Spontaneous Intracranial Hypotension – Diagnosis and Management

Introduction
Spontaneous intracranial hypotension (SIH) produces a headache similar to a post lumbar puncture headache. Although the terms ‘hypotension’, ‘low CSF pressure’ and ‘low CSF volume’ are often used interchangeably, the syndrome can occur in the setting of ‘normal’ CSF pressures. Loss of CSF volume rather than pressure better explains the clinical features and imaging abnormalities.1

Classification of low volume headaches
The international classification of headache disorders recognises three subsets of low CSF volume headache.2 These are post-dural (post-lumbar) puncture headache, CSF fistula headache and headache attributed to spontaneous low CSF volume/spontaneous intracranial hypotension. Criteria needed for these diagnoses are summarised in Table 1. The cardinal feature indicating low CSF volume headache is aggravation of symptoms within 15 minutes of sitting or standing. In post-dural puncture headache symptoms should improve within 15 minutes of lying down.

Aetiology and risk factors
SIH has been associated with abnormalities of the cervical spine and chiropractic manoeuvres. Although there may be a clear trigger such as a Valsalva manoeuvre or trauma, SIH may occur without a clear precipitant. The cause is thought to relate to a breach of dural diverticulae, or tearing of nerve root sheaths. Connective tissue disorders have been suggested as possible predisposing factors, as SIH has been reported in patients with Marfan’s and Ehlers-Danlos syndromes.

Not all patients with spontaneous intracranial hypotension have low CSF pressures when measured at lumbar puncture. This implies that there may be significant individual variation in CSF pressures, and also that the rate of CSF loss may be more important in producing the syndrome than the residual CSF pressure or volume. CSF leaks are not identified in every case of apparent SIH. In part this may relate to the limitation of investigations. However patients with a typical history, without clear evidence of a leak, and who have failed ‘blind’ blood patches, often prove very difficult to treat. It is possible in such cases that a CSF leak may have occurred, with a residual effect on CSF dynamics (eg lowered pressure setting in the choroid plexus, and sensitisation of meningeal afferents). Based on similarities between post lumbar puncture headache (PLPH) and SIH, a number of inferences can be made. PLPH is less common at the extremes of age and this has been attributed to reduced epidural distensibility in the very old and very young.3 A higher risk has been reported in young females with a low body mass index.4 Patients with dementia appear to have a very low risk of PLPH and this has been attributed to low pain sensitivity, rigid dural fibres, arteriosclerotic vessels, and large CSF spaces due to cerebral atrophy. PLPH occurs less frequently in those with higher CSF opening pressures.4 These factors may also be of relevance in SIH.

Pathophysiology
Two main theories have been proposed to explain the cause of headache in patients with low CSF volume headache. They have been outlined in greater detail by Paldino et al.2

1) Traction on pain sensitive structures
Under normal conditions, CSF supports the brain reducing its weight from 1500g to only 48g within the cranium. This remaining weight is supported by suspension from several pain-sensitive structures. These include the meninges, cerebral and cerebellar veins (tributaries of the sagittal and transverse sinuses, respectively) as well as the fifth, ninth, and tenth cranial nerves and the superior three cervical nerves. Descent of the brain and traction on these structures, explains the orthostatic nature of the headache.

However tonsillar descent is not found in all patients with SIH. This may be because displacement of the brain is underestimated (because the patient lies supine during brain imaging). It may also be because there are additional pathophysiological mechanisms.

2) Dilatation of pain sensitive intracranial vascular structures
The mean recumbent CSF pressure is approximately 150mm of water at all levels. In the erect posture, a pressure gradient occurs; highest in the lumbar sac, about 0 at the level of the cisterna magna, and around -85mm H2O in the ventricles. Venous engorgement in both brain and spine occurs in SIH. According to the Monro–Kellie doctrine, the upright posture should be associated with further dilatation of pain-sensitive intracranial venous structures. In support of this theory is the finding that coughing or Valsalva manoeuvres (that decrease the venous return to the heart and therefore increase intracranial venous volume) can reproduce headache in a patient with SIH even when supine.

