be considered in
combination with intracranial/aural pressure waves, and perhaps other factors mentioned above, as a predisposition for imbalance.

4.2 The Origin of Tinnitus Associated with IIH: Postulate

The current research clearly demonstrates that most BIH adults report low frequency or pulsatile tinnitus but this is not usually present in children and adolescents. However, all ages of patients exhibit cardiovascular pulsation of the inner ear pressure that in turn can reflect that of the intracranial pressure. In addition, no patient for whom the TMD test demonstrated a sealed intracranial-cochlear fluid communication suffered from the characteristic low frequency tinnitus. In consideration of this, we postulate that the characteristic IIH low frequency tinnitus is associated with an open intracranial-cochlear pathway in combination with narrowing of the aqueduct lumen. This narrowing will naturally occur with age. Furthermore, the possibility that the cardiovascular intracranial pressure wave is generating tinnitus as a result of fluid turbulence within the restricted cochlear aqueduct of the adult needs to be investigated. The intracranial cardiovascular pressure wave has a fundamental frequency of 1 to 2 Hz, however, fluid turbulence would generate noise significantly above this frequency and within the acoustic bandwidth of the ear. It is postulated that such fluid turbulence stimulates the hearing receptors and is perceived as low frequency or pulsatile tinnitus. The current research records common descriptors for the tinnitus as ‘wind-like’, ‘the roaring of water’, ‘rushing water’, ‘sea-like’, ‘like the sound of steam locomotive’ and these may have characteristics synchronous with the cardiovascular cycle. These descriptors are consistent with the postulated source of the noise being turbulence.

The above postulate is also consistent with cochlear aqueduct morphology, in that it is opening in children and progressively becomes sealed with age. Future research needs to investigate the above more thoroughly and the proposed postulates need to be tested experimentally (see Appendix A: Testing the Hypothesis).

4.3 Diversity of Symptoms with Intracranial Hypertension

There is a considerable diversity of symptoms within the IIH patient population which may, in part, be explained by differing underlying pathophysiological processes such as:-

- increased mean intracranial pressure
- abnormal intracranial pressure waves.
- reduced compliance of the cerebrospinal fluid systems e.g. a type I Chiari malformation as discussed in later sections.

The current study provides evidence that abnormal pressure waves of intracranial origin may underlay certain forms of both paediatric and adult Benign Intracranial Hypertension (BIIH). Traditionally, only the absolute mean intracranial pressure is considered since pressure waves cannot be accurately measured via conventional lumbar puncture methods. Further research is required to support this finding as intra-aural pressure waves may turn out to be the underlying intracranial pathology in a number of cases. In turn, correct diagnosis will lead to more effective treatments.

Co-researcher Dr. E. Good, Consultant Neurologist and NASA Flight Surgeon, has coined the name ‘Normal Pressure Pseudo Tumor Cerebri’ for this condition. It is accepted that the condition may exist with or without normal baseline intracranial pressure.
Our research has provided the opportunity to compare IIH with certain cerebral vascular disorders, Chiari Malformation type 1, and adult aqueductal stenosis, all of which share a similar symptom profile (Sismanis, 1998; Milhorat et al, 1999; Barlas et al, 1983). Tinnitus has been shown to be a common factor in these disorders and our limited experience appears to show subtle difference in this symptom between disorders. These differences may provide a basis for differentially diagnosing these disorders. Much of the research in this area has been undertaken by Sismanis (1998). Figure 6 is our interpretation of his work based on our own preliminary findings.
### Figure 6: Neurological Disorders and Symptomatology -- Discussion Document Only

