Offprint from
Advances and Technical Standards in Neurosurgery, Vol. 30
Edited by J.D. Pickard

Cranial Venous Outflow Obstruction and Pseudotumor Cerebri Syndrome

B. K. Owler[1,2], G. Parker[3], G. M. Halmagyi[1], I. H. Johnston[1], M. Besser[1,2], J. D. Pickard[4], and J. N. Higgins[5]

[1] T. Y. Nelson Departments of Neurosurgery and Neurology, Institute of Clinical Neurosciences, Royal Prince Alfred Hospital, Sydney, Australia
[2] Department of Surgery, University of Sydney, Sydney, Australia
[3] Department of Radiology, Royal Prince Alfred Hospital, Sydney, Australia
[4] Department of Neurosurgery, Academic Neurosurgical Unit, University of Cambridge, Addenbrookes Hospital, Cambridge, UK
[5] Department of Neuroradiology, Addenbrookes Hospital, Cambridge, UK

With 14 Figures

Contents

Abbreviations

ACCS	Average Combined Venous Conduit Score
AVM	Arteriovenous Malformation
BMI	Body Mass Index
CBF	Cerebral Blood Flow
CBV	Cerebral Blood Volume
cmCSF	centimetres of CSF
cmH_2O	centimetres of water
$CMRO_2$	Cerebral Metabolic Rate of Oxygen
CPP	Cerebral Perfusion Pressure
CSF	Cerebrospinal Fluid
CT	Computed Tomography
CVT	Cerebral Venous Sinus Thrombosis
DRCV	Direct Retrograde Cerebral Venography
ICP	Intracranial Pressure
kg/m^2	kilograms per square metre
mmHg	millimetres of Mercury
mmHg/ml/min	millimetres of Mercury per millilitre per minute
MR	Magnetic Resonance
MRI	Magnetic Resonance Imaging
MRV	Magnetic Resonance Venography
PTS	Pseudotumor cerebri syndrome
R_{csf}	Resistance to CSF absorption
SSS	Superior Sagittal Sinus
SVC	Superior Vena Cava

Abstract

The pathophysiology of PTS including idiopathic intracranial hypertension or 'BIH', remains controversial. The older literature frequently referred to pathology in the cerebral venous drainage but more modern imaging techniques (CT and early MR) failed to reveal gross venous pathology. The role of impaired cranial venous outflow has recently been re-examined in the light of new methods of investigation (advanced MR venography and direct microcatheter venography with manometry) and of treatment (venous sinus stenting).

Venous sinus obstruction in PTS is a more common factor in the pathogenesis of the condition than previously recognised. Venous obstruction may be primary, that is, it is the underlying aetiological factor in PTS. Venous sinus obstruction may also be secondary to raised CSF pressure which may exacerbate problems with intracranial compliance and raised CSF pressure. Early experience with venous stenting suggests that it may be a helpful treatment for patients with PTS but more experience

and longer follow-up is required to define the subgroups of patients for whom it is most appropriate.

Keywords: Pseudotumor cerebri syndrome; idiopathic intracranial hypertension; benign intracranial hypertension; papilloedema; intracranial pressure; cerebral venous drainage; venous stent, MR venography.

Introduction

There has been a recent revival of interest in the role of impaired cranial venous outflow in the causation of the PTS, even to the point of proposing that this may be the one underlying factor in all cases [78, 86]. For a general review of PTS please see reference 169a. Although the evidence is insufficient to establish such a unifying hypothesis on causation, nonetheless there is enough to suggest that some form of venous outflow pathology is present in a significant number of cases, the presence of which is likely to have been overlooked in the period when CT scanning was the basis of diagnosis [74]. Two recent developments make this an issue of significance. First, the means are now available as never before to detect the presence of cranial venous outflow tract pathology – advanced MR imaging methods [43, 64] and microcatheter venography with manometry. Second, there are now techniques available for direct treatment of intracranial venous sinus obstruction – endovascular clot lysis [88] and venous sinus stenting [63, 65, 128, 130]. Such developments, in their importance for the diagnosis and treatment of PTS, make a review of the subject of cranial venous outflow obstruction in this condition both pertinent and timely.

Historical Perspective

The association between cranial venous outflow obstruction and PTS dates back to the earliest descriptions of the latter condition, indeed even prior to the reports of Quincke [138, 139] and Nonne [123] which are generally taken to represent the first recognition of a specific condition initially called either meningitis serosa (Quincke, 1893) or pseudotumor cerebri (Nonne, 1904). Thus Taylor wrote in the 1890 edition of *The Practice of Medicine*: ''It is important to remember what has now been verified in numerous cases that in mastoid suppuration there is often double optic neuritis with an entire absence of meningitis or abscesses proved by post-mortem examination, or by recovery after simple trephining of the mastoid cells.'' The link with ear disease was through involvement of the lateral sinuses by the disease itself, or through internal jugular vein ligation as a means of treatment. For example, Newton Pitt, also in 1890 [121], described three patients, all of whom had papilloedema but no other CNS signs, and who

recovered, one having had a lateral sinus explored with clot removal, and the internal jugular vein ligated.

In the first three decades of the 20th century there were numerous reports of PTS occurring in conjunction with chronic suppurative otitis media and mastoiditis to the extent that Symonds [170] in 1931 felt able to define a condition of otitic hydrocephalus in which CSF excess due to over-production or impaired absorption followed cranial venous sinus, particularly but not exclusively transverse sinus obstruction, occurring secondary to chronic middle ear or other infection. In addition, Liedler in 1928 [102] was probably the first to describe PTS after ligation of one or both internal jugular veins in the treatment of chronic ear disease. Symonds' concept did not, however, survive the neuroradiological developments of the 1930s when the newly introduced techniques of encephalography and ventriculography showed that there was no demonstrable increase in the volume of fluid in the intracranial CSF-containing spaces in these cases. This has, of course, been an enduring difficulty in establishing a disturbance of CSF hydrodynamics as primary in PTS. Whatever the precise mechanism, the association of PTS with chronic ear disease and venous sinus pathology remained important. Thus in other significant reports from the 1930s, six of the fifteen cases reported by Davidoff & Dyke [33] had chronic suppurative otitis media or other infection whilst all of Gardner's [48] cases had chronic ear disease, the majority also having lateral sinus occlusion.

In parallel with the literature on so-called 'otitic hydrocephalus' a series of cases was published describing "traumatic hydrocephalus" [109]. This misnomer was used to describe cases of PTS occurring after closed head injury, either with or without skull fractures. The association between closed head injury and venous sinus obstruction was first proposed by Ecker in 1946 [40] but was not confirmed using venography until later by several other groups [11, 84, 109]. These cases were distinct from those in which there was a depressed fracture fragment or a penetrating injury. Most cases involved either a non-displaced linear occipital skull fracture crossing the sinus or a closed head injury without a fracture.

By the 1950s the relation between PTS and cranial venous sinus pathology, particularly secondary to chronic ear infection, was well-established, although hydrocephalus had been excluded. In an important paper in 1955, Foley [45] collected from the literature 46 cases of benign intracranial hypertension (a term which he introduced) which he labeled as otitic and described 60 cases of his own of which 13 were otitic or cerebral venous in origin. In 25 cases with right-sided otitis media mastoidectomy was performed in 21. Thrombosis of the lateral sinus was proven at surgery in 14 cases whilst another 6 had some type of sinus involvement such as perisinus abscess. Of the 13 cases with left-sided otitis media, mastoidectomy

was performed in 9 with lateral sinus thrombosis in 3 and other involvement of the lateral sinus in 2 more. Five cases had bilateral ear disease and of these 4 went on to mastoidectomy. In 2 there was left-sided lateral sinus thrombosis and in 2 the sinuses were apparently normal. Foley proposed that lateral sinus thrombosis, presumably of the dominant sinus, rather than thrombosis of the superior sagittal sinus (SSS), was the primary pathology in otitic PTS.

Four other aspects of the possible link between PTS and cranial venous outflow obstruction were also documented by this time. First, Evans [42] gave further evidence of PTS following internal jugular vein ligation although in reviewing other reports as well as his own cases he found that none of the 7 patients having bilateral ligation for non-otitic problems developed papilloedema whereas the 3 cases who had the procedure in relation to ear disease did. Of 6 cases who had unilateral ligation for bilateral ear disease only one developed papilloedema. Second, there were several reports linking PTS with chronic respiratory disease and cardiac failure with the presumption of increased venous pressure [6, 21, 155]. Third, there were the first reports linking PTS with blood disorders which could be presumed in some instances to act through venous obstruction [38, 103, 172]. Fourth, and most significant, was the study by Ray and Dunbar [141] who used the technique of direct sinography in which a catheter was introduced via a burr-hole into the anterior segment of the SSS. They studied 4 patients, 2 of whom were identified as having PTS without any antecedent factors. Both had failed to respond satisfactorily to subtemporal decompression and both showed evidence of obstruction in the posterior segment of the SSS with elevation of intra-sinus pressure, one going on to clot removal with apparent benefit. A third case, described as a typical case of 'otitic hydrocephalus', was found to have complete obstruction of the right transverse sinus and a small left transverse sinus. There was measured elevation of SSS pressure [320 mmH_2O]. Their remaining case would not qualify for the diagnosis of PTS. The authors recommended sinography be introduced for the investigation of patients with PTS. They also proposed that the formation of collaterals after venous sinus obstruction was the mechanism for the spontaneous resolution of symptoms. Foley [45] also performed venography on a wider population of patients with PTS. Sixty cases were reviewed; 11 of which were classified as otitic hydrocephalus. Angiography was performed in 13 cases, however, only the patency of the SSS drew direct comment.

In the period between 1960 and 1980 the connection between PTS and cranial venous outflow obstruction fell out of prominence for a number of reasons. Among these may be numbered the introduction of effective antibiotic treatment which sharply reduced the incidence of chronic middle ear infection, the considerable number of other putative aetiological factors in

PTS which would not be thought to act through venous sinus obstruction, and the introduction of CT scanning which reduced the likelihood of recognizing cranial venous outflow tract pathology. The report of Janny *et al.* [71] in 1981 might, however, be taken as signalling the return of focus on the role of cranial venous outflow in PTS, a focus which has sharpened over the last two decades with the technical advances referred to in the introduction. Their study, and those that have followed, will be considered in detail in what follows.

Prevalence of Cranial Venous Outflow Obstruction in Pseudotumor Cerebri Syndrome

The study of Janny *et al.* [71] was a landmark in the study of PTS. The authors studied 16 patients with primary PTS using a combination of ventricular CSF pressure monitoring, SSS pressure monitoring and direct antegrade venography via a midline frontal burr-hole. They demonstrated venous sinus obstruction in 5 of 16 patients. In 4 of these patients the obstruction was at the level of the transverse sinus, being bilateral, or single in a functionally predominant sinus. Although issues of lesion morphology or aetiology were not addressed it suggested that the prevalence of venous sinus obstruction in primary PTS may be higher than previously appreciated.

Unfortunately, the issues raised by Janny *et al.* received little attention in the literature with only sporadic reports on the topic of PTS and venous sinus pathology. One example is that of Bortoluzzi *et al.* [17] who reported a case of PTS with severe radiculopathy in whom obstruction of a dominant right transverse sinus was clearly demonstrated with venography. Cremer *et al.* [27] also reported a single case of bilateral transverse/sigmoid sinus stenosis with pressure gradients on manometry, probably due to giant arachnoid granulations, in a patient with PTS.

In the mid-1990's two important papers detailed the findings of direct retrograde cerebral venography (DRCV) with manometry in the study of PTS patients. The first was that of King *et al.* [86] who studied 11 patients. All had undergone CT, static MRI and conventional angiography. One patient was suspected of harbouring a SSS thrombosis on MRI but this was not confirmed on other investigations. Venous manometry demonstrated elevated SSS pressures in 9 patients; the remaining 2 patients were those in whom minocycline had been implicated in the aetiology. Of the patients with elevated SSS pressures, there were focal pressure gradients (of at least 10 mmHg) at the junction of the middle and distal thirds of the transverse sinuses bilaterally in all patients. Venography demonstrated morphological abnormalities in these regions ranging from mild to severe focal narrowing. In some cases there appeared to be intraluminal filling defects and in others

the sinus appeared smoothly tapered. These morphological characteristics were much more easily appreciated using venography than on conventional angiography. Shortly after a report from Karahalios *et al.* [78] suggested that venous sinus hypertension was the universal mechanism of PTS. In their study of 10 patients with PTS, 5 patients were found to have focal venous sinus obstruction. Later, in King *et al.'s* [85] second paper, a total of 21 patients with PTS for which no obvious cause was found (for example minocycline) were examined using venography and manometry. With the exception of 2 patients, SSS and CSF pressures followed each other closely and there were transverse sinus obstructions with significant pressure gradients.

The findings of Karahalios [78] and of King *et al.* [85, 86] of venous obstruction in PTC using DRCV were at odds with the conventional opinion regarding the pathophysiology of PTS. This probably reflects the fact that investigations of the venous sinuses in PTS were usually performed on the basis of four incorrect assumptions. First, the cause of venous sinus obstruction was thrombosis rather than stenosis or some other lesion. Second, the site of the obstruction was usually in the SSS. Third, static CT or MRI had sufficient sensitivity to detect the obstructing lesion. Fourth, when MRV was performed and was focused on the transverse sinuses, absence of flow in a transverse sinus was interpreted as a normal variant due to sinus hypoplasia or an artefact such as inflow turbulence.

The importance of the focus of the investigations and index of suspicion was evident from the report of Johnston *et al.* [74] who retrospectively reviewed 188 patients with PTS who had presented between 1968 and 1999. The group included 29 children. The overall incidence of venous sinus obstruction, they termed cranial venous outflow obstruction, was 19.7%. Of these 37 cases, an underlying cause of the obstruction could be identified in 20. Presumed aetiologies included thrombophilia (7 cases), trauma (2 cases), tumour (2 cases), and congenital jugular foraminal narrowing and infective internal jugular vein thrombosis with retrograde thrombosis. The remaining cases of idiopathic cranial venous outflow obstructions were all female patients. As cases had been accumulated over a 30 year period, investigations for PTS varied considerably as did the index of suspicion for venous sinus obstruction. In the first decade the incidence was only 4.2%, compared to 15% in the second and 31% in the third. In the final decade patients were likely to be investigated with MRI/MRV. While the patients in the first decade often underwent cerebral angiography rarely was the investigation focused on the venous sinuses which probably explains the low incidence of venous obstruction in that group. These authors also found the transverse and sigmoid sinuses to be the most common sites of obstruction (20/37 cases). In 11 cases obstruction was bilateral. Of the 9 patients with unilateral obstruction, the transverse sinus was

definitely dominant in 6 cases and probably dominant in 2. In one case it was considered to be the non-dominant sinus although DRCV with manometry was not performed. Interestingly, only when the SSS became involved did obtundation or venous infarction become evident.