Clinical Features
The onset of headache following SIH may be gradual or subacute but a thunderclap form is also well recognised in about 14% of cases.4 Associated clinical features are neck stiffness, tinnitus, hyperacusis, photophobia, nausea, interscapular and radical upper limb pain, vertigo, visual field defects, and cranial nerve palsies.

As SIH becomes chronic, the postural aspect of the headache may become much less apparent, and an index event may not be recalled. SIH should therefore be considered in the differential diagnosis of new onset persistent daily headache.9

Rare presentations of SIH include sudden deafness, orthostatic tinnitus, rapid onset encephalopathy and coma (attributed to diencephalic compression resulting from brain descent), Parkinsonism, and chronic behavioural features suggestive of frontotemporal dementia.10-12 Radiculopathy due to cervical epidural venous engorge ment has also been associated with SIH.13

It is also important to note that orthostatic headaches have been described without CSF leakage as the major clinical manifestation of postural tachycardia syndrome (a disorder characterised by chronic orthostatic symptoms and a dramatic increase in heart rate on standing, but that does not involve orthostatic hypotension).15

Investigations
Investigation of patients with suspected SIH may help corroborate the diagnosis and identify the site of CSF leakage.

Magnetic Resonance Imaging (MRI)
MRI brain with contrast is the initial investigation of choice in suspected SIH. Meningeal enhancement is the earliest and most frequent feature, occurring in more than 80% of subjects; tonsillar descent is seen in more than

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Management Topic
### Post-dural (post-lumbar) puncture headache
- Headache that worsens within 15 minutes after sitting or standing and improves within 15 minutes after lying
- One of neck stiffness, tinnitus, hyperacusis, photophobia or nausea
- Dural puncture has been performed
- Headache develops within 5 days after dural puncture
- Headache resolves spontaneously within 1 week or within 48 hours after effective treatment

### CSF fistula headache
- Headache that worsens within 15 minutes after sitting or standing and improves within 15 minutes after lying
- One of neck stiffness, tinnitus, hyperacusis, photophobia, or nausea
- A known procedure or trauma has caused persistent CSF leakage with at least one of the following: low CSF pressure evidence on MRI, evidence of CSF leakage on conventional myelography, CT myelography or cisternography and CSF opening pressure <60 mm H2O in sitting position
- Headache develops in close temporal relation to CSF leakage
- Headache resolves within 7 days of sealing the CSF leak

### Headache attributed to spontaneous (or idiopathic) low CSF pressure
- Diffuse and/or dull headache that worsens within 15 minutes after sitting or standing, with at least one of the following:
  - One of neck stiffness, tinnitus, hyperacusis, photophobia, or nausea
- A known procedure or trauma has caused persistent CSF leakage with at least one of the following: low CSF pressure evidence on MRI, evidence of CSF leakage on conventional myelography, CT myelography or cisternography and CSF opening pressure <60 mm H2O in sitting position
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### Doppler Flow Imaging
This is predicated on the basis that the superior ophthalmic vein is a tributary of the cavernous sinus and it might therefore reflect the engorgement of the intracranial venous sinuses that occurs in this condition. Increased diameter and maximum flow velocity of the superior ophthalmic veins has been demonstrated in patients with SIH using transor-bital colourflow Doppler imaging. One study suggests this technique has very high specificity and sensitivity, though clearly does not assist in identifying the site of leakage.

### Radionuclide Cisternography
Radionuclide cisternography frequently demonstrates ‘surrogate’ markers of a low volume CSF state. These include limited ascent of the tracer to the cerebral convexity in 91% of cases, early appearance of the radioisotope in the bladder in 65%, and early soft tissue uptake of radioisotope in 43%. Actual leakage of CSF has been identified in 52% of cases, most commonly at the cervico-thoracic junction or in the thoracic spine. Intermittent leaks may go undetected and the technique may be insufficiently sensitive to identify small leaks.