#### Symptoms common to all:- Chronic fatigue, ‘brain fog’, memory loss

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<thead>
<tr>
<th>Ideopathic Intracranial Hypertension – BIH</th>
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<tbody>
<tr>
<td>• Low frequency tinnitus – if pulsatile then clearly identified as being synchronous with heartbeat.</td>
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<tr>
<td>• Localised within ears.</td>
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<tr>
<td>• Often described as ‘whooshing’, ‘like the sea or water’, ‘a wind noise’, ‘like a steam train’.</td>
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<tr>
<td>• Tinnitus often reduces or is completely obliterated by head turn towards to tinnitus ear or light digital pressure over the internal jugular vein</td>
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<tr>
<td>• 30% of tinnitus high frequency</td>
<td></td>
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<tr>
<td>• Headache tends not to respond to analgesics</td>
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<tr>
<td>• Headaches tend to be across forehead and sometimes behind eyes, usually described as being ‘dull’ or a pressure sensation which also extends to ears. Not always present.</td>
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<tr>
<td>• Dizziness occasionally can be a full rotary vertigo, however, is frequently mild imbalance. Distant object can appear to ‘wobble’ and patients can stumble but rarely completely loose balance.</td>
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<tr>
<td>• Meniere’s like, however, the experience clinical practitioner identifies it to be not ‘classical’ Meniere’s presentation</td>
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<tr>
<td>• Patient may have papilleodema, however, many do not.</td>
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<td>• See also Appendix C</td>
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<tr>
<th>Atherosclerosis</th>
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<tr>
<td>• Tinnitus usually identified as being pulsatile and usually clearly synchronous with heartbeat</td>
<td></td>
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<tr>
<td>• Patient is often confused or finds it difficult to localise the tinnitus within an ear – it is often ‘sensed’ within head.</td>
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<tr>
<td>• Tinnitus does not appear to diminish with head-turn or digital pressure over the internal jugular vein.</td>
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<tr>
<td>• Reports of bruit within neck</td>
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<tr>
<td>• Mild imbalance</td>
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<tr>
<td>• ‘Brain fog’, memory loss often significant and can be disabling or stated as being the main symptom</td>
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<tr>
<th>Cerebral Vascular</th>
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<tr>
<td>• Tinnitus usually identified as being pulsatile and usually clearly synchronous with heartbeat</td>
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<tr>
<td>• Tinnitus may be reported within head</td>
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<tr>
<td>• Pulsatile headaches</td>
<td></td>
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<tr>
<td>• Distinct bruit</td>
<td></td>
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<tr>
<td>• ‘Brain fog’, memory loss significant and can be disabling or stated as being the main symptom</td>
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<tr>
<th>Fibromuscular Dysphasia</th>
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<tr>
<td>• As for ‘cerebral vascular’ with multiple focus bruit which can be clearly identified.</td>
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<tr>
<td>• Bruit can be identified within head and neck and, significantly, within the chest.</td>
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<tr>
<td>• Significant ‘Brain fog’, memory loss significant.</td>
<td></td>
</tr>
<tr>
<td>• Reportedly can be virtually identical to Meniere’s disease and an endolymphatic hydrops symptom complex</td>
<td></td>
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<tr>
<td>• Can include a fluctuating hearing loss</td>
<td></td>
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<tr>
<td>• Occipital headaches can be distinctive.</td>
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<tr>
<th>Chiari I Malformation</th>
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Section 5

Possible Associations between Ideopathic Intracranial Hypertension and Ménière’s Disease

Independent TMD based research indicates that the pathophysiology of Ménière’s Disease is, in some cases, associated with the interconnecting pathways between the inner ear and the intracranial fluid space (for more details see Appendix B). In most cases this connection is presumed to be the cochlear aqueduct although the internal auditory meatus can provide an alternative route main in association with some congenital malformations (Ernst et al, 1995a). The underlying physiology of this relationship is not understood and is difficult to understand simply in terms of the mechanical properties of this pathway and static pressures (Densert et al, 1981). It seems probable that the hydrodynamics of the intracranial/labrinthine interface need to be considered and that the newly discovered intracranial pressure waves will feature in our understanding.

5.1 Chiari Malformation Type I (CMI) in Association with Ménière’s Disease

Milhorat et al (1999) in their study of 364 patients with Arnold Chiari malformation type I (CMI) found this condition to be characterised by ‘a Ménière’s disease-like syndrome’. They further conclude that ‘Clinical Manifestations of Chiari I Malformation seem to be related to cerebrospinal fluid disturbances which are responsible for headaches, pseudotumor-like episodes, endolymphatic hydrops ......’. They found that a significant proportion of their patients had a diagnosis which was fully consistent with Ménière’s disease. The symptoms included aural pressure, disequilibrium and peripheral vestibular dysfunction, tinnitus and low frequency hearing loss. They found that these symptoms were particularly sensitive to physical activities, including Valsalva manoeuvres. They conclude that ‘these findings fulfil the criteria for endolymphatic hydrops.