Two prospective case-control studies designed to investigate the prevalence of venous sinus obstruction in PTS have recently been published. Farb *et al.* [43] used a 3-D gadolinium enhanced MRV to examine the venous sinuses of 29 patients (age 37.2 years) with PTS and 59 control patients (age 60.3 years). The control group consisted of cancer patients that were undergoing MRI of the brain as a screening test for cerebral metastases. Patients with intracranial pathology were excluded from the study. The MRV of each patient was examined by 3 blinded radiologists. For each patient, an average combined venous conduit score (ACCS) of 2–8 was produced. For each side the patency of the transverse sinus was scored from 1–4 (1 = hypoplasia or severe stenosis and 4 = normal and patent). There was very high inter-observer reliability. With the exception of 2 patients, all had an ACCS of less than 5 (93.1%). Four of 59 controls (6.8%) had an ACCS of less than 5. Thus, an ACCS of less than 5 had a 93% specificity and sensitivity for PTS. For patients, there was no correlation between CSF pressure and ACCS. The morphology of the obstructing lesions amongst the PTS patients appeared extraluminal in 45 and intraluminal in 13 patients.

MRV was used by Higgins *et al.* [64] to examine 20 patients with PTS and 40 controls subjects. The control group consisted of patients who were recruited from patients presenting for MRI of another body region. Control patients were screened for headache and neurological disorders. Those with symptoms apart from very occasional minor headache were excluded. The PTS patients and asymptomatic controls were matched for sex and age. The MRVs were assessed for the existence of flow gaps in the transverse sinuses. No flow gaps could be seen in the transverse sinuses of any control patient on either side. In the PTS group, there were bilateral transverse flow gaps in 13 patients (65%). In only one patient were the sinuses normal bilaterally.

Interaction Between Venous Sinus Hypertension and CSF Pressure

The aforementioned recent observations demonstrating a much greater prevalence of venous sinus obstruction in patients with PTS raise the question of what role venous sinus obstruction occupies in the aetiology of PTS. Clearly, in cases of cerebral venous sinus thrombosis the role has been defined. However, the nature of venous sinus obstruction in PTS is different. Both intrinsic and extrinsic lesions have been identified and both characteristically are found in the region of the junction of the middle and dis-

tal thirds of the transverse sinus close to the asterion of the skull. Before attempting to answer the question of whether the lesions are the cause or effect of raised intracranial pressure, the effects of primarily raising venous pressure on CSF pressure, and the reverse, will be examined in both the experimental and clinical settings.

Effects of Raised Venous Pressure in Adults and Children

Experimentally, early studies aimed not to produce PTS but rather hydrocephalus by increasing venous sinus pressure. Attempts to produce sustained increases in venous sinus pressure, particularly by occluding large venous conduits, usually failed [8, 32]. Dixon & Halliburton [37] increased venous sinus (torcular) pressure acutely in the dog and found a small increase in CSF pressure (approximately 25% of the increase in venous pressure). The difficulties in these earlier experiments probably related to the difficulties in isolating the venous circulation in most species of laboratory animals, the propensity for the development of venous collaterals and the existence of alternative routes of CSF drainage by pathways such as the cribriform plate [135].

The first study in which adequate occlusion of cranial venous outflow was achieved was that of Bering & Salibi [15] in dogs. The external and internal jugular veins were ligated in the neck proximal to the facial vein. The condyloid foramen was also occluded. After one week, a neck dissection was performed and any collateral venous drainage was ligated. Of the 21 dogs subject to this procedure 13 developed hydrocephalus. In almost all animals both the CSF and SSS pressures were elevated. In dogs that developed hydrocephalus, CSF pressure fell after a few days and remained below the SSS pressure. However SSS pressure also fell with time and was associated with the development of collaterals as demonstrated using sinography. Of the 8 animals that did not develop hydrocephalus, ligation was incomplete in one while another was killed the day of completion of the surgery. In the remaining six animals both the CSF pressure and SSS venous pressures increased. Also examined were the pulse pressures of the CSF and SSS. In the eight animals so examined, 3 developed hydrocephalus and these animals had higher pulse pressures than those that did not. The results were taken as evidence of a long suspected link between hydrocephalus and venous sinus obstruction. However later studies did not confirm Bering and Salibi's findings. Guthrie *et al.* [57] obstructed the torcular and transverse sinuses of 10 adult dogs using cotton pledgelets in an attempt to produce hydrocephalus. Over a period of up to 29 weeks SSS pressure increased significantly as did CSF pressure. However both pressures fell towards 5 weeks and was associated with the development of venous collaterals around the torcular. There was no difference in ventric-

ular size at post-mortem. The result of the experiment, at least initially, was thus not hydrocephalus but PTS. It has also been suggested that the extent of dissection required to isolate the venous circulation in the animals of Bering and Salibi's study was so great that alterative routes of CSF drainage including the lymphatics were also compromised.

Clinically, venous sinus hypertension due to obstruction is known to result in PTS. The most common clinical example of this is the venous obstruction of the cerebral sinuses that occurs in cerebral venous sinus thrombosis (CVT). Cerebral venous thrombosis is the most well recognized cause of venous sinus hypertension and when venous sinus thrombosis is limited to the lumen of the sinus and does not involve cortical veins the clinical picture may be identical to PTS [18, 147]. The acknowledgement of venous sinus thrombosis as a cause of PTS syndrome is evident in the need to exclude venous sinus thrombosis in cases of PTS [98]. This distinction between CVT and PTS is justified by the differences in management and prognosis of the two conditions [99]. These issues aside CVT does demonstrate the clinical effects of venous sinus obstruction on CSF and intracranial pressures.

Venous sinus obstruction may also occur from non-thrombotic venous sinus obstruction. There are a few small series and a large number of case reports documenting PTS due to mass lesion both intrinsic and extrinsic to the venous sinuses that result in PTS. A non-exhaustive list of these published cases are presented in Table 1. Furthermore relief of the obstruction by removal of the offending lesion usually results in a reduction in CSF pressure and relief of clinical symptoms.

Venous sinus obstruction causes an increase in venous sinus pressure proximally. The effects of this raised cranial venous outflow pressure on the brain and CSF do not occur in isolation and so need to be considered together. Elevated venous sinus pressure affects both CSF absorption and production. The main site of CSF absorption is thought to be the arachnoid villi of the lateral lacunae and SSS's. The absorption process is a pressure-dependent process. Davson [34] demonstrated that the absorption of CSF depends on a pressure gradient between the subarachnoid space and the venous sinus of approximately 3 mmHg in health. Thus when venous sinus pressure is raised, CSF pressure must also rise in order for CSF absorption to continue. This explains why CSF pressure is usually a few millimetres of mercury higher than venous sinus pressure in cases where both pressures are monitored simultaneously. In addition to causing an increase in CSF pressure, venous sinus hypertension may also effect production. CSF production is for the most part a pressure-independent process in respect to CSF pressure. However, venous sinus hypertension will affect venous outflow from the site of CSF production, that is, the choroid plexus. As part of the mechanism of CSF production is filtration of plasma

Table 1. *Case Reports and Series of Patients with a Pseudotumor Syndrome Secondary to Venous Sinus Obstruction of Various Aetiologies*

Reference	Pathology	Number of cases
[89] Kollar et al. 1999	AVM deep venous system – post embolisation	1 (child)
[97] Lee et al. 2001	Torcular epidermoid	1 (adult)
[92] Lam et al. 2001	Torcular epidermoid	1 (adult)
[91] Lam et al. 1992	Radical neck dissection/sigmoid sinus ligation	3 (adults)
[91] Lam et al. 1992	CVC thrombosis	2 (adults)
[53] Goldsmith et al. 1991	Ca prostate metastasis: SSS compression	1 (adult)
[132] Plant et al. 1991	Plasmacytoma & Ewing's sarcoma	2 (adults)
[80] Keiper et al. 1999	Suboccipital/translabyrinthine craniectomy	5 (adults)
[17] Bortoluzzi et al. 1982	Bilateral lateral sinus obstruction ?cause	1 (adult)
[132] Plant et al. 1991	Occipital skull tumours	2 (adults)
[82] Kim et al. 2000	Metastatic prostate cancer	1 (adult)
[133] Powers et al. 1986	Cholesteatoma	1 (adult)
[27] Cremer et al. 1996	Small meningioma & thrombosis	1 (adult)
[93] Lamas et al. 1977	Dural posterior fossa AVM	1 (adult)
[46] Ford et al. 1939	Occlusion left lateral sinus	1 (adult)
[48] Gardner 1939	Unilateral sinus occlusion	3 (adults)
[56] Greer 1962	Lateral sinus thrombosis – mastoiditis	3 (adults)
[117] Medlock et al. 1992	Depressed Skull Fracture	1 (adult)
[90] Kuker et al. 1997	Epidermoid	1 (adult)
[3] Angeli et al. 1994	Glomus Jugulare	1 (adult)
[9] Beck et al. 1979	Glomus Jugulare	1 (adult)
[141] Ray et al. 1951	SSS thrombosis	3 (adults)
[72] Jicha et al. 2003	Cardiac septal defect – L-R shunt	1 (adult)

across the choroid, the increase in venous sinus pressure, if the deep system is affected, might increase the hydrostatic pressure in the capillaries of the choroids plexus and increase CSF production. Kollar *et al.* [89] reported a case of PTS in a 5 year-old boy who had undergone embolisation of a deep temporal lobe AVM that drained via large venous varix into the vein of Galen. After embolisation a cerebral angiogram demonstrated that the vein of Galen did not fill and only sluggish flow in the straight sinus. The other dural sinuses were patent. The authors speculated that the venous outflow of the deep venous system would increase transcapillary CSF production in the choroid plexus. If this production was in excess of absorptive capacity, as may be the case if the system was underdeveloped, then PTS might result.

The other effect of raising venous sinus pressure is on venous outflow from the brain itself. Apart from perhaps the lumbar subarachnoid space, the cerebral venous system contributes most to the compliance of the intracranial space. Therefore, an increase in venous sinus and cerebral venous

pressure increases the volume of the venous system proximal to the obstruction and reduces the compliance of the craniospinal axis. When venous sinus obstruction occurs, the high compliance cerebral venous system should increase in size and should be reflected in the observation of increased cerebral blood volume (CBV). In fact, Dandy [31] hypothesised that PTS was a result of increased CBV. Mathew *et al.* [113] calculated cerebral blood flow (CBF) and CBV before and after treatment using carotid injections of Xe^{133} and Tc^{99m}. Both patients demonstrated increased CBV and this decreased towards normal when CSF pressure had been reduced. CBF was also slightly reduced in both cases prior to treatment and increased after CSF pressure reduction. Mathew *et al.* [113] stated that the cases provide evidence of venous engorgement. Raichle *et al.* [140] studied CBF, cerebral metabolic rate oxygen ($CMRO_2$) and CBV using carotid injection of ^{15}O-labelled water, oxyhaemoglobin and carboxyhaemoglobin. Compared to normal values there was a small but significant reduction in CBF of 18.5% ($n = 9$) and an increase in CBV of 33% ($n = 8$). In 3 patients, the studies were repeated after CSF was removed to lower ICP. CBF remained unchanged but there was a 10% reduction in CBV. Most patients had undergone cerebral angiography and no evidence of venous outflow obstruction was reported. In contrast, Brooks *et al.* [19] used positron emission tomography and steady-state inhalation of $C^{15}O_2$, $^{15}O_2$ and ^{11}CO to study regional CBF, $CMRO_2$ and CBV. No difference in any of these variables could be demonstrated between the 5 patients and 15 controls. In one patient, the study was repeated after lumbo-peritoneal shunting. CBF and $CMRO_2$ appeared improved, at least in white matter. There was no change in CBV. Thus there is at least tentative evidence in a limited number of studies for an increase in CBV in PTS. Modern imaging techniques have yet to be applied to the study of CBV in PTS.

An increase in cerebral venous pressure will alter the Starling equation across the capillary bed as the venous outflow pressure and therefore capillary hydrostatic pressure is increased. This would normally result in an increase in ultrafiltrate and vasogenic oedema. There is little direct evidence for brain oedema in PTS. Although Sahs, Hyndman and Joynt [149, 150] provided histological evidence of brain oedema at post-mortem, their findings have been questioned on the basis of tissue preparation and artefact. Wall [176] could find no evidence of brain oedema in 2 patients with non-active PTS at post-mortem. However it should be clear that although there is no histological evidence supporting the finding of brain oedema there is no good evidence to refute such a claim.

More information has become available using MR imaging which has the ability to detect increased brain water. Early studies using low strength magnets without the benefits of diffusion weighted scans were contradictory. Connolly *et al.* [24] using qualitative examination of images obtained

on a 0.15 Tesla magnet reported no signal change in 7 children with PTS. The same finding was reported by Silbergleit *et al.* [154] in 6 patients with PTS using a 0.35 Tesla magnet. Benefiting from improved technology, Moser *et al.* [120] used a heavily-weighted T2 MR technique (1.5 Tesla) to investigate the brain water content in 10 patients with PTS. They found an increase in the signal white matter free water content as reflected in prolongation of the T2 relaxation time. The authors concluded that this represents a diffuse low level of oedema. In addition, a triple-echo sodium MR technique was used to study 5 patients. Three demonstrated no change in their sodium signal. However, two patients who were clinically the most severely affected demonstrated increases in their sodium signal. As most sodium is extracellular, the authors concluded that the increase in brain water was likely to represent a vasogenic oedema. Sorenson *et al.* [161, 162] using diffusion sensitive sequences at 1.5 Tesla found that self-diffusion of white matter was increased. In some cases this was restricted to the periventricular region while in others it was distributed throughout the brain.

Gideon *et al.* [50] investigated a group of patients with PTS using diffusion-weighted MR imaging. They applied a diffusion gradient in one direction only and found that diffusion was increased in 10 patients with PTS. These studies indicate that there is a small but significant amount of brain oedema in PTS. In contrast, a more recent study by Bastin *et al.* [5] in 10 patients could demonstrate no evidence of brain oedema in PTS. These authors also used diffusion-weighted imaging (1.5 Tesla) but obtained their images using diffusion gradients in three orthogonal directions and used echo planar imaging. This allows very short acquisition times and minimises the effects of bulk brain motion. Using echo-planar imaging and diffusion tensor imaging at 3 Tesla we performed a regional analysis of the brains of 5 patients with PTS and 6 normal healthy controls [129]. Apart from small focal decreases in trace (diffusivity) in some grey matter regions, there were no differences in trace or the anisotropy of white matter regions between the two groups.

The effects of an increase in venous sinus pressure are therefore several although competing. Obstruction to cranial venous outflow appears to produce a balance between an increase in CSF pressure, capillary hydrostatic pressure, intraparenchymal pressure and CBV. This is brought about by these components being enclosed within the rigid cranium (the Munro-Kellie hypothesis). Although there is possibly a small increase in CBV, the pressure exerted on the parenchyma by an increased CSF pressure increases intraparenchymal pressure and so negates the ability of the increased capillary hydrostatic pressure to produce brain oedema. Thus the morphology of the brain does not appear to change although the intracranial pressure is increased and the compliance significantly reduced. A disturbance of this balance may be the reason for an increase tendency to-

wards slit ventricle syndrome in PTS after ventricular shunting and the formation of the acquired Chiari syndrome after lumboperitoneal shunting in PTS. That is to say, reducing CSF pressure in the presence of continued raised venous pressure will leave the increased capillary hydrostatic pressure unbalanced resulting in brain oedema and an increase in cerebral volume.