### CT Myelography
CT myelography has been found to demonstrate the level of a CSF leak in 67% of patients overall, compared with only 50 and 55% for spinal MR imaging and radionuclide cisternography. In no case did radionuclide cisternography reveal the leak when CT myelography did not. Unfortunately CT myelography can be very time consuming, as it requires CT slices be obtained through the skull base and the entire spinal axis. Spinal imaging and radionuclide cisternography may perhaps be helpful as guides for focusing on particular areas with CT myelography.

### Lumbar Puncture
Lumbar puncture should be considered only if the features are equivocal and should be avoided before MRI with contrast as this can interfere with interpretation of the results. CSF opening pressure is typically low (usually 0–5cm CSF). It may however be normal in up to 17% of cases. CSF constituents are usually normal although high protein concentration and lymphocytic pleocytosis may be seen.

### Treatment
#### Medical
Conservative measures like bed rest are the first line treatment for low intracranial pressure headache. If not effective, intravenous caffeine at a dose of 500mg in 500ml saline over two hours (repeated once or twice) is often used although the evidence base is limited. Cardiac monitoring is necessary as caffeine can induce arrhythmias. There is also some evidence to suggest that theophyllines may be efficacious. It has been proposed that methylxanthines produce arterial constriction through the blockade of adenosine receptors. Consequently, intracranial blood flow and, presumably, venous engorgement are decreased. Abdominal binding with a surgical corset may help, while glucocorticoids or mineralocorticoids have been used in some studies but are of questionable effect.

#### Interventional
**i) Autologous epidural blood patch**
The technique was initially based on the observation that PLPH was less severe after a ‘bloody tap’ compared with a ‘clear tap’. The mode of action is not clear but may be due to a tamponade effect. It is performed by slowly injecting autologous blood into the same interspace or the interspace below the site of leak.

In contrast to PLPH the site of CSF leakage may not be certain in SIH. It may not be critical to identify the site of leakage. There is some evidence that lumbar epidural blood patching may be effective over nine spinal segments when the patient’s head is lowered to 30°. A recent report suggests that early ‘blind’ epidural blood patching within one week of onset is effective; demonstrating complete cure in 77% of 30 patients (with or without typical MRI changes) after one (57%) or two (20%) blood patches. These patients did not have lumbar punctures, nor was the site of CSF leakage identified.

**ii) Other treatment modalities**
Epidural saline injection has been reported to give immediate relief for headache. This is thought to be by reduction in the distensibility of the epidural space. This manoeuvre could also be life saving in obtunded patients with SIH.

A small group of patients with a typical history but no clear evidence of a leak, may fail ‘blind’ blood patches. These patients often prove very difficult to treat. It is possible in such cases that a CSF leak may have occurred, with a residual effect on CSF dynamics (eg lowered pressure setting in the choroid plexus, and sensitisation of meningeal afferents).

### Conclusion
Loss of CSF volume best explains the syndrome often designated ‘low-pressure headache’. CSF pressures may not always be low. Patients with chronic symptoms of SIH may not volunteer or recall a
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Department of Clinical Neurosciences
Joint meeting of Neuroscience for Clinicians 13 & Brain Repair Spring School 2006
28-30 March 2006
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The themes of the meeting are Molecular Plasticity, Systems Neuroscience, Cognitive Function and Mechanisms of repair. At the beginning of the meeting will be a clinical session where basic scientists have the opportunity to meet patients and learn about their conditions. A poster session is open to all participants for the display of their original work. To submit a poster, please send a completed abstract form to vas33@cam.ac.uk, by the registration deadline of Friday 10 March 2006. The Steering Group will select some of the abstracts submitted and invite the lead author to give a short presentation. If you do not wish to be considered for this please state this clearly on your abstract submission form.

Cost: £200 (without accommodation)
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The Guantors of Brain have offered a bursary to UK clinically qualified delegates which will fund all but £50 of the meeting fee. Registration deadline 10th March, 2006.