The work of Milhorat et al (1999) also suggests that Chiari I malformations may be more prevalent in the population than it is currently consider to be the case. It may be related to minor head trauma, infection, coughing, sneezing or pregnancy. It is known that CMI will reduce the intracranial fluid volume and increase the intracranial compliance. As a result greater than usual fluctuations should occur with respiration, the cardiac pulse, Valsalva manoeuvres and changes in posture. Several cases in the current clinical trial appear to demonstrate a reduced CSF compliance that is not solely due to raised intracranial pressure. One patient with CMI was confirmed amongst our ENT referrals. The possibility that CMI may be the underlying pathology in other patients with abnormal intra-aural pressure waves is being investigated. Discussions are ongoing with this research group who are awaiting approval of a proposal to conduct further investigations using the TMD technique and our research protocols.

5.2 Intracranial Pressure Waves – A Cause of Endolymphatic Hydrops ?

If a turbulent fluid flow exists within the intracranial-cochlear routes (cochlear aqueduct), then according to principles of fluid mechanics, pressure gradients can be established between the inter-linking fluids (perilymph/endolymph and the intracranial fluids). It is postulated that such pressure differentials may change the mechanical properties of the Basilar membrane and create an equivalent of a endolymphatic hydrops condition. Endolymphatic hydrops
created in such a manner would be consistent with our findings and those of other research
groups including that of Milhorat et al (1999). If this postulate is correct, then the
pathogenesis of endolymphatic hydrops by this means may sometimes occur as a natural
progression associated with ageing of the cochlear aqueduct.

Further research needs to be undertaken to investigate the endolymphatic hydrops postulate
and also the associations with other pathologies such as certain cerebral vascular disorders,
Chiari Malformation type 1, and adult aqueductal stenosis.

*Please refer to Appendix C for more detailed coverage of other TMD research findings with
Ménière’s disease.*
Section 6

Treatment of Tinnitus and Dizziness Associated with IIH

The current research shows that IIH related tinnitus frequently resolves with medication in the form of diuretics (e.g. acetazolamide, frusemide) with or without a short two week course of a steroid (e.g. prednisone). If weight is an issue, then diet management should also be considered. Other drugs may prove to be effective for controlling the intracranial pressure and, therefore, the tinnitus and dizziness. Research is currently investigating non steroid anti-inflammatory drugs such as indomethacin (e.g. ibuprofen) as a means of reducing intracranial pressure. It has been shown that these drugs reduce the cerebral blood flow without influencing the cerebral metabolism (Bundgaard et al, 1997; Dahl et al, 1998; Jensen et al, 1997). Vasoconstriction results in a small reduction in intracranial blood-volume and consequently a reduction in the intracranial pressure. Further research is being undertaken to investigate this claim with the assistance of the TMD technique as a non-invasive method of monitoring intracranial pressure changes. Walsted et al (2001) could not prove a significant reduction in intracranial pressure in healthy normal subjects. However the reason for this may be because in these subjects the intracranial pressure was already normal and any subsequent reduction in intracranial pressure with medication was insignificant. This study needs to be extended to patients with known raised intracranial pressure.

In cases where conservative IIH treatments fail to resolve tinnitus and imbalance, then a surgical approach may need to be considered. Surgery may include the insertion of a lumbar or ventricular peritoneal shunt to reduce and control the intracranial pressure. Major surgery may include decompression surgery in cases of Chiari I Malformation (Milhorat et al, 1999). Dr. Weider of the Dartmouth-Hitchcock Medical Center in the US, has surgically blocked the cochlear aqueduct via an intracranial approach. This surgery was performed on four patients suffering from recurrent perilymphatic fistulae, and in all cases, the tinnitus and balance problems diminished or resolved following the blockage (Weider and Musiek, 1998). Further work may show that cochlear aqueduct occlusion may be appropriate ‘last resort’ surgery in cases of intractable and chronic tinnitus.

Our research may also influence treatment of vertigo by intratympanic Gentamicin. Dr. Walsted has postulated that unpredictable cases of profound hearing loss after intratympanic Gentamicin may be caused by decreased patency of the cochlear aqueduct. If the main communication route between the cerebrospinal fluid and the perilymph is blocked, then a reduced flow or diffusion away from the cochlear will occur and result in an enhanced ototoxic effect. It is proposed that the TMD technique is used to assess the patency of intracranial-perilymph communication prior to treatment so that this risk factor may be ascertained (Walsted, 2000).
Section 7

Future Research

1. Collaboration and meetings are taking place with Drs. Kula and Milhorat of the Departments of Neurosurgery and Neurology, State University of New York Health Center at Brooklyn. This group is currently researching Chiari I Malformation in a number of children and adults. In a paper detailing a study of 364 symptomatic patients, they propose that this condition is more prevalent than currently thought and that patients will frequently report Ménière’s Disease like symptoms and even exhibit endolymphatic hydrops due to disturbances of the intracranial-labyrinthine fluid dynamics.