Effects of Raised Venous Pressure in Infants

In neonates and infants the effects of raised venous sinus pressure are different from those in adults and children. Haar and Miller [60] as well as Rosman & Shands [146] catalogued a handful of cases of venous sinus obstruction with CSF circulation disorders. In patients under 18 months of age hydrocephalus developed while in those over 3 years of age PTS resulted. Both groups concluded that whether venous sinus obstruction results in hydrocephalus or PTS depends on the state of the cranial sutures [60, 146]. This difference in clinical expression of venous sinus hypertension was demonstrated experimentally by Olivero & Asner [126]. Occlusion of the posterior sagittal sinus in 10 craniectomised rabbits caused a moderate but significant increase in ventricular size compared to 5 animals that had undergone sinus occlusion but not craniectomy (distance from head of caudate to junction of septum pellucidum and corpus callosum: $7.2 +/- 0.7$ mm compared to $4.6 +/- 0.5$ mm).

Clinically, like in adults and older children, there are a large number of case reports in which various problems have caused venous hypertension (Fig. 1). However, instead of PTS, these cases develop hydrocephalus. These case series and reports are presented in Table 2. Although in some reports or series the age of the patients is greater than 18 months almost all cases had evidence of increasing head circumference from in the neonatal period. In some cases relief of the obstruction may produce relief of hydrocephalus and/or megalencephaly.

Due to these observations, there has been a gradual recognition of the role of venous sinus hypertension in the aetiology of some forms of infantile hydrocephalus and megalencephaly that have previously been thought to occur through other mechanisms. This is particularly true in achondroplasia [182] and patients with myelomeningoceles. More recently, venous outflow obstruction has been implicated in the aetiology of ventriculomegaly commonly seen in various forms of osteopetrosis [29].

Achondroplasia is frequently associated with hydrocephalus and megalencephaly. Growth in head circumference is most prominent in the first few months of life and is followed by a period of stabilisation between the 4^{th} and 24^{th} months. Pierre-Kahn *et al.* [131] found clinical evidence of increased prominence of venous collateral circulation in 17 of 18 patients with achondroplasia. One patient underwent angiography that depicted

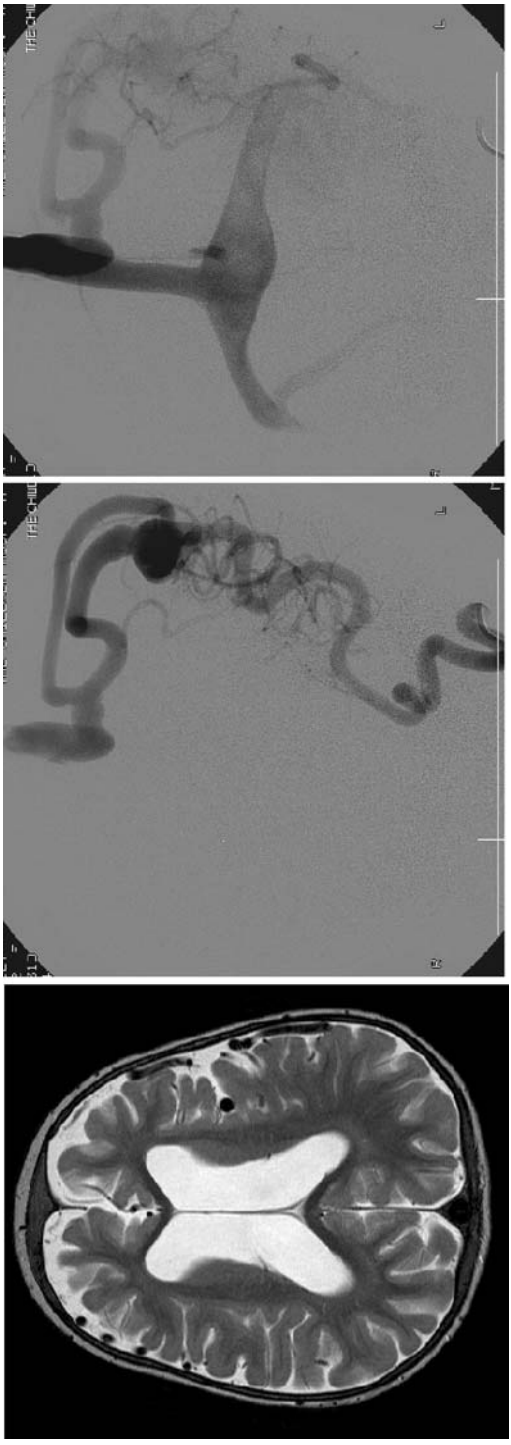

Fig. 1. Example of a 23 month old girl who presented with increasing head circumference and hydrocephalus. She was found to have an AV fistula fed by the middle cerebral arteries and which drained into the SSS

Table 2. *Case Series and Reports of Hydrocephalus Resulting from Venous Sinus Obstruction of Varying Aetiology*

Reference	Pathology	Number of cases
[58] Guttierrez et al. 1975	Agenesis of arachnoid granulations	2 (children)
[146] Rosman et al. 1978	CCF/Glenn procedure	1 (infant)
[41] Emery et al. 1956	Congenital abnormality SSS	2 (children)
[116] McLaughlin et al. 1997	SVC syndrome	3 (infants)
[79] Katznelson 1978	Cystic Fibrosis	3 (infants)
[83] Kinal 1966	Posterior fossa tumour compressing lateral sinus	4 (children)
[151] Sainte-Rose et al. 1984	Craniostenosis and achondroplasia	4 (children)
[182] Yamada 1981	Achondroplasia and jugular foramen stenosis	10 (children)
[60] Haar et al. 1975	SVC syndrome	1 (infant)
[67] Hooper 1961	SVC syndrome (thymic hyperplasia)	1 (infant)
[35] de Lange et al. 1970	AVM draining to both lateral sinuses	1 (16 years)
[28] Cronqvist et al. 1972	Cerebral AVM	2 (infants)
[49] Gibson et al. 1959	Cerebral AVM – vein of Galen	1 (infant)
[164] Stewart et al. 1975	Jugular vein thrombosis – TPN	4 (infants)

severe bilateral sigmoid sinus stenosis at the level of the jugular foramen. Friedman & Mickle [47] also reported a case with bilateral venous outflow obstruction at the level of the jugular bulb. Steinbok *et al.* [163] studied four achondroplastic children with active hydrocephalus using retrograde venography and documented significant venous hypertension in at least 2 patients associated with jugular vein stenosis and superior vena caval obstruction at the level of thoracic outlet. Furthermore, Lundar *et al.* [105] reported a case of achondroplasia with active hydrocephalus. Digital subtraction angiography demonstrated severe bilateral venous outflow obstruction at the foramen magnum. Operative decompression of the right sigmoid sinus and its junction with the jugular vein at the foramen was undertaken. A bony spur was found to be kinking the vein. Improved venous outflow was confirmed radiologically. Head circumference decreased and growth normalised.

Venous sinus obstruction is also common in craniosynostosis. Rollins *et al.* [143] using MRV studied 17 patients with craniosynostosis and a mean age of 7.3 years (4 months–34 years). The authors concentrated on the patency of the sigmoid sinus and jugular veins. No comments were made on the transverse sinuses. In 12 patients the MRV was abnormal. In 9 patients there was venous outflow obstruction at the sigmoid sinus and/or jugular bulb while in 3 patients there was jugular vein obstruction. Of these patients 9 had hydrocephalus. Venous sinus obstruction was associated

with enlargement of collateral venous drainage particularly via the posterior condylar veins. Two of 11 patients with hydrocephalus had a normal MRV. However, the results of this study are difficult to interpret given the age of the patients and the time since the initial surgery in most cases. Taylor *et al.* [171] studied 23 such patients with digital subtraction angiography. ICP monitoring confirmed raised pressure in 21 cases and in 2 cases plain X-ray suggested the presence of large transcalvarial venous collateral drainage. In a total of 24 angiograms there was a greater than 50% stenosis or no flow in the sigmoid-jugular venous complex in 18 patients; in 7 unilateral and 11 bilateral. Of these 18 angiograms, florid transcalvarial collateral venous flow via a large stylomastoid emissary vein was observed in 11 cases. The severity of the stenosis did not correlate with ICP but did appear age-related. The mean age of patients with bilateral stenosis was 20.4 months, unilateral stenosis 25 months and 54 months in those with mild or no stenosis. The authors conclude that patients with more severe venous outflow obstruction tend to present with raised ICP earlier.

The importance of the state of the cranial sutures for the clinical manifestation of venous sinus obstruction is exemplified by the condition of craniosynostosis. If ICP is raised, this may manifest itself in several ways. Most commonly, raised ICP is noted after investigation for behavioural alteration or papilloedema. In the presence of normal or small sized ventricles, raised ICP is frequently attributed to inadequate intracranial volume and craniostenosis. However hydrocephalus is also recognised as occurring in association with craniosynostosis, particularly in syndromic cases where multiple sutures and the skull base are involved [44]. Hydrocephalus may occur with or without head enlargement [52]. Hydrocephalus with head enlargement may occur in the presence of sufficient uninvolved sutures or after the surgical suture release or cranial vault remodelling.

Cinalli *et al.* [23] reviewed 1727 cases of craniosynostosis. Of the 1447 cases of non-syndromic craniosynostosis, the prevalence of hydrocephalus at presentation requiring shunt insertion was just 0.28%; similar to the normal population. Two of these cases with complex craniosynostosis exhibited bilateral jugular foraminal narrowing. In comparison, syndromic cases of craniosynostosis (280) had a prevalence of hydrocephalus requiring a shunt of 12.1%. Non-progressive ventriculomegaly was seen in 15.7%. Hydrocephalus was most common in patients with Crouzon's disease (54%) and all of these patients had either their coronal, sagittal or both sutures open at the time of ventricular enlargement. In the other patients hydrocephalus occurred after surgical correction and all of these had had more severe craniosynostosis with fusion of both the coronal and sagittal sutures. Angiography demonstrated bilateral jugular vein stenosis in 13/16 patients (81.3%) examined. Of the patients with Apert's syndrome, progressive hydrocephalus requiring shunting was less common (6.5%) al-

though 18 (23.7%) had non-progressive ventriculomegaly at presentation and another 12 developed ventriculomegaly not requiring shunting after surgery. Thirteen patients underwent angiography and 7 demonstrated jugular venous obstruction (53.8%).

To summarise, venous sinus hypertension produces an increase in CSF pressure. Whether hydrocephalus or PTS results depends on the state of the cranial sutures. Where the cranial sutures are fused, such as in adults, older children and infants with severe forms of craniosynostosis, raised venous pressure causes a PTS syndrome. There is an increase in CSF pressure and a reduction in intracranial compliance. Available evidence suggests that brain oedema does not occur and that there may be either a small or no increase in CBV. If the cranial sutures are patent, such as in the infant, hydrocephalus results as the raised CSF pressure is allowed to act on the cerebral mantle and cranium.

Effects of Raised CSF Pressure

In conditions that affect the CSF circulation and raise CSF pressure there are secondary effects on the cerebral veins and the dural venous sinuses. The cerebral veins must cross the subarachnoid space in order to reach the sinuses or lateral lacunae. At this point they are prone to compression by raised CSF pressure. The lateral lacunae, because of their wide surface area, are even more prone to compression and may assist in maintaining the patency of the cerebral venous outflow. It is also proposed that in health, these structures act as Starling resistors regulating CSF absorption according to changes in CSF pressure. That is when CSF pressure is high, the lacunae collapse, decreasing venous flow, dropping sinus pressure, increasing the gradient across the arachnoid villi and increasing CSF absorption.

The dural sinuses are enclosed between the two layers of the dura. The SSS and the transverse sinuses are triangular in cross section with their base on the dura lining the skull. At the apex of the triangle the other dural leaves fuse such that the walls of these sinuses are held open by the falx cerebri and tentorium cerebelli. The sigmoid sinus also appears protected as it usually runs in a deep groove to the jugular foramen. The assumption usually made is that the sinuses are not compressible due to the structures that maintain their shape. However, the sinuses, particularly the transverse sinuses, may be compressed due to significantly raised intracranial pressure as demonstrated by a number of experimental and clinical studies (*vide infra*).

Cushing [30] studied the effects of raised CSF pressure on the SSS of the dog and reported that increased CSF pressure resulted in SSS collapse. Wright [181] later repeated the study, again in the dog, but found that this collapse only occurred when the dura surrounding the sinus had been incised. He did however demonstrate that pressures within the SSS were af-

fected by CSF pressure in the subarachnoid space. Both Becht [7] and Weed & Flexner [180] reported that venous sinus pressures were not influenced by changes in CSF pressure. In contrast Dixon & Halliburton [37] reported that increases in CSF pressure were accompanied by increases in torcular venous pressure. However, Wright [181] and Bedford [10] noted that increases in CSF pressure caused a small decrease in venous sinus pressure. This effect was usually seen as CSF pressure was initially being increased and most likely represented a compressive effect on the cerebral veins in the subarachnoid space and a decrease in venous return to the SSS. In terms of the relationship between the venous sinuses and CSF pressure, the arrangement of venous sinuses in the dog is different from that in humans in that the torcular and lateral sinuses are encased in bone and thus protected from any compressive effects. The applicability of these early studies to human physiology is therefore questionable.

Langfitt *et al.* [94] reported the effects of increasing ICP using a subdural balloon in the rhesus monkey. Initially, SSS pressure decreased, increased or was unchanged. When ICP approached 30 mmHg SSS pressure began to rise. The transverse and sigmoid sinus pressures were influenced far less by changes in ICP. The authors reported that a gradient was demonstrated in some instances between the SSS and distal transverse sinus. In an extension of that study, Shapiro *et al.* [152] described the morphological changes of the cerebral venous system that took place in the rhesus monkey during fatal increases in ICP due to brain oedema. These animals demonstrated collapse of the SSS and straight sinuses presumably secondarily to compression. However, as ICP approached arterial pressure in these animals the implications of the results are not clear. Johnston & Rowan's [77] study of the effects of raised intracranial pressure on cerebral venous blood flow in baboons also demonstrated that the sinuses may collapse with increasing ICP. Using saline infusion into the cisterna magna of 6 baboons to raise ICP, cortical venous pressure was noted to rise linearly with ICP and remained above subarachnoid CSF pressure at all times. Animals demonstrated two distinct patterns of SSS pressure response. In 3 animals SSS pressure remained less than 20 mmHg while in the other 3 animals SSS pressure rose linearly once ICP reached 40 mmHg and remained just below cortical venous pressure.

In man, Greenfield & Tindall [55] performed cerebral angiography on 3 patients at normal and raised CSF pressures and found compression of the cerebral veins in the subarachnoid space or of the venous sinuses. Kinal [83] performed sinography on 4 patients (age 7 months–15 years) who presented with evidence of a posterior fossa lesion. In all patients the lesions had resulted in obstructive hydrocephalus with raised pressure. Sinography revealed bilateral transverse/sigmoid sinus stenosis with development of venous collateral circulation. Removal of the posterior fossa lesions resulted

in improvement in venous sinus flow demonstrated by opacification of the transverse/sigmoid sinuses and the disappearance of venous collaterals on sinography.

Osterholm [127] performed antegrade cerebral venography in patients with subdural (4 patients) or extradural (1 patient) haematomas. SSS pressure was measured and venography was performed immediately prior to operative decompression. Venous sinus pressure was 21–46 cm saline and venography demonstrated bilateral transverse sinus stenosis with opacification of venous collaterals. Cerebral decompression resulted in a fall in venous pressure to 0–4 cm saline and venography showed normally filling transverse sinuses without opacification of venous collaterals. To further examine the secondary collapse of the venous sinuses as a result of increasing ICP, Osterholm [127] also performed experiments on 3 fresh human cadavers. Into the anterior SSS was perfused 600 ml/min of saline. Distally the SVC was open. Ventricular and cisterna magna CSF pressures were monitored. Infusion of normal saline into the cisterna magna allowed ICP to be raised in 10 mmHg increments. No change in SSS flow was appreciable below 20 mmHg. At 50 mmHg there was a 30% flow reduction, at 70 mmHg there was a 60% SSS flow reduction and at 200 mmHg SSS flow was arrested.

Martins *et al.* [110] monitored CSF pressure and SSS pressure simultaneously in 12 patients undergoing ventriculography who were subsequently found to have cerebral tumours. In 9 patients SSS pressure was not related to CSF pressure and remained below 14 mmHg in the presence of spontaneous or artificial increases in CSF pressure up to 75 mmHg. On venography performed in 2 of these patients there was no change in CSF pressure while in the third patient there was a partial collapse of the transverse sinus at 40 mmHg despite there being no change in SSS pressure when CSF pressure was higher. In 3 patients, SSS pressure changed with ICP. In 2 patients it increased but to a lesser extent than CSF pressure while in another patient CSF pressure and SSS pressure remained closely related throughout. In one patient who demonstrated an increase in SSS pressure with increased CSF pressure there was partial collapse of the sagittal and transverse sinuses at 40 mmHg. In addition Martins *et al.* [110] noted that 3 patients had pressure waves during recording. In 2 patients the duration was less than 1 minute. These patients had no change in SSS pressure during the pressure wave. In contrast, the third patient experienced a pressure wave of 5 minutes and this was associated with an increase in SSS pressure.

The ability of increased CSF pressure to cause venous sinus obstruction is also seen in infants with hydrocephalus. Shulman and Ranshoff [153] measured CSF and SSS pressures of 15 such cases of varying causes and included both communicating and non-communicating forms of hydrocephalus. They found a close relationship between the SSS pressure and CSF

pressure and the ratio of the former to latter was 1.08. By plotting the SSS pressure versus the CSF pressure they found a regression co-efficient of 0.95 with a standard error of 0.08 indicating that SSS pressure and CSF pressure were closely related in these patients. In some patients CSF was allowed to drain while CSF pressure and SSS pressure were recorded simultaneously. The regression slop of this curve was 1 and bisected the SSS pressure axis at approximately 30 mmH_2O (probably reflecting the venous outflow pressure). The authors postulated that the increase in SSS pressure was secondary to increased CSF pressure collapsing the sinus near the point of outflow from the skull. In 3 infants antegrade venography was performed. In 2 infants the sinuses appeared normal while in a third the lateral sinuses appeared to taper on each side and end in the jugular foramen. Collateral drainage was provided by enlarged parietal and mastoid emissary veins.

Norrell *et al.* [124] studied SSS and CSF pressures in 30 infants with hydrocephalus. Eleven patients had myelomeningoceles. CSF pressure exceeded SSS pressure in 12 patients, SSS pressure exceeded CSF pressure in 8 cases and the pressures were equal in 10 cases. SSS pressure was elevated more frequently in patients with myelomeningoceles (9/11) compared to those without (9/19). Of the non myelomeningocele group none of the patients with aqueduct stenosis had elevated sinus pressures compared to 9 of the 14 patients with communicating hydrocephalus. Adequate venography was performed in 28 patients. In 18 cases both lateral sinuses were opacified whereas only one sinus opacified in 10 cases. In the 17 patients without myleomeningoceles, the anatomical position and arrangement was considered normal. In one case there was stenosis of the lateral sinus. In 11 patients with myelomeningoceles, anatomical arrangement of the venous system was abnormal and consisted of a low lying torcular with the transverse/sigmoid sinuses running directly forward around the foramen magnum to the jugular bulb. Four of these patients had venography performed at CSF pressures of 10 and 60 cmCSF. This increase in ICP caused a partial or complete collapse of the lateral sinuses, an increase in opacification of emissary collateral veins, delayed sagittal sinus emptying time and a parallel rise in SSS pressure in all cases. Lateral sinus obstruction was not seen when the CSF pressure was elevated in hydrocephalic infants without myelomeningoceles and there was no change in emptying time.

These findings demonstrate that the falx cerebri and tentorium cerebelli do not afford protection of the cerebral venous sinuses from increased CSF pressure. There also appears to be considerable differences between individuals as to when secondary collapse of the sinuses occurs. The most common site of secondary compression of the venous sinuses is the distal transverse sinus; the same site that venous sinus obstruction is observed in PTS. It is possible that secondary venous sinus compression may be important in

maintaining the patency of more proximal venous channels and or have some other important role. In addition, it appears that in some conditions such as myelomeningocele with Chiari malformations, abnormally positioned venous sinuses may be more exposed to CSF pressure elevations.

Venous Sinus Obstruction in Pseudotumor Cerebri Syndrome: Cause or Effect?

Whether venous sinus obstruction in PTS is cause or effect remains unresolved. The experimental and clinical evidence discussed above indicates that there is potential for primary venous sinus pathology to cause PTS and there is also potential for secondary venous sinus obstruction due to raised intracranial pressure. We discuss below the available evidence and also present a unifying theory based on the establishment of a disordered positive feedback cycle. The discussion will centre on the site of venous obstruction, the morphology of venous sinus obstruction and the effects of removing venous sinus obstruction.

Venous sinus obstruction in PTS is most commonly, although not exclusively, seen in the transverse sinus. This is very commonly at the junction of the distal and middle thirds of the sinus. It co-incides with the area of the skull at which a number of bony sutures meet called the asterion. Other regions that may demonstrate stenosis are the other portions of the transverse sinus, posterior third of the SSS, sigmoid sinuses and jugular bulb. This point appears to be the same site at which compression of the venous sinuses takes place when CSF pressure is raised in experimental and clinical studies. If the venous sinuses are considered as a series of collapsible tubes then collapse of the tubes in such a system tends to occur at its distal end. However, it is also the most common site for the location of large arachnoid granulations that are known to cause obstruction of the transverse sinuses.

The symmetrical bilateral nature of the obstructions is also a consistent finding. This is important because, although the right transverse sinus is dominant in most cases, there is usually sufficient communication through the torcular Herophili to overcome a unilateral obstruction. The exception occurs in cases where one sinus is atretic or hypoplastic; usually the left. In these cases unilateral venous sinus obstruction may be sufficient to compromise venous outflow sufficiently to produce symptoms.

Morphologically, there are four basic types of lesions that obstruct the venous sinuses: extrinsic compression and intrinsic lesions of three main forms (Fig. 2). Extrinsic compression may be implied from the appearance of a smooth tapering of the sinus. This appearance tends to indicate that increased CSF pressure may be secondarily collapsing the venous sinus. Intrinsic lesions are of three main types: 1) broad-based lesions with an undu-

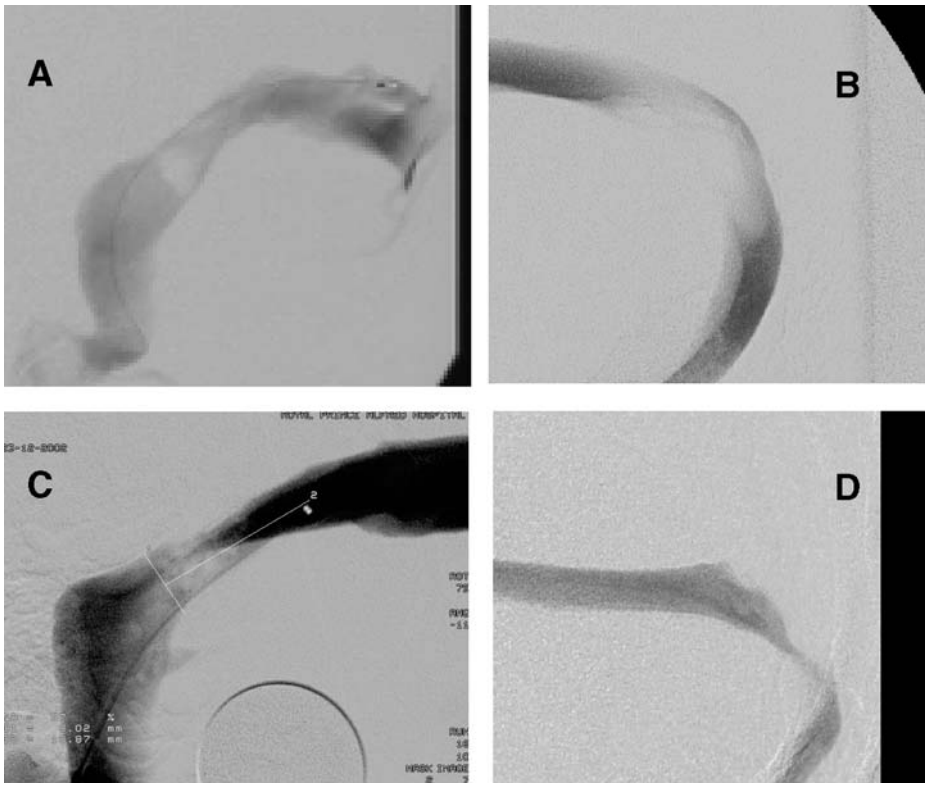

Fig. 2. Various forms of focal venous sinus obstruction in the transverse sinuses of 4 patients. Intrinsic filling defects are obvious in the top two radiographs being an arachnoid granulation (A) and a broad based undulating lesion (B). Of the lower two, the radiograph on the left (C) could be a focal stricture or extrinsic compression while the radiograph on the right (D) appears to indicate secondary venous sinus compression or irregularity due to old thrombus

lating surface that are of unknown aetiology. These may be difficult to distinguish from extrinsic compression but may require significant pressure application during stent deployment indicating the presence of a focal stenotic lesion (Fig. 3); 2) Abnormally large arachnoid granulations forming a round well defined filling defect in the venous sinus (Fig. 4), and; 3) Irregular lesions suggesting old thrombus.

Arachnoid granulations are most frequently reported as incidental findings on angiography, contrast enhanced CT or MR imaging [22, 142]. The true incidence and range of variation of 'normal' arachnoid granulations in a large series of asymptomatic individuals is yet to be established. On angiographic studies, arachnoid granulations of small to moderate size are frequently seen as filling defects of the sagittal and transverse sinuses. An example of a likely arachnoid granulation causing venous sinus obstruction

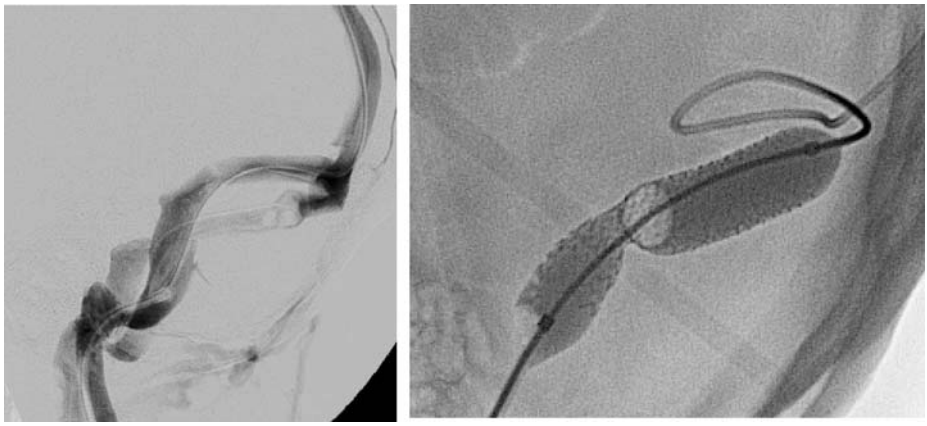

Fig. 3. Bilateral venous sinus obstruction. During the deployment of the stent, significant pressure was required in order to overcome this focal venous sinus stenosis

was provided by Arjona *et al.* [4] who reported a case of PTS in a 51 year-old man where the venous phase of cerebral angiography demonstrated the lesions protruding into the transverse sinus. On contrast enhanced CT arachnoid granulations are usually seen as round or oval hypodense lesions within the dural sinuses. They are best appreciated on fine slice contrast enhanced CT which may be more sensitive than MR for small lesions [96]. On MR, arachnoid granulations are of variable signal on T1-weighted images and hyperintense on T2 weighted images. Compared to CSF, arachnoid granulations are usually isointense to CSF on T1 weighted, T2 weighted and FLAIR MR imaging but may also have signal characteristics suggesting fat content. Their appearance is variable on proton density images [70] and may be altered by the presence or absence of calcification [142]. Oblique views on MR venography may give the impression of elongated lesion that may be mistaken for thrombus [142].

Roche & Warner [142] reported 41 arachnoid granulations in 32 patients (17 males and 15 females) on either CT or MR imaging in a 5 year period. Thirty-five (85.4%) of the arachnoid granulations were found in the distal or middle thirds of the transverse sinus. One or more vessels were closely associated with the granulation in 16 cases and appeared to enter 4 granulations. There were 2 arachnoid granulations located at the torcular and 4 in the sigmoid sinuses. Leach *et al.* [96] found 168 arachnoid granulations in 138 patients (24%) on reviewing 573 contrast enhanced CT scans; 92% of the granulations were found in the transverse sinus, especially in the middle and lateral parts. A vein entered the sinus adjacent to the granulation in 62% of cases and there was a tendency to increased incidence with age. There was no difference in the male to female distribution. On reviewing 100 MR scans there were 14 granulations identified in 13

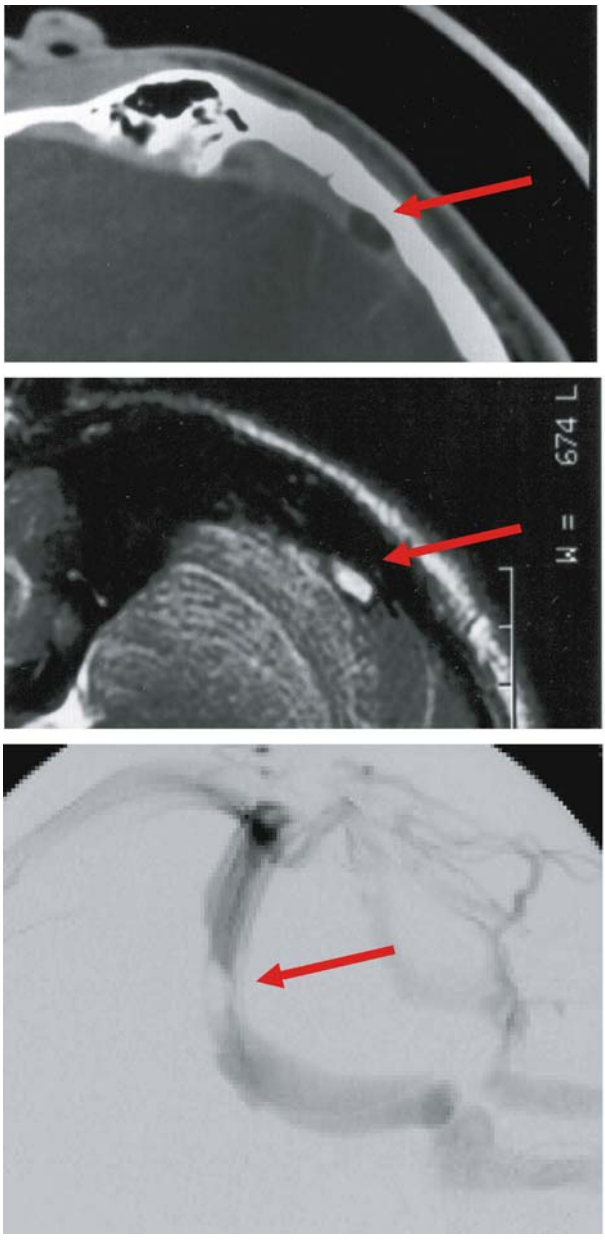

Fig. 4. A Patient with PTS with an intrinsic lesion on venography with a pressure gradient. On review of the MR images focal lesions were demonstrated in the transverse sinuses of both sides. These may represent either large arachnoid granulations or fat within the sinuses

patients; 85% were closely associated with a vein draining into the sinus. Ikushima *et al.* [70] reviewed static MR images of 1118 patients. Arachnoid granulations were present in 8.3% of males and 12.2% of females. A total of 134 arachnoid granulations were found with an overall incidence of 10%. In 14 patients there were was more than one granulation. The most common site of the granulations was the transverse sinus (85.8%).