2. Professor Robinson, Consultant Paediatric Neurologist, Newcomen Centre, St Thomas’ Hospital, London, will be using our CCFP (TMD) Analyser to research children with Benign Intracranial Hypertension and other neurological disorders.

3. The Alfred’s Hospital, Melbourne, Australia, will be using the CCFP Analyser, questionnaire and protocols based on the ‘Defeating Deafness’ research to test for IIH as the underlying cause of tinnitus and imbalance in certain ENT patients. Confirmation of the diagnosis will include lumbar puncture where indicated.

4. Dr Dudley Weider and Dr Frank Musiek, Section of Otolaryngology, Department of Surgery Dartmouth-Hitchcock Medical Center, in the US, will be researching ENT patients for underlying IIH. Patients of particular interest are those with recurrent perilymphatic fistulae in association with raised cerebrospinal fluid pressure as proven by lumbar puncture.

5. Our work is now being funded by the NASA Johnson Space Center. The project concerns the use of our non-invasive intracranial pressure assessment technique in combination a NASA Langley technique. The purpose is to investigate ‘The Role of Intracranial Pressure in Space Adaptation Syndrome’ (see Appendix F). Under the leadership of Dr. Good, the work will investigate space sickness and the problems experienced by astronauts on return to Earth, and during four Space Shuttle missions. The NASA Langley ultrasonic method of measuring intracranial pressure waves will be combined with our measurements of baseline intracranial pressure and intra-aural pressure waves, ECG and blood flow measurements. This research provides an ideal opportunity to more fully investigate the nature of the cardiac and respiratory related acoustic pressure waves and to perfect apparatus for non-invasive intracranial pressure.

6. At a Department of Trade and Industry Telemedicine Meeting (December 2000), the Community Outreach Section of the Texas Medical School announced their intention to collaborate in clinical trials using the Southampton CCFP measurement technique.

7. The CCFP measurement technique is being independent validated by Professor Mendelow and Dr. K Banister, Departments of Neurosurgery and Medical Physics, Newcastle General Hospital, UK. They have published findings which corroborate our own published research (Banister et al, 2000; Samuel et al, 1998).

8. A number of other Clinical Research Centres are using our CCFP Technique for investigating Ménière’s like disorders and neurological disease (See CCFP references, Section 9.1). This includes the work by Dr Boucara and colleagues, Hôpital Beujon, Paris and Konradsson and colleagues, Lund, Sweden, who are investigating the underlying pathology of Ménière’s Disease (Appendix B).

9. The third in our series of international conferences on the work outlined in this report and associated research is planned for Berlin 2003. The proposed topic is ‘Communication at the Cranial and Sensorineural Interfaces in Health and Disease’. Co-organisers are Professor Arne Ernst, BG-Unsallklinikum, Berlin and Mr. Andrew Reid, Head of Audiological Services, Royal United Hospital, Bath.
Section 8

Conclusions

1. Extraordinary intra-aural pressure waves were consistently measured in children and adults with known intracranial hypertension and other neurological disorders. These pressure waves were of cardiovascular and respiratory origins and could, in some cases, be shown to be directly of intracranial pressure origin.

2. The current research is in agreement with a consensus that considers low frequency tinnitus to be the most well defined symptom of iodeopathic intracranial hypertension (IIH). Other symptoms usually include headache and chronic fatigue frequently described as ‘brain fog’.

3. In the main, IIH is difficult to diagnose on the basis of symptoms alone unless papilloedema is present and papilloedema is reported to occur in less than 20% of cases. The TMD system provides a means of estimating the mean intracranial pressure and is particular sensitive for tracking pressure changes.

4. Tinnitus and imbalance is usually present in adults, but seldom occurs in children or adolescents.

5. In children is especially difficult, if not impossible, to diagnose IIH on the basis of symptoms alone. Children do not have the ‘tell-tell’ tinnitus and infrequently report imbalance. Without papilloedema, then the only distinguishing symptom may be chronic fatigue or ‘brain fog’ with or without headache.

6. The current research supports the hypothesis that turbulent fluid flow within cochlear aqueduct is the source of the low frequency tinnitus perceived by most adults with IIH. Histologically studies show that in children the cochlear aqueduct provides a free-flow of fluid/pressure between the intracranial and cochlear spaces. It is for this reason that it is believed that tinnitus does not exist in most children and adolescents with IIH.

7. There is a growing consensus of opinion between TMD research centres that intracranial-perilymph fluid pressure transfer features in the pathogenesis of Ménière’s Disease and endolymphatic hydrops. It is too early to determine the exact nature of this association at the current stage of knowledge. The current research adds to our understanding by highlighting the need to consider intracranial pressure waves and the possibility of turbulent fluid flow within the cochlear aqueduct.

8. Our research highlights the need to undertake comparative studies of IIH with certain cerebral vascular disorders, Chiari I Malformation, and adult aqueductal stenosis, all of which share a similar symptomatology. Tinnitus and imbalance have been shown to be symptoms common to these disorders.

9. This research raises the possibility that certain neurological conditions such as IIH, cerebral vascular disorders, Chiari I Malformation, and aqueductal stenosis, not only mimic the symptoms of Ménière’s Disease, but in some cases cause endolymphatic hydrops due to disturbances of the intracranial-labyrinthine fluid dynamics. If this is indeed the case, then it seems likely that the newly discovered aberrant intra-aural/intracranial pressure waves are manifestations of these fluid disturbances. The possibility that endolymphatic hydrops is induced in such a manner, needs to be thoroughly researched in case controlled studies using electrocochleography and any other measures of hydrops.
Section 9

Acknowledgements

I wish to acknowledge the support of ‘Defeating Deafness – the Hearing Research Trust’ for sponsoring this research and without this support it would not have been possible. I wish also to thank Mr David Burge FRCS, Diane Turner, Eirwen Jones and Professor Mark Lutman for their invaluable assistance with the experiment planning and collecting of test data. The contributions from Melanie Ferguson, Professor Linda Luxon and Dr Rosalyn Davies allowed a clinical questionnaire to be compiled which I am confident will assist other clinicians to appropriately cross-refer patients with intracranial pressure disorders to neurology.

I am grateful to the Clinical Staff of the Wessex Neurological Centre and other UK clinics that kindly referred patients to the study. I would also like to thank Dr Good, Bay Area Neurology, Webster; Drs Kula and Milhorat, State University of New York Health Center and Dr Weider, Dartmouth-Hitchcock Medical Center, for providing me with an insight into their own research and for arranging for me to spend time in their clinics.

Finally I wish to thank Miss Dorothy Lang FRCS of the Wessex Neurological Centre and Professor John Warner and the staff of Southampton University Child Health for their continuing support over the past years.
Section 10

References and Bibliography

10.1 A selection of Publications from Research Centres using the Southampton Cerebral and Cochlear Fluid Pressure Analyser


10.2 Books and Dissertation


10.3 General References and Related Research


Appendix A: Fluid Turbulence within the Cochlear Aqueduct as a Generator of Tinnitus: Testing a Hypothesis

We postulate that the characteristic IIH low frequency tinnitus is associated with an open intracranial-cochlear pathway in combination with narrowing of the aqueduct lumen. Furthermore, that the cardiovascular intracranial pressure wave can generate tinnitus as a result of fluid turbulence within the restricted cochlear aqueduct of the adult. Such fluid turbulence stimulates the hearing receptors and is perceived as low frequency or pulsatile tinnitus.

This postulate is consistent with the known cochlear aqueduct morphology, in that it is usually open in children and progressively becomes sealed with age. This does not, however, preclude the possibility that tinnitus can be generated by turbulence within the jugular bulb or from elsewhere within the cranial cavity. The above postulate needs to be investigated in terms of a hypothesis that can be tested experimentally.

The proposed hypothesis is that there will be relationship between the frequency bandwidth and the amplitude of the intra-aural cardiovascular pressure waves for a group of untreated BIH patients, or any group of patients where generation of this intra-aural pressure wave is extrinsic to the ear. That is, as the frequency bandwidth decreases, there will be a tendency for the pressure wave amplitude to also decrease. Psychometric tests should also demonstrate inter-dependencies with the perceived intensity and frequency characteristics of the tinnitus. The rational is that for extrinsically generated intra-aural pressure waves, that is intracranial cardiovascular pressure waves, then reduced patency of the intracranial-labyrinth routes will affect both the amplitude and frequency bandwidth of the resulting intra-aural pressure wave.

There will be large inter-subject variations and other factors will affect the morphology of intracranial generated pressure waves. Therefore, a carefully designed experiment is required which uses modified TMD equipment to measure the spectrum of the intra-aural pressure wave.