In Browder *et al.'s.* [20] report arachnoid granulations were described as benign tumours of the cerebral venous sinuses. In an anatomical study of 295 sinuses, 25 arachnoid granulations were identified; all but 2 were in the transverse sinuses. Of those in the transverse sinuses they were almost always associated with the vein of Labbe as it entered the sinus. Mamourian & Towfighi [107] studied 10 patients without known venous sinus disease, 2 patients were found to have giant arachnoid granulations of the distal transverse sinus. In one patient there were bilateral lesions. Leach *et al.* [96] reported on the inspection of the sinuses of 29 cadavers for the presence of focal intraluminal protuberances. Ninety-one protuberances were observed in 19 cases (66%) and ranged in size from less than 1 mm to 8 mm diameter. Ninety-five percent were located in the transverse sinus – predominantly the left. In Rosenberg *et al.'s* [145] report of 4 cases of giant arachnoid granulations presenting as osteolytic skull lesions, histological examination demonstrated loss of the normal stromal organisation. Instead large CSF filled cystic spaces were seen. Upton *et al.* [175] reported on the structure of arachnoid granulations obtained from 23 autopsies. There was a tendency for the granulations to become larger and more complex with age.

Given the typical site and the correspondence with intrinsic lesions seen on MRV or DRCV, arachnoid granulations may represent a proportion of the obstructing lesions in PTS. While the natural occurrence suggests a primary role for these lesions, they may increase in size secondary to increases in CSF pressure for a number of reasons. In animals, arachnoid granulations may increase in size with increases in CSF pressure [54, 100]. It may also be that increased CSF pressure increases the CSF component of the arachnoid granulation which becomes incarcerated in the lumen of the sinus further exacerbating the increased CSF pressure. An increase in the size of the collagenous core of the granulation may also increase its size. Chronic inflammation of this core may result in such an increase [175]. Hayes *et al.* [62] studied the effects of dietary vitamin A deficiency in calves and rats and confirmed Eaton's [39] finding that it resulted in increased CSF pressure. Histological examination of the arachnoid granulations in rats and calves revealed the granulations to be larger in the vitamin A deficient animals compared to controls. This was particularly so along the transverse sinuses of the calves. The increase in size of the granulations was associated with an increase in collagen with stimulation of fibroblasts with an increase and extreme dilation of the golgi endoplasmic reticulum

of these cells. Hernias of brain tissue into the core of arachnoid granulations may also result in enlargement of the granulation. Kollar *et al.* [87] reported a case of where an abnormally large arachnoid granulation was removed and the histological sections published clearly demonstrate a hernia of brain into the granulation. The authors at the time described this as 'ectopic' brain tissue but the true nature of the lesion is evident. Small hernias of brain tissue are frequently seen in the bases of arachnoid granulations at craniotomy (*M Besser; personal communication*).

There are various other pathological entities that may be represented in the spectrum of obstructive intrinsic venous sinus lesions. Fat deposits in the dural sinuses on CT was reported by Tokiguchi *et al.* [173]. These authors reported 8 cases in which macroscopic, non-obstructing fat deposits were demonstrated in the walls of the sinuses. In 5 cases fat was located at the torcular while in 3 it was located in the SSS. Anatomical proof that these lesions did indeed consist of fat was supplied in a later report where 2 of these patients had later undergone autopsy [174]. Finally, nodules of cavernous tissue have been identified in the sinuses, especially at the junction of the straight sinus and vein of Galen [13, 95]. The nodules, distinct from arachnoid granulations, were common at autopsy and were composed of endothelium lined sinusoids resembling erectile tissue.

Cerebral venous sinus thrombosis (CVT) may also contribute a proportion of the cases of PTS. Acute CVT should be distinguished from chronic CVT. In the former, provided the thrombus does not involve the cortical veins, the condition may certainly cause a pseudotumor syndrome [14, 99, 159]. The approach to management of these patients is quite different. The prevention of thrombus propagation and dissolution of the thrombus are important in the management [12]. Thus anticoagulation either systemically or locally via the endovascular route are used. Persistence of thrombosis with reorganisation and recanalisation may result in improved cerebral venous outflow. In such cases intrinsic venous sinus obstructive lesions may represent old thrombus. However, more frequently such chronic CVT cases appear to have less focal stenosis and may be difficult to treat.

There is also significant circumstantial evidence for a role of occult CVT in PTS from the association of a large number of prothrombotic states. These associations include the thrombophilias [81, 101, 112, 119] as well as other prothrombotic states such as essential [118] and iron deficiency anaemia [69]. This association between prothrombotic conditions and PTS was reviewed by Sussman *et al.* [169]. A mixed group of 38 retrospectively and prospectively accumulated patients. Eighteen patients were subject to angiography and three patients were found to have venous sinus thrombosis although the location and other details were not given. Each of these patients had a prothrombotic disorder.

In order to test whether the venous obstruction is primary or secondary one may either relieve the obstruction and observe the effects on CSF pressure or, reduce CSF pressure and observe the effects on venous obstruction. However even these measures may not produce a conclusive result due to the nature of positive feedback loops which can be interrupted without producing conclusive information on causation. For example, stopping chickens breeding does not determine whether the chicken or the egg came first.

King *et al.* [85] reduced CSF pressure in a total of 21 patients with PTS for which no obvious cause was found (for example minocycline) were examined using venography and manometry. With the exception of 2 patients, SSS and CSF pressures followed each other closely. In these patients there were transverse sinus stenoses with significant pressure gradients. Of these patients 8 underwent C1-2 puncture with removal of 20–25 mls CSF. Manometry was then repeated. The procedure was also performed on 3 patients with so-called non-idiopathic PTS. The drop in CSF pressure produced by C1-2 puncture was measured in only 3/11 patients. The reductions were 40, 23 and 10 cm CSF. All patients had a reduction in the proximal venous sinus pressures. In 5/8 idiopathic PTS patients, the pressure gradient in the transverse sinus disappeared. In 2 other patients in this group the gradient remained although it was reduced. One patient had no transverse sinus obstruction or gradient before C1-2 puncture. Of the 3 patients with so-called non-idiopathic PTS who were examined after C1-2 puncture, two patients had no venous pressure gradient to begin prior C1-2 puncture. The results of the patient with a high CSF pressure and a transverse sinus pressure gradient prior to C1-2 puncture are difficult to interpret as although proximal venous pressure fell to 10 mmHg, the distal sinus pressure was not recorded.

Given the reduction in venous sinus pressures and associated pressure gradients after C1-2 puncture and the CSF pressure reduction, the authors [85] and others [25] concluded that transverse sinus obstruction in PTS was a result of raised CSF pressure but not the cause. However, such a conclusion is difficult to justify on the basis of these results. First, although no normal healthy controls were examined, venography and manometry were performed on 10 patients with diseases other than idiopathic PTS. CSF pressure was raised in 7 patients (20–50 cmCSF) but venography and manometry demonstrated transverse sinus gradients in only 3 (43%) of these patients. In the other four there was no evidence of venous sinus hypertension. In comparison, of the 21 patients with idiopathic PTS venous sinus hypertension with transverse sinus pressure gradients were found in 19 (90%). Although the average CSF pressure was higher in the idiopathic PTS group, the higher incidence of venous sinus hypertension indicates that it may be an aetiological factor. Second, the results indicate that venous sinus pressure fell almost universally after C1-2 puncture. This is an

expected outcome even in the presence of a fixed venous sinus stenosis. In at least 2 patients, the venous sinus gradient remained although reduced. Finally, the authors avoided the issue of morphological change in the stenoses after C1-2 puncture. Although they allude to the presence of either tapering or intraluminal filling defects on pre-C1-2 puncture venograms they were unable to state whether these lesions were present or absent after CSF pressure reduction. The heterogeneous nature of the stenosing or obstructing lesions means that the conclusions of the authors may only be valid for one subtype of obstructing lesion, in particular extrinsic compression.

In support of King *et al.* is a case report by McGonigal *et al.* [115] who document a case of bilateral transverse sinus obstruction in a 19 year old with quite severe PTS. The obstructions had the appearance of a smooth tapering on CT venogram. After insertion of a lumboperitoneal shunt symptoms resolved and there was marked improvement in the degree of narrowing bilaterally. Higgins and Pickard [66] also reported resolution of venous sinus obstruction in a very similar case after lumboperitoneal shunting. We have also observed this phenomenon after ventriculoperiteoneal shunting in one case. In contrast, morphological and functional venous sinus obstruction in the presence of a functioning shunt has been observed in 2 of 8 cases from our series and in 2 patients in the series of Higgins *et al.* [63].

Sainte-Rose *et al.* [151] studied the relationship between CSF and venous pressures in 31 infants (age 1–23 months). These patients consisted of 6 cases of communicating hydrocephalus, 6 cases of hydrocephalus associated with a myelomeningocele, 14 cases of craniostenosis, 3 cases of achondroplasia and a case each of aqueduct stenosis and subdural haematoma. In the first part of the study, consisting of a group of 11 infants mainly with craniostenosis, intraventricular CSF and SSS venous pressures were recorded simultaneously. In all patients the difference between CSF and SSS venous pressures were small (< 3 mmHg). CSF pressure was elevated (15–25 mmHg) in 8 patients but there was no relationship between underlying pathology and pressure recordings. In the second part of the study, a second ventricular catheter was also introduced to allow CSF pressure reduction via CSF withdrawal. The jugular venous pressure was also monitored. In 16 of 20 patients, after withdrawal of CSF to reduce CSF pressure to zero, SSS venous pressure also fell to the jugular venous pressure. Re-injection of the same volume of CSF usually restored CSF pressure to the same or a slightly higher CSF pressure than at baseline. SSS venous pressure also increased to baseline. In these patients there was no evidence of sigmoid sinus compression on sinography. In the remaining 4 patients; two with achondroplasia and two with craniostenosis; SSS did not decrease to the jugular venous pressure when CSF pressure was reduced to zero. Instead illustrated traces demonstrate a modest fall in SSS pressure.

Also suggestive of a fixed obstruction was the finding that reinjection of CSF produced a rise in SSS pressure above baseline. Fixed venous sinus obstruction of the transverse or sigmoid sinus was confirmed on sinography.

The effects of relieving the venous sinus obstruction in PTS have also been studied. The results of these studies will be considered fully in the section on treatment (*vide infra*). However, it is clear that reduction of venous sinus hypertension in PTS may result in rapid clinical resolution and a reduction in CSF pressure. Of the cases reported to date, significant clinical improvement was apparent in 4 of 4 cases in our series [130] and in 8 of 12 cases in the series from Cambridge [63]. These results, along with the observation that some obstructions are intrinsic, indicate that venous sinus obstruction in PTS may have a primary aetiological role, possibly exacerbated by raised ICP due to disordered positive biofeedback.

It is clear that arguments exist for primary and secondary aetiological roles for venous sinus obstruction in PTS. Certainly there are cases in which either may exist. Failure of treatment of venous sinus obstruction in a handful of cases indicates that it may be important to differentiate between the two. However, there may be a role for treatment of the obstruction whether the obstruction is primary or secondary. The argument for treatment of primary lesions is intuitive; however secondary venous sinus obstruction may exacerbate any underlying CSF circulation disorder; an argument supported by King [85] and Quattrrone *et al.* [137]. When CSF pressure becomes increased and venous sinus obstruction ensues, the compliance of the craniospinal axis is reduced because of engorgement of the cerebral venous compartment. Therefore small increase in CSF or blood volume will cause rapid increases in CSF pressure. More importantly though, if CSF pressure is increased sufficiently to overcome venous pressure and collapse the sinuses, venous pressure must increase in order to overcome the obstruction and maintain adequate cranial venous outflow. Venous sinus hypertension therefore becomes increased. If the primary problem is one of CSF absorption and raised R_{csf}, then in order for CSF absorption to continue, the pressure gradient between the subarachnoid CSF must be even higher than the normal gradient of 3 mmHg. CSF pressure must rise further and thus a vicious circle of rising CSF pressure, venous sinus obstruction and rising venous sinus pressure is established. Treatment of the venous sinus obstruction may interrupt this positive feedback loop and restore the normal compliance of the cerebral venous compartment.