Further consideration of the above should be given in relation to:-

- the disequilibrium and sometimes vertigo experienced by IIH and other patients with neurological disorders.
- possible inter-relationships with spontaneous otoacoustic emissions, since the existence of fluid turbulence is paramount to an acoustic energy source within the inner ear.
Appendix B: Other TMD Related Research -- An Underlying Neurological Condition for Ménière’s Disease?

Konrádsson, Nielsen and Carlberg are researching Ménière’s Disease using the TMD technique. They find that posture induced changes in perilymphatic pressure are significantly greater in the diseased ear compared with the healthy ear (Konrádsson, 1999a; Konrádsson et al, 2000). They interpret this finding as a more efficient intracranial-cochlear pressure transfer in the diseased Ménière’s ear, compared with the good ear.

“The results also indicate that for the patients tested, the routes of communication are more effective in the diseased ear than in the healthy ear – a condition that may relate to the pathogeneses of Ménière’s disease.”

The suggestion being made is that there is a greater degree of patency of the intracranial-cochlear routes in the ear with Ménière’s Disease, and therefore, the cochlear is more susceptible to the continuous fluctuations in intracranial pressure. However, the opposite situation and the possibility of narrowing of these routes should also be considered. That is, the larger that expected change in the perilymphatic pressure both reflects the expected change in pressure with posture (as seen in the good ear) plus a component due to intracranial pressure waves causing a pressure ‘pumping’ action as a consequence of cochlear aqueduct narrowing. If this exists, I speculate that this pressure ‘pumping’ action could create intracranial-perilymph-endolymph pressure differentials and may be responsible for endolymphatic hydrops in some cases. It is not clear which of the two alternative explanations is valid and perhaps both are significant.

It is interesting to consider the work of the Konrádsson research group in the context of findings published by Boucarra et al (1998).

Konrádsson et al (2000) exposed 16 patients with Ménière’s Disease to hypobaric conditions within a pressure chamber. A statistically significant relationship was found between those patients demonstrating the greatest change in perilymphatic pressure with posture as indicated by the TMD technique, and those showing the greatest improvement in hearing threshold at the low frequencies (250 Hz and 500 Hz) with treatment provided by hypobaric exposure. Konrádsson et al conclude that the TMD may have a predictive value regarding the outcome of hypobaric exposure for patients with Ménière’s Disease. Furthermore, they conclude that there appears to be a relationship between the efficiency of the route of pressure transfer and the observed effect of hypobaric exposure. Again there appears to be an association between the intracranial-cochlear routes of communication (cochlear aqueduct) and the Ménière’s Diseases process.

Boucarra et al (1998) compared a control group with normally hearing (n=7), with those with non-progressive sensorineural hearing loss (n=9), a group with fluctuating hearing loss which had been hospitalised during a phase of deterioration (n= 8), and similarly a group with

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2 The chamber pressure was set at 20 daPa/s to levels of –180 to –480 daPa (mean –285 daPa) relative to the prevailing atmospheric pressure, and the maximum hypobaric pressure was individually chosen so as to avoid opening of the Eustachian Tube and equilibration of the middle ear pressure. By this method the cochlear is exposed to a relative overpressure compared to that of the intracranial pressure, for duration which will depend on the degree of patency of the cochlear aqueduct (or any other intracranial-cochlear connecting pathways). The number of episodes of hypobaric exposure were 4 to 13 (mean 7.4) and the total duration was 24.4 ± 9.8 minutes. Just before normalisation of chamber pressure the recorded relative middle ear over pressure was 185 ± 105 daPa.
Ménière’s Disease in an active phase (n=25). The control group and those with sensorineural hearing loss demonstrated normal perilymphatic pressure as assessed by TMD for the group as a whole. However, all the patients with a fluctuating hearing loss in an acute phase demonstrated raised perilymphatic pressure (inwards TMD). About 50% of the Ménière’s Group similarly demonstrated raised perilymphatic by TMD assessment. Boucarra et al postulate the existence of two subgroups amongst the Ménière’s Disease patients, and that these subgroups suggest the presence of normal and high pressures. Furthermore, they propose that two separate pathogenesis for Ménière’s Disease may exist, or alternatively that a single pathogenesis exists with a fluctuating evolution of the pressure (i.e. about 50% of the patients were tested during a normal pressure phase). Their proposition is also that the high pressure group may have a pathogenesis common with the fluctuating hearing loss group which similarly show raised cochlear pressure.