We therefore propose the following unifying hypothesis. Normally, increased CSF pressure leads to increased CSF drainage and restoration of normal CSF pressure, representing classical physiological biofeedback control where the response of the system has a negative effect on the stimulus (Fig. 5) [59]. In PTC, with venous abnormalities, the presence of the lesion in the venous outflow system creates a possibility for an abnormal

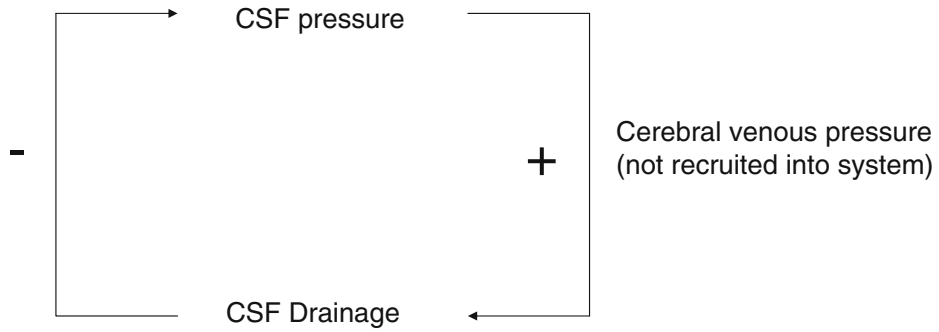

Fig. 5. Normal negative feedback. Increases in CSF pressure are controlled by an increase in the rate of CSF absorption as it is a pressure dependent process

positive biofeedback to develop as increases in CSF pressure can worsen the degree of venous compromise leading to a further increase in CSF pressure, a further increase in venous obstruction, and so on (Fig. 6). The degree to which cerebral venous pressure is recruited into the control system could determine the extent to which CSF pressure rises until other negative feedback mechanisms (for example, CSF absorption through other routes) become significant and re-establish control of CSF pressure at a higher level. Recruitment of cerebral venous pressure into this control system is variable, and due to a variety of factors, potentially explaining the variability of PTC symptoms over time. The prolonged benefit produced by a single CSF tap in PTC patients may be understood in this way if one postulates that removal of CSF reduces secondary venous compression and improves CSF drainage due to uncoupling of cerebral venous pressure from the control system for a period much greater than that required to re-

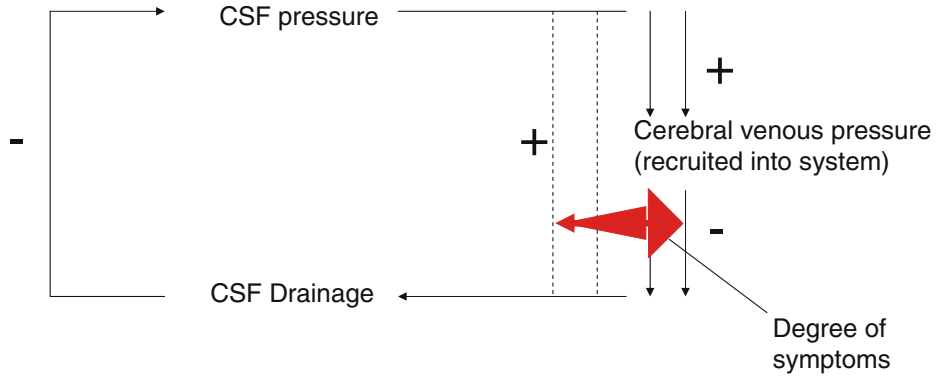

Fig. 6. Disordered positive feedback. Recruitment of the cerebral venous sinuses into the feedback loop due to venous sinus collapse, secondary to increased CSF pressure, causes venous sinus pressure (particularly SSS pressure) to increase. This inhibits CSF drainage and results in further increases in CSF pressure and so on

place the volume of CSF removed. Permanent decoupling of cerebral venous pressure by stenting an obstructive cause may be therapeutic, regardless of the initial cause.

Non Obstructive Venous Hypertension

Venous sinus hypertension also occurs in the absence of venous sinus obstruction. Karahalios *et al.* [78] drew attention to systemic venous hypertension in their series of patients studied with venography. There are several case reports in which cardiac lesions have been associated with PTS [72] or hydrocephalus [134]. However, the most well-studied scenario is that of morbid obesity and its association with venous sinus hypertension and PTS.

Obesity is strongly associated with development of PTS in both men and women [36, 51, 178]. Johnston & Paterson [75] found that of 110 patients with PTS, 35 were moderately or grossly obese. These patients were all female and 27 of them had no recognisable aetiology. Foley [45] found that only 1 of 46 cases with 'otitic hydrocephalus' compared to 20 of 60 cases with 'toxic hydrocephalus' were obese. In a prospective study of 50 patients with PTS by Wall & George [177] 94% were noted to be overweight.

Corbett & Mehta [26] investigated CSF pressure in 116 acute PTS patients, 8 chronic PTS patients, 41 normal obese volunteers and 15 normal non-obese volunteers. CSF pressure was only slightly higher in the normal obese subjects compared with normal non-obese subjects. There was no correlation with the degree of obesity and CSF pressure in this study. Patients with acute PTS all had CSF pressures markedly higher than both patients with chronic papilloedema and normal subjects. In a study of 19 patients (mean BMI 39.3 kg/m^2) randomly selected from an obesity clinic CSF pressure was recorded during lumbar puncture [61]. CSF pressure was elevated ($>$ 20 mmHg) in 15 patients (79%); in 8 patients it was greater than 25 mmHg and in 2 patients it was greater than 30 mmHg. The authors could not find any correlation between CSF pressure and BMI. No patient reported headaches and no patient had papilloedema.

There has been much speculation on the relationship between obesity and PTS. Numerous hormonal and metabolic links between obesity and raised CSF pressure have been proposed. In some cases a weight reduction can result in clinical improvement. There are reports of dramatic clinical improvement in patients with extreme obesity and PTS who have undergone surgically induced weight loss. Noggle & Rodning [122] reported a case of PTS in a morbidly obese patient who was successfully treated (weight reduction from 150 to 86 kg; resolution of clinical PTS) with gastric exclusion surgery. Furthermore symptoms recurred 3 years later with failure of the gastroplastic stapling line and recurrent weight gain. After

revision of the gastric surgery, significant weight loss and clinical PTS resolved. At around the same time Amaral *et al.* [2] reported a similar case (138 kg) in whom surgically induced weight loss resulted in clinical resolution of PTS and a reduction in CSF pressure.

In 1995 Sugerman *et al.* [167] reported resolution of symptoms of PTS in morbidly obese patients (BMI $49 +/- 3$ kg/m^2) following surgically induced weight loss. At mean follow-up of 34 months average CSF pressure had reduced from $35.3 +/- 3.5$ to $16.8 +/- 1.2$ cmH_2O. These initial results were confirmed in a second study of 24 severely obese patients (mean BMI $47 +/- 6$ kg/m^2) previously diagnosed with PTS [168]. Mean CSF pressure was $32.4 +/- 8.3$ cmH_2O. Twenty three patients underwent gastric bypass and one had laproscopic gastric banding. Follow-up was $62 +/- 52$ months. At the time of the report, one year follow-up was available in 19 patients who had lost an average of $71 +/- 18\%$ of their excess weight ($45 +/- 12$ kg). Headache and pulsatile tinnitus resolved within 4 months of surgery with the exception of one patient. Papilloedema and cranial nerve dysfunction improved in all patients. Interestingly, 2 patients who had initially lost weight and experienced resolution of their symptoms developed recurrent PTS on regaining weight. As a non-surgical solution, Sugerman *et al.* [165] designed a counter-traction mechanism to reduce intra-abdominal pressure and central venous pressures. Improvement in headache and pulsatile tinnitus was reported with the nocturnal application of this external negative abdominal pressure device to the abdomen of 5 patients with severe obesity and PTS.

Sugerman *et al.* [166] studied 6 obese patients (mean BMI $45 +/- 3$ kg/m^2) with PTS undergoing gastric banding. Mean ICP was $29.3 +/- 8.0$ cm H_2O. Intra-abdominal pressure ($22 +/- 3$ cmH_2O), central venous pressure ($20 +/- 6$ mmHg; $n = 5$) and transoesopohageal pleural pressure ($15 +/- 10$ mmHg; $n = 3$) were all elevated in these patients. The authors concluded that central obesity raises intra-abdominal, pleural and cardiac filling pressures. The later impedes cranial venous outflow and causes PTS. Gastric bypass or laproscopic gastric banding in these patients resulted in significant weight loss. At the time of the report 5 of the 6 patients had resolution of their PTS symptoms, including pulsatile tinnitus. One patient had only recently undergone their surgery. Although the right atrial pressures demonstrated using venography and manometry in the study of Karahalios *et al.* [78], the mechanism that these authors propose may still be plausible. However, as Sugerman and colleagues themselves noted, there remains no satisfactory explanation for why some obese individuals develop PTS but most do not. In addition, why are women more commonly affected than males given that the proposed mechanism is increased intra-abdominal pressure and males tend to have more central obesity compared to females.

Experimentally, Luce *et al.* [104] demonstrated that in anaesthetized dogs, an increase in pleural pressure increases lumbar and intracranial CSF pressure. This increase in CSF pressure was secondary to elevation of venous pressure in the superior vena cava. In the swine, Bloomfield *et al.* [16] demonstrated that elevation of intraabdominal pressure 25 mmHg above baseline caused an increase in central venous and intracranial pressures (7.6 +/− 1.2 to 21.4 +/− 1.0 mmHg). In addition there was a reduction in cardiac index and CPP decreased. Expansion of intravascular volume returned cardiac index and CPP to normal and also resulted in a further increase in ICP (27.8 +/− 1.0 mmHg). Decompression of the abdomen returned ICP to normal. The effects on central venous pressure and ICP were negated by sternotomy and pleuropericardotomy [16]. Even when ICP was already artificially elevated (mean 25.8 mmHg) increases of 15–25 mmHg in intra-abdominal pressure resulted in significant increases in intra-thoracic pressure and ICP (25.8 to 33.8 and 39.0 mmHg, respectively) [148].

There exists, therefore, a co-hort of patients with systemically increased venous sinus pressure without focal obstruction. These patients appear to be those with morbid obesity. It should be stressed that the degree of obesity in the patients that Sugerman *et al.* have dealt with surgically is much greater than that in the average overweight patient with PTS. In addition, it should also be noted that venous sinus obstruction, from both intrinsic lesions and extrinsic compression does also occur in obese patients. Non-obstructive venous sinus hypertension are a particularly difficult group to diagnose as there are no static CT or MR examinations that will demonstrate this aetiology. Instead cerebral venography with manometry including right atrial pressures, preferably in the awake patient, should be performed. These patients are also difficult to distinguish from a co-hort of patients with normal veins, normal venous pressures and increased CSF pressure possibly due to disordered function of the arachnoid granulations.

Cerebrospinal Fluid Dynamics in Pseudotumor Cerebri Syndrome

Johnston & Patterson [76] proposed that PTS resulted from either a problem of CSF absorption at the level of the arachnoid villi or cranial venous outflow obstruction. To determine whether there is an obstruction to CSF absorption at the level of the arachnoid villi, the resistance to CSF absorption (R_{csf}) is calculated using the CSF infusion study. In Martin's [111] study, 4 patients with PTS were studied and had a similar R_{csf} value to 2 patients with venous outflow obstruction. Sklar *et al.* [158] reported their findings in 10 patients with PTS who underwent a total of 17 investigations using the constant-pressure variable infusion rate method at various stages of their disease. The results of their study are difficult to interpret as at least

half of the patients had normal baseline CSF pressures and several patients were being treated with diuretics or steroids. While the authors interpreted their findings as demonstrating evidence of an CSF absorption deficit in PTS, 6 of the studies in 2 patients were normal. Ropper & Marmarou [144] presented a case of PTS secondary to Guillain-Barre syndrome in whom serial measurements of R_{csf} were made. R_{csf} was elevated at presentation and fell to normal with clinical improvement. However, the authors calculated the contribution of this raised R_{csf} to the elevated CSF pressure and concluded that the R_{csf} recorded was insufficient to produce this extent of pressure elevation. They proposed that elevation of the venous sinus pressure must also contribute to the elevation in CSF pressure in their patient. Lamas *et al.* [93] reported a case of a dural AVM with PTS and raised SSS pressure. A constant-infusion lumbar CSF infusion study had to be terminated at a pressure of 50 mmHg before reaching equilibrium. Calculating R_{csf} on the basis of this result gives a value of at least 36 mmHg/ml/min. There was no evidence of any other CSF circulation disorder in that patient.

In most series the R_{csf} is measured using a perfusion or infusion technique and the average R_{csf} measured in patients with PTS is raised. However, patients are usually analysed as a group. One of the most valuable studies therefore was that of Janny *et al.* [71] who, using a constant intraventricular CSF infusion technique, measured the R_{csf} and differentiate patients with venous sinus obstruction from those without. In the patients without venous sinus obstruction mean R_{csf} was 46.6 mmHg/ml/min while in the patients with venous sinus obstruction it was 14.5 mmHg/ml/min. In addition, Janny *et al.* [71] demonstrated a reversal of the normal pressure gradient between the SSS and CSF in patients with venous sinus obstruction causing a PTS syndrome. The mean pressure was 3.16 mmHg higher in the SSS. In contrast, their patients without venous sinus obstruction ($n = 12$), the mean pressure was 9.5 mmHg higher in the CSF. The difference suggests that in patients without venous sinus obstruction the underlying problem may be that of CSF absorption.

The results of CSF infusion studies in PTS are difficult to interpret. Studies of CSF dynamics are performed using the potentially invalid assumption that the venous sinus pressure remains stable during mock CSF infusion. Using the constant infusion CSF study, baseline CSF pressure is monitored and then mock CSF is infused at a constant rate until a new equilibrium CSF pressure is reached. The R_{csf} is calculated on difference in CSF pressure at equilibrium and baseline divided by the infusion rate. However, as noted in the earlier discussion regarding the effects of raised CSF pressure on the venous system, elevations of CSF pressure may cause venous sinus collapse, secondary venous obstruction and an elevation of venous sinus pressure. Therefore, as CSF absorption depends upon a pres-

Table 3. *Classification of Venous Sinus Pathology in PTS*

Classification of PTC based on Venous Sinus Pathology
A. Raised Venous Sinus Pressure
i. Obstructive
Intrinsic Vs Extrinsic
Primary Vs Secondary
ii. Non-obstructive
B. Normal Venous Sinus Pressure

sure gradient between the subarachnoid space and venous sinus, CSF pressure must rise further. Therefore, the increase in CSF pressure required to reach equilibrium may be falsely high. Likewise in the presence of a primary venous sinus obstruction, venous sinus pressure will be high. If during increases in CSF pressure the venous sinus pressure remained at the same level then the increase in R_{csf} should be normal. However, due to the low compliance of the venous compartment, elevation of CSF pressure may produce increases in venous sinus pressure and therefore may result in falsely high calculated R_{csf} values. It should be noted that measurement of R_{csf} in situations where CSF pressure is very high prior to testing makes such studies technically difficult.

Despite these problems there is sufficient evidence to conclude that most cases of PTS are related to either problems of venous sinus obstruction or problems of increased R_{csf} at the level of the arachnoid villi as proposed by Johnston and Patterson [73, 76, 77], and we have seen patients with PTC with normal veins and normal venous pressures and elevated CSF pressure.

It is clear therefore from the above discussion that there is no single cause of PTC and that a multitude of pathological states may cause the symptom complex. We have found it useful to divide patients into venogenic and non-venogenic groups based on the results of DRCV and manometry studies which provides guidance for therapeutic options Table 3.

Investigation of Venous Aetiology in Pseudotumor Cerebri Syndrome

The high proportion of patients with venous sinus obstruction coupled with the ability to treat such obstruction should be an indication to investigate all patients with PTS for the existence of venous sinus obstruction. In performing these investigations one should be cognisant of the location and morphology of the venous obstruction that is sought.

The most important distinction in the investigation of venous sinus obstruction in PTS is that between thrombosis and stenosis. Until recently, almost all papers reviewing and recommending management strategies for PTS concentrate on the exclusion of cerebral venous thrombosis rather

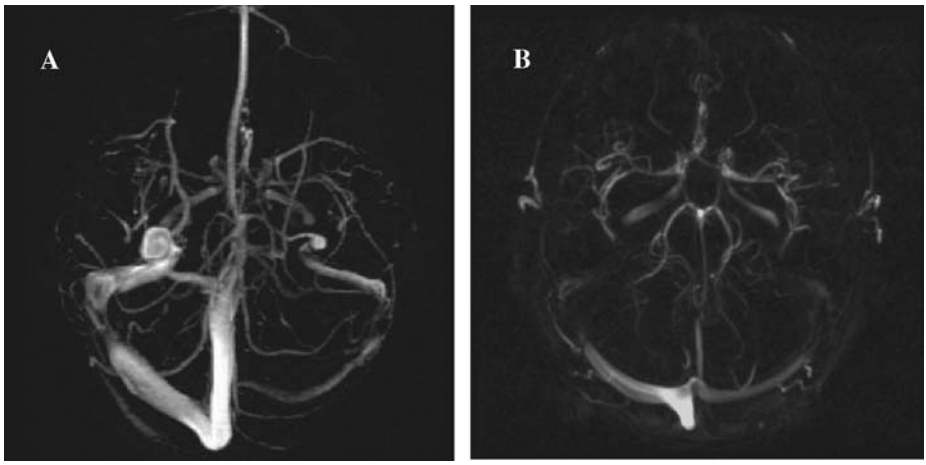

Fig. 7. Axial MRVs of two different patients. (A) There is a dominant large right dominant transverse sinus with absence of flow in the distal third. This patient later went on to have a venous sinus stent. (B) Another patient with a dominant right transverse sinus. Both patients also have obstructions in the small left transverse sinuses confirmed using DRCV and manometry

than stenosis [98, 99, 160]. The possibility of the other causes of obstruction is rarely mentioned. Strategies that aim to exclude thrombosis often use CT and/or static MRI with most attention given to the SSS, for example, the empty delta sign. CT, even with contrast enhancement, should not be relied upon for the diagnosis of venous sinus obstruction in PTS. This is exemplified by Leker *et al.'s* [98] report of 46 cases of PTS with normal CT results. When conventional angiography or MRI/MRV was performed, 12 patients (26%) had evidence of venous sinus thrombosis.

We recommend that as a minimum static MR as well as MR venography with full coverage of the cerebral venous system should be used to investigate patients with PTS for venous sinus disease (Fig. 7). The combination of these exams should be able to identify most cases of thrombosis or venous sinus stenosis. MR also has the advantages of identifying intraluminal lesions such as giant arachnoid granulations. Absence of flow in the distal transverse sinuses in particular should be treated as a real finding and not attributed to artefact.

Conventional angiography may detect venous sinus obstruction. However, the sensitivity for venous sinus obstruction is less than for DRCV. King *et al.* [86] as well as Karahalois *et al.* [78] found that even with benefit of hindsight, venous sinus obstruction was more difficult to identify on conventional angiography than on DRCV. In addition, there is a risk of embolic stroke or arterial dissection with cerebral angiography that is not

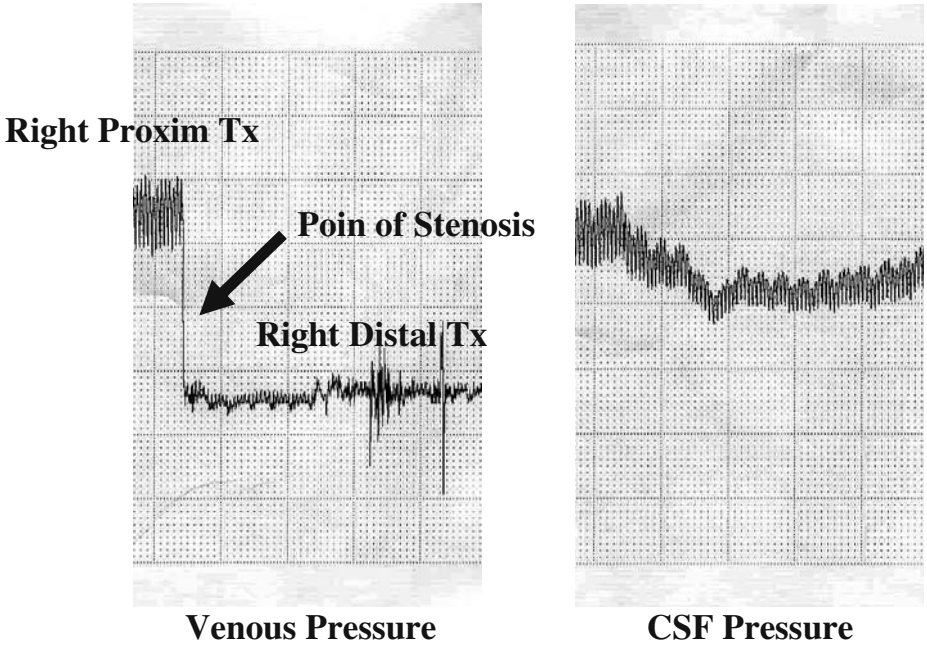

Fig. 8. Venous sinus manometry and CSF pressure recordings. The venous catheter has been pulled back across the point of stenosis during pressure recording demonstrating the venous sinus pressure gradient

present with DRCV. However, conventional angiography may be useful when there is a suspicion of a dural AV fistula.

Direct retrograde cerebral venography (DRCV) combined with manometry is the investigation of choice for venous sinus obstruction in PTS. It is probably the most sensitive investigation for detecting venous sinus obstruction. However, because of its more invasive nature, in cases where venous sinus obstruction has been demonstrated and medical therapy is to be trialled, presuming there is no immediate threat to vision, it is reasonable to keep DRCV with manometry in reserve until treatment of the stenosis is contemplated.

The advantages of DRCV with manometry are that it provides the most accurate information regarding the nature of venous sinus flow and allows measurement of venous sinus pressures to be obtained. Unlike either MRV or conventional angiography, manometry affords information regarding the functional significance of the obstruction. It allows determination of whether venous sinus pressure is raised and whether any pressure gradients exist across morphological obstructions (Fig. 8). If there is doubt regarding the presence or absence of a lesion due to inflow or contrast streaming, manometry will provide clarification. King *et al.* [86] commented that in some cases the filling defects were not impressive on venog-

raphy, or when initially examined, these changes were not appreciated on the venous phase of the carotid angiogram or were attributed to streaming of the contrast medium. In addition central venous pressures can also be measured using manometry and allows patients with systemic venous hypertension to be identified.

The advantages of venography and manometry over conventional angiography were exemplified in a case of PTS reported by Cremer *et al.* [27]. A small (1 cm diameter) falcine meningioma caused partial obstruction of the posterior one-third of the SSS. Conventional angiography had been revealed a normal arterial and venous systems. Venography however revealed the obstruction of both transverse and sigmoid sinuses. Manometry demonstrated venous pressures to be 40 mmHg through the entire SSS and transverse sinuses and dropped to 3–5 mmHg in the distal sigmoid sinuses. There was no pressure gradient at the meningioma itself.

Manometry should be performed with patient awake unless the patient is unable to co-operate fully. DRCV and manometry are usually well tolerated however the sinuses are sensitive to stimuli, particularly stretch and intermittent discomfort from the catheters may be reported. Anaesthetic agents and positive pressure ventilation may interfere with accurate measurement of venous pressures by changing both the ICP and the intrathoracic pressures. Therefore for diagnostic purposes the procedure should be performed, if feasible, in the awake patient.

Venous pressures should be measured for all segments of the venous sinuses including the SSS, torcular, transverse and sigmoid sinuses, jugular bulb, internal jugular vein and right atrium. Where a morphological obstruction has been demonstrated, the pressures proximal to, at and immediately distal to the stenosis are recorded. By pulling the catheter back across the stenosis under radiological control and recording the pressure simultaneously, a sudden fall in venous pressures is often recorded demonstrating the functional significance of the stenosis. By measuring right atrial pressures non obstructive venous hypertension can be demonstrated and is particularly relevant in the grossly obese patients.

Venography and manometry are invasive procedures compared to MR imaging. The risks however are less than those of conventional cerebral angiography, for example, embolic stroke. There is however a risk of perforation of a vein or sinus, for instance, if the guidewire inadvertently enters a fragile draining cerebral vein. Another potential risk is the formation of a thrombosis around the catheter which might case pulmonary embolus. Overall however the risks of DRCV and manometry appear lower than those of conventional angiography.

We have performed DRCV with manometry in 22 patients diagnosed with PTS. In 11 (50%) there were either bilateral venous sinus obstructions (7 cases) or a unilateral venous sinus obstruction in a dominant venous si-

nus (4 cases). These obstructions were all associated with pressure gradients across the point of stenosis. Pressure gradients ranged from 7–41 mmHg (mean 18.3 +/− 10.6 mmHg). The resulting SSS pressure in this group ranged from 17–43 mmHg (mean 27.9 +/− 9.3 mmHg). In comparison, the other 11 patients had gradients of less than 5 mmHg. The mean SSS pressure in these patients was 15.0 +/− 6.8 mmHg. However, 5 of these 11 patients had venous sinus pressures of 15 mmHg or above. The mean of the right atrial pressures in the 11 non obstructed patients was 8.1 +/− 5.3 mmHg compared to 4.7 +/− 4.4 mmHg in those with venous sinus obstructions. Therefore some of the patients in the group without morphological obstruction or focal pressure gradients still had significantly raised venous sinus pressures that may be contributing to their PTS.

The location of obstructing lesions was always within the distal two-thirds of the transverse sinus. The morphology of the obstructions varied as described previously. In some cases the obstructions appeared to be intrinsic and were well defined rounded filling defects. Other cases appeared exhibit the features of a tight primary stenosis. In some cases the obstruction was less well defined and may have been consistent with extrinsic compression.

Treatment of Venous Sinus Obstruction

In most cases of PTS spontaneous resolution of the condition will occur. In these cases, removal of any offending agent such as tetracyclines, conventional medical therapy including acetazolamide and/or steroids, and intermittent lumbar punctures will enable sufficient control of the condition until spontaneous resolution occurs. However, consideration should be considered to more aggressive intervention when the condition is refractory to medical therapy, it does not undergo spontaneous resolution within a reasonable period, vision is threatened or in the rare case where PTS exhibits a fulminant course.

The options for surgical treatment that currently exist are CSF shunting, usually either lumbo-peritoneal or ventriculo-peritoneal, optic nerve sheath fenestration or bilateral subtemporal decompressions. These procedures all have their own limitations and certainly are not always effective. Ventriculoperitoneal shunting, even with use of stereotaxis, may be difficult and the shunt prone to blockage in small ventricles. Lumbo-peritoneal shunts have the added problem of the acquired Chiari malformation. Optic nerve sheath fenestration may help with vision but do not always effectively reduce ICP and headaches. Finally subtemporal decompressions provide symptomatic relief by increasing the effective intracranial compliance but do not address the underlying aetiology. As an alternative to these treatments, where a venous sinus obstruction has been identified, consideration should be given to treatment of the venous sinus obstruction itself.

The options for treatment include direct surgical treatment of lesion and/or surgical venous bypass or endovascular therapy, the most useful of which appears to be venous sinus stenting.

Direct Surgical Treatment

There is limited experience with direct surgical treatment of venous sinus obstruction in PTS. From a historical perspective, Ray & Dunbar [141] reported a 49 year old woman with PTS of 14 months duration who was found to have an obstruction at the junction of the posterior and middle thirds of the SSS. At surgery a sterile thrombus was removed from the sinus but a partial obstruction remained on the post-operative venogram although pressure was slightly reduced and she was clinically improved.

Venous sinus bypass surgery has been performed by Sindou and Auque [156, 157] in 5 cases of PTS. The underlying aetiology was post-otitic sinus thrombosis, surgical internal jugular vein ligation, a torcular meningioma and dural AV fistula excision with sinus thrombosis in two cases. In 4 of 5 cases internal saphenous vein was used and the authors describe excellent clinical outcome with post-operative patency documented on angiography. In one case, a Gore-Tex graft was used but this became occluded. The authors emphasize the importance of post-operative anticoagulation.

Sainte-Rose *et al.* [151] reported 3 infants with craniostenosis and fixed venous sinus outflow obstructions related to bony stenosis who were treated with a saphenous vein bypass. In the first patient (8 months of age) the graft progressively dilated over a 6 month period with a gradual reduction in ICP. The authors emphasized the problems related to the size of the saphenous vein grafts in infants (about 1 mm diameter). In the other two patients, both with craniostenosis and fixed venous sinus obstruction, saphenous vein grafts did not reduce ICP after surgery and to protect vision a VP shunt was required. However, in both patients the grafts dilated and cranial remodelling could proceed without jeopardizing the venous collaterals in the scalp.

Direct treatment of venous sinus obstruction, as yet, has not been undertaken in PTS. However, the role of surgery, especially in removing intrinsic venous sinus obstructing lesions should be considered. Although, there are obvious risks of haemorrhage and thrombosis, there is the potential benefit of avoiding placement of a permanent venous sinus stent.

Endovascular Treatment

Endovascular therapy for venous sinus obstruction in PTS may be divided into those treatments aimed at thrombolysis and those aimed at mechanical relief of the obstruction. The later includes venous sinus angioplasty and venous sinus stenting.

Thrombolysis is effective in cases of venous sinus thrombosis. The first reported application of anticoagulation in patients with PTS was that of Ray & Dunbar [141] which was successful in 2 patients. However, apart from cases of acute thrombosis thrombolysis is usually ineffective in cases of PTS. For example, thrombolysis was also attempted in 2 patients by Karahalios *et al.* [78] using urokinase but without success. King *et al.* [86] reported their unsuccessful attempt at clot dissolution using urokinase in one patient with transverse sinus narrowing and PTS. The authors speculate that as the lesion had been present for some months dissolution is unlikely as a mural thrombus would probably have organised and become epithelialised. In contrast, Kollar *et al.* [88] attempted thrombolysis using urokinase in 2 patients with mixed success. In one patient with symptoms of 3 weeks duration, thrombotic occlusion of the transverse sinus was effectively treated with urokinase and systemic anticoagulation. A second patient, also with a short duration of symptoms and an apparent transverse sinus thrombosis underwent thrombolysis with urokinase followed by systemic anticoagulation. Recurrent thrombosis was problematic and raised CSF pressures responded to acetazolamide. The later two cases are really cases of cerebral venous sinus thrombosis and the role of thrombolysis in such acute cases is well established. However, most cases of PTS with venous sinus obstruction will not have thrombosis as their primary pathology. In these cases of course there will be no effect of thrombolytic therapy.

Venous Sinus Angioplasty

Balloon angioplasty of venous sinus obstructions would be the ideal treatment for patients with venous sinus obstruction as the need for implanting a stent would be avoided. However, the results of venous sinus angioplasty have been disappointing due to a high rate of recurrence. Karahalios *et al.* [78] attempted angioplasty in 2 patients with sigmoid sinus stenosis and 1 patient with jugular bulb stenosis. While in 2 patients the stenosis initially improved, one patient developed restenosis in one year and another experienced no resolution despite a good hemodynamic result. In their report of PTS syndrome secondary to venous sinus stenosis after suboccipital craniotomy or translabyrinthine craniectomy, Keiper *et al.* [80] described a case of post-operative stenosis in a dominant sinus with a pressure gradient of 24 mmHg on manometry. Repeated balloon angioplasty reduced that gradient to 14 mmHg although the patient remained symptomatic. An attempt to place a stent across the stenosis was unsuccessful although the details of why this was were not provided. Kollar *et al.* [88] utilized angioplasty for bilateral transverse sinus lesions in a patient who had been symptomatic for 3 years. One lesion was consistent with a large arachnoid granulation. Symptomatic improvement was found post-procedure but she

experienced a recurrence of symptoms after 3 months and underwent surgical therapy. There are two reasons why recurrence of stenosis might occur after venous sinus angioplasty. First, the situation is not akin to performing angioplasty of stenosing arterial plaques instead the obstructing lesions, whether enlarged arachnoid granulations or venous sinus strictures, appear to have elastic properties and reconstitute their shape. Second, if the stenosis is secondary to raised CSF pressure then the cause of the obstruction has not been addressed. Due to these reasons, we do not recommend venous sinus angioplasty in the treatment of venous sinus obstruction secondary to PTS.