Unfortunately Boucarra et al do not report the state of the intracranial-cochlear pressure exchange as assessed by using TMD and postural manoeuvres. However, if we assume that most of these Ménière’s and ‘fluctuating hearing loss’ patients do have communicating intracranial-cochlear fluids, then raised perilymphatic pressure implies raised intracranial pressure and/or the presence of abnormal intracranial pressure waves. That is, the findings of Boucarra et al imply that in at least 50% of cases, the underlying pathology of Ménière’s Disease is of a neurological origin.

Could Benign Intracranial Hypertension (BIH) be the neurological disorder underlying Ménière’s Disease? This is unlikely since, although BIH is known to clinically present with Ménière’s Disease like symptoms, adult BIH is predominately a female condition and Ménière’s of a classical form is approximately equally prevalent in males and females. The Ménière’s Group tested by Boucarra was 11 men and 14 females, although they note a small female predominance, this was not statistically significant and also does not support the BIH conjecture. So BIH would not appear to be the most likely neurological candidate. There are several other aspects of the clinical presentation of the BIH condition that makes it dissimilar to Ménière’s Disease. Other striking differences are that the tinnitus with BIH is usually low frequency in character and it is likely to be bilateral. However, BIH cannot be considered to have a single pathogenesis as in 80% of cases the cause is of an ideopathic nature. It leaves the possibility that a subgroup of BIH population group will be the same as a Ménière’s neurological sub-group. In addition other conditions need to be considered as candidates for Meniere’s subgroups, such as Chiari I Malformation as proposed by Milhorat et al (1999), aqueductal stenosis as proposed by Barlas et al, 1983, or cerebral vascular disorders.

Finally, a clear distinction should be made between the existence of distinct neurological pathologies that underlay subgroups of Ménière’s Disease and merely a neurological association. In the later case, the possibility that some ears are simply just more susceptible to intracranial pressure waves should not be overlooked.

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2 Ménière’s Disease as defined by the American Academy of Otolaryngology, Head and Neck Surgery criteria.
Appendix C

A Typical Profile for Idiopathic Intracranial Hypertension

Predominantly female - at least 4 to 1, female/male ratio. The patient may be 20% or more overweight. Typical age range - 18 to 45 years.

Likely to be suffering from a low frequency tinnitus which will be described as 'hum', 'roaring', 'whoosing' or perhaps 'sea like' with sometimes characteristics which are synchronous with the heart beat. About 60% of patients will report tinnitus and of these about 60-70% (36-42% of total) will be of a low frequency type. In cases of unilateral tinnitus, gentle compression of the internal jugular vein will often result in a reduction in the intensity of the tinnitus or even a complete cessation. Likewise turning the head to the ipsilateral side will often reduce the tinnitus.

Most patients will report a mild imbalance or 'unsteadiness on their feet'. About 40% of those with tinnitus will be suffering some form of objective vertigo. This will be described as episodes when the 'room appears to move' and this can last for several minutes and sometimes hours. This is often not fully developed rotary vertigo. The feeling is often associated with nausea, but only infrequently vomiting.

The patient will be suffering from a malaise which will often be associated with a 'deterioration in memory', 'mental slowing' or 'dulling of mind'. The patient will commonly report headaches, however, in most cases these headaches will be mild, sometimes described as a 'dull' headache. The headache may be associated with a pressure or fullness sensations in the head, ears or behind the eyes. If a significant headache occurs, then there should be little or no associations with 'stress' and it is unlikely to respond to analgesics. It may occur daily and may be present on rising from bed in the morning and perhaps improves as the day progresses.

If investigated, papilloedema will only probably be found in less than 10% of cases. Interestingly, although visual deficits are often found, these or visual disturbances frequently go unreported by the patient. If these occur, they may include 'greying' or 'tunneling' which may occur - as with other symptoms - with change of posture and subsequently last for several minutes.

Low frequency and/or fluctuating hearing losses are also symptoms, but only rarely are significant enough to be noticed by patients.

The most distinguishing associations of intracranial hypertension are probably 'female' and 'low frequency and/or pulsatile tinnitus'. Nevertheless, if this latter symptom alone was taken for a 'clinical screen' for this condition, then we would expect to miss over 50% of the patients.