Venous Sinus Stenting

The first report of deployment of stents in the transverse/sigmoid sinuses is attributed to Marks *et al.* [108]. The first of two cases was a 25 year-old woman with disabling right sided tinnitus but no evidence of PTS. There were bilateral transverse sinus stenoses and the right was dominant. There was a 20 mmHg pressure gradient across the stenosis which was abolished, along with the tinnitus, after deployment of a stent. The second case was an 8 year-old boy with episodic ischemic symptoms and absence of a deep venous drainage who also demonstrated bilateral sigmoid sinus stenoses with a 14 mmHg pressure gradient. The right sided stenosis, which was resistant to angioplasty, was successfully stented. However his episodic symptoms remained.

Hunt *et al.* [68] reported two cases of papilloedema secondary to what was reported to be venous sinus thrombosis. In both cases patients developed right sided venous sinus thrombosis. The first patient had systemic lupus erythematosis and the second had undergone a right radical neck dissection. In both cases left sided focal venous obstruction was also demonstrated; one patient in the sigmoid sinus and one in the transverse sinus. Thombolysis was not followed by clinical improvement in either case. Therefore the left sided focal stenosis was stented in both cases with good effect and resolution of papilloedema. Detail regarding the anatomical arrangement of the cerebral venous system in these cases was not provided.

The first reported case of venous sinus stenting for PTS was that of Higgins *et al.* from Cambridge [65]. This 30 year-old obese woman (30.1 kg/m^2) with a 22 month history of typical PTS refractory to medical therapy was shown to have bilateral transverse sinus stenoses on MRV and venography that were associated with 18 mmHg pressure gradients on manometry. A stent was deployed across the right sided stenosis with dramatic clinical improvement. CSF pressure fell from 20.6 to 13.7 mmHg while intracranial compliance was normalised from 3.6 mL to 16.7 mL. She remained well although with persisting mild residual headache at 1 year.

After that initial report two other single case reports were also published. The Sydney Group reported the case of a woman with a previous diagnosis of PTS who had presented with CSF rhinorrhoea and striking radiological evidence of raised pressure [128]. Following a craniotomy and repair of the anterior cranial fossa defect, a large subgaleal collection developed that required shunting. Venography and manometry demonstrated a filling defect in the right transverse sinus that was associated with a pressure gradient of 14 mmHg and a SSS pressure of 22 mmHg. The left transverse sinus was hypoplastic. Deployment of a stent reduced the gradient to 1 mmHg and subsequently the LP shunt was removed. Ogungbo *et al.* [125] reported a case of typical PTS in a 37 year old woman. CSF pressure was 40 cm CSF and an MRV showed a focal obstruction in the right transverse sinus which was dominant; the left transverse sinus was hypoplastic. There was a pressure gradient of 25 mmHg with a proximal venous pressure of 40 mmHg. Deployment of a stent across the lesion re-established normal venous flow, complete resolution of clinical symptoms with a reduction in CSF pressure to 26 cm CSF.

The Sydney Group reported 4 patients with PTS treated with stent placement of a series of 9 consecutive patients investigated with DRCV and manometry [130]. One of those stented was the subject of the earlier case report [128]. Of the other 3 patients who underwent venous sinus stenting, clinical improvement was seen in all. The first patient, an obese 17 year old girl had bilateral transverse sinus obstruction on DRCV with associated pressure gradients of 23 and 25 mmHg. Stenting of the left side resulted in a dramatic reduction in CSF pressure (35 to 11 mmHg) and resolution of headache. Unfortunately despite these changes vision acuity did not improve due to optic atrophy. A 27 year old thin male had typical PTS with bilateral papilloedema. Again there were bilateral transverse sinus obstructions that appeared intrinsic in nature. A review of the MR scan revealed symmetrical lesions in the transverse sinuses that at the time we suggested might represent fat but they may also represent large arachnoid granulations. Stenting resulted in a reduction in CSF pressure and resolution of papilloedema and headache. After a period of 18 months there was some recurrence of headache although less than previously but vision and fundi remained normal. The third patient was another obese young woman (27 years). Bilateral transverse sinus obstructions with 25 mmHg pressure gradients were demonstrated. These obstructions had the appearance of large arachnoid granulations. The right lesion was stented with restoration of normal CSF pressure and clinical resolution. Apart from a short period of mild left-sided headaches which resolved she remains well. Of the other 5 patients, one had bilateral transverse sinus obstructions with moderate gradients; in this case we opted for a ventriculo-peritoneal shunt. The other four, all of which had chronic PTS and had undergone numerous other

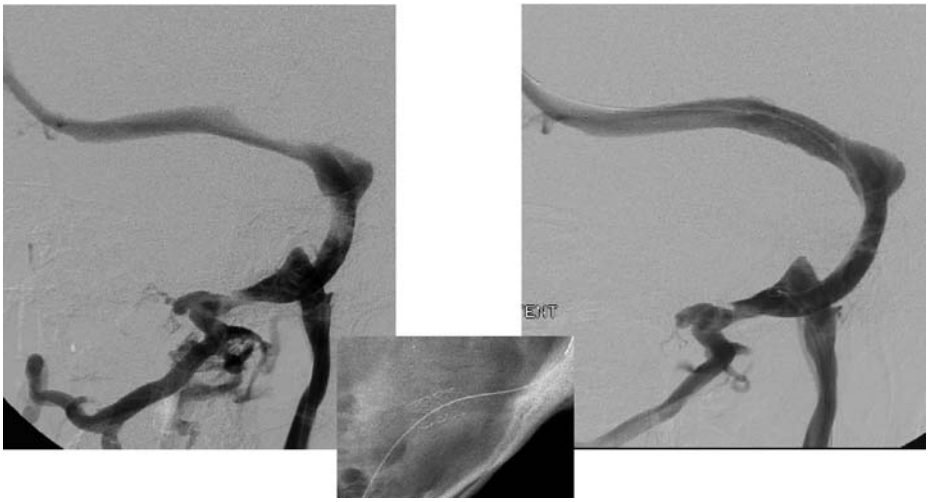

Fig. 9. Venous sinus obstruction treated with a venous sinus stent

treatments did not demonstrate morphological or functional transverse sinus obstructions.

More recently, a series of 12 patients with PTS treated with venous sinus stenting was reported from Cambridge by Higgins *et al.* [63]. All had headache and some form of visual disturbance prior to stenting. The duration of symptoms ranged from several months to 12 years and 5 patients had undergone surgical intervention (at least 10 months prior) for their PTS. All 12 patients had significant pressure gradients across obstructions of the transverse sinuses. After stenting of the transverse sinuses 5 patients were asymptomatic, 2 were improved but with residual headache and 5 were unchanged. There were apparently no predictors of clinical improvement after stenting in these patients. Papilloedema was present in 8 cases prior to stenting and follow-up was available in 7 cases; it resolved in 4, improved in another and in the 2 cases where there was no change papilloedema had been chronic.

The Sydney Group has have now had experience in 8 cases of stenting in eight cases of PTS (Fig. 9). In 7 cases there is long term follow-up available. Headache has improved in all cases. Pain over the region of the stent has been reported in all but one cases and generally resolves over a period of days to weeks with simple analgesia. In 2 cases there was return of a mild headache. This was slightly difference in nature in certainly much less severe than their previous PTS headache. In one case, a second contralateral venous sinus stent was deployed (*vide infra*) with some improvement. Vision improved in 6 of 7 patients. In one patient, optic atrophy developed despite a reduction in CSF pressure. In some cases improvement of vision was dramatic changing in one case from light perception only

to almost normal vision within weeks. One patient also had resolution of bilateral sixth nerve palsies. Papilloedema was present in all patients prior to stenting and resolved in all. There was one case of recurrence after stenting in which the first procedure produced immediate and dramatic clinical improvement and the patient returned a few months later with her previous symptoms. Venous sinus obstruction was again noted and treated with dramatic clinical improvement once more (*vide infra*).

The longest published follow-up of the Cambridge series of patients was 26 months with a mean of 14.1 months. In no series has stenosis of the stent due to endothelial proliferation or venous sinus thrombosis been observed during long term follow-up. Of the patients published in the original series from Sydney, the longest follow-up is 30 months with a mean of $22 +/- 8.5$ months. However, we are cognisant of the longer follow-up that is required. We inform all patients and their families of the unknown long-term performance of venous sinus stents. It is obviously important that patients treated in the Sydney and Cambridge groups to be followed over an extended period of time in order to assess these issues.

In cases with bilateral transverse venous sinus stenosis where stenting of one side has either not resulted in clinical improvement or the patient is improved but not asymptomatic presents the therapeutic dilemma of whether to stent the contralateral side. In the Cambridge series [63] 2 patients received bilateral transverse sinus stents. The first patient, who improved after an initial stent, improved further after a contralateral transverse sinus stent but was still not asymptomatic. In the second patient, no improvement was demonstrated after the initial stent and a partial but non-sustained improvement was evident after a contralateral stent. The 27 year-old male of the previous series from Sydney [130] also underwent bilateral transverse sinus stenting (Fig. 10). Initially he had bilateral transverse sinus stensoses with pressure gradients of 13 mmHg across each. The right transverse sinus was successfully stented. Although there was resolution of papilloedema, improvement in headache and he had returned to work, some headache remained. CSF pressure had fallen to 11 mmHg on last lumbar puncture. Stenting of the contralateral sinus resulted in marginal improvement in headache and he remains well at 7 months. It is difficult to argue that stenting of the contralateral venous sinus will produce further clinical improvement if there is free communication of the transverse sinuses at the torcular. However, in cases where the transverse sinuses appear to drain the deep and superficial cerebral venous systems independently and venography with manometry demonstrates that there is a persistent stenosis with a pressure gradient, stenting the second transverse sinus may be useful.

Complications of venous sinus stenting have been few in the cases reported so far. Higgins *et al.* [63] performed venograms on some patients in the immediate post-stent period due to concern about stent patency.

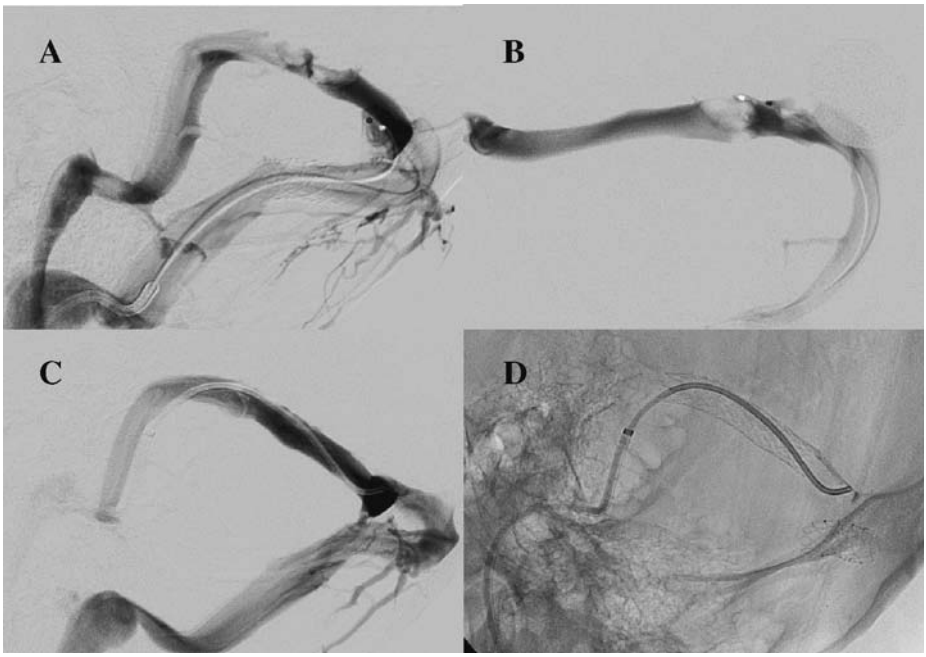

Fig. 10. A case of bilateral transverse sinus stenting. (A) Lateral DRCV demonstrating stented right transverse sinus with normal calibre and an obstruction of the left transverse sinus. (B) AP view of left transverse sinus with filling defect. (C) Lateral DRCV demonstrating that the left transverse sinus has also now been stented. (D) Plain film showing the bilateral transverse sinus stents in situ

Although all stents were patent, probable intraluminal thrombi were observed in 2 patients and were successfully treated with thrombolytic therapy. Transient hearing loss ipsilateral to the side of stenting was observed in both the patients from Sydney (2 patients) and Cambridge (2 patients). Hearing returned to normal within a few days. Higgins *et al.* [63] also reported one patient who complained of unsteadiness temporarily.

There was one life-threatening complication of venous sinus stenting – an acute subdural haematoma on a previously unpublished case from Sydney. This patient presented with severe global headache, gross papilloedema, bilateral sixth nerve palsies and marked visual loss with light perception only. CSF pressure was >64 cmCSF. She underwent optic nerve sheath fenestration and had an external ventricular drain inserted to control her CSF pressure. Venography and manometry were performed and demonstrated the bilateral transverse sinus stenoses in the typical location with large pressure gradients. During the venogram the CSF pressure was noted to rise and blood was noted in the external ventricular drain. The right transverse sinus was stented successfully and CT scan immediately after the procedure demonstrated a left acute subdural haematoma. The pa-

tient was immediately taken to the operating theatre for evacuation of the subdural. The bone flap was left out. The brain did not swell and she made recovered rapidly with improvement of her vision to normal and resolution of her sixth nerve palsies. The bone flap was replaced and she remains well without headache, visual disturbance or papilloedema at 12 months follow-up. The cause of the subdural was probably the inadvertent puncture of a draining vein by a guide-wire during venography of the contralateral transverse sinus rather than the stenting *per se*. Indeed, in this case, the stent may well have been life-saving.

The Sydney Group has had one case of re-stenosis after venous sinus stenting. A 23 year-old woman was referred with severe headache, bilateral papilloedema and a CSF pressure of 23 mmHg. DRCV with manometry was performed via a right femoral vein puncture. Extremely high venous pressures were demonstrated in the SSS that fluctuated between 45/30 (38) mmHg to 70/45 (56) mmHg. The pressure at the torcular was 69/41 (50) mmHg. Both transverse sinuses had tight obstructions. On the right side this was localized to its anterior portion with pressures of 66/42 (54) mmHg falling to 16/12/(13) below the obstruction. On the left the stenosis was more diffuse with proximal pressures of 62/41 (50) mmHg decreasing to 18/14 (12) mmHg. After a discussion with the patient, informed consent was obtained and the patient was returned to the angiography suite. Under general anaesthesia, a 10×30 mm and a 8×20 mm Wall stent were placed in the right transverse and sigmoid sinuses (Fig. 11). The pressure gradient was reduced but not completely obliterated. The pressure proximal to the stent was 41/26 (32) and was 20/17 (18) mmHg distal to the stent. The patient was recovered and returned to the neurosurgical high dependency unit on heparin and oral antiplatelet medications. Post-procedure the patient was improved. Her headache resolved and she reported that her vision had also improved. However she complained of muffled hearing. This resolved after several days. The LP was repeated under fluoroscopy and this demonstrated CSF pressure to be reduced 13 cm CSF (10 mmHg). She was discharged home under ophthalmological surveillance and on antiplatelet medication.

However, she experienced recurrence