Robert Marchbanks, Feb 2000

From research sponsored by 'Defeating Deafness – the Hearing Research Trust'.
Appendix D

Principles of Static and Dynamic Interactions between the Middle ear, Intracranial and Intralabyrinthine Fluids

First presented in entirety by Robert Marchbanks at the ‘Irish Society of Audiology Meeting’, Mater Hospital, Dublin on 5 November 1999

On consideration of research into the intracranial-labyrinthine-middle ear mechanics and clinical research findings, I have proposed the following theorems:

Theorem 1: Given a patent cochlear aqueduct, the intracranial pressure will always provide the reference pressure for the endolymph and perilymph within the limits set by:
- Dynamics properties of the cochlear aqueduct
- Resting tension of the Reissner’s membrane

Theorem 2: Given a patent cochlear aqueduct, pressure waves of intracranial origin will be transmitted to the labyrinth in a manner dependent on the:
- Hydromechanical properties of the cochlear aqueduct
- Mechanical properties of the cochlear windows
- Middle ear pressure and any tension applied to the oval window via the ossicles

Theorem 3: Direct stimulation of the vestibular system and manifestations of tinnitus can occur due to intra-aural amplitude and phase variations in transmitted intracranial pressure activity brought about by:
- Raised intracranial pressure
- Changes in the compliance of the cochlear windows such as secondary to changes in middle ear pressure

Theorem 4: Intracranial-labyrinthine fluid impedance mismatch is important in limiting the degree of mechanical stress and therefore possible labyrinthine structural damage which may occur for given pressure pulses of intracranial or middle ear origins.

Theorem 5: Differential pressures may exist between the cerebral fluid, endolymph and perilymph due to:
- The existence in some cases of a finite opening pressure across the lumen of the cochlear and vestibular aqueducts
- Non-linear hydromechanical properties of the cochlear and vestibular aqueducts which allow pressure waves of intracranial origin to pass more readily to the labyrinth in one direction compared to the other direction

Theorem 6: In consideration of the non-linear properties of the cochlear and vestibular aqueducts (Theorem 5), then the perpetual pressure fluctuations within the cerebral fluid of cardiovascular and respiratory origins may produce sustainable pressure differences between the cerebral, endolymphatic and perilymphatic fluids which are important to:
- Normal labyrinthine physiology and fluid homeostasis
- The pathogenesis of conditions such as endolymphatic hydrops

Theorem 7: The physiology and pathophysiology of the labyrinth will be dependent on changes in and interactions occurring between the mean intracranial pressure, and pressure waves of cardiovascular and respiratory origins, and also:
- The substantial pressure increases which occur with intracranial plateau waves
- Airway flow restrictions and nasal obstruction
The Role of Intracranial Pressure in Space Adaptation Syndrome

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Monitoring Center: JSC
Initial Funding Date: 1999
Students Funded Under Research: 0
Expiration: 2002
Post-Doctoral Associates: 0

Flight Information:
Experiment ID: 9802148
Flight Mission|Program: Shuttle
Flight Assignment: TBD
Required Hardware:

Task Description:
Symptoms of space adaptation syndrome (SAS) are experienced by more than two-thirds of space travelers during their first few days in flight. These symptoms, which include headache, malaise, lethargy, anorexia, vomiting, nausea, and gastric discomfort, can affect the productivity, well-being, and safety of flight crews. Some of the symptoms of SAS resemble those arising from increased intracranial pressure (ICP) and cerebral edema. The possibility that the headward fluid shift associated with early exposure to microgravity could raise ICP, thereby giving rise to SAS symptoms, has not been tested directly because of the invasiveness of previous methods for measuring ICP. However, new noninvasive methods have become available. We propose to measure ICP noninvasively by using the Cerebral and Cochlear Fluid Pressure (CCFP) Analyzer, a devise that links tympanic-membrane displacement to variations in intracranial cerebrospinal fluid pressure. Measurements will be obtained from control subjects in various positions (seated, supine, head-down tilted) on Earth and during parabolic flight on the NASA KC-135 aircraft. These measurements will be examined for correlation with SAS symptoms (quantified according to the Grabiel motion-sickness criteria) and with ICP dynamics assessed by pulsed phase-lock loop [PPLL] ultrasound, a technique developed by Dr. Hargens. Finally, measurements will be collected from crewmember volunteers before, early during, and after brief Space Shuttle missions. The overall goal is to determine whether ICP increases during space flight, and if so, whether that increase correlated temporally and in magnitude with symptoms of SAS. If changes in ICP are found to be associated with SAS, then countermeasures that shift ICP toward ground-based norms could be effective in eliminating or reducing the symptoms of SAS. Moreover, this noninvasive ICP technology can be used to answer other critical problems related to human adaptation to microgravity in addition to space adaptation syndrome, e.g., ICP effects on brain perfusion, cerebrovascular regulation, and postflight orthostatic intolerance.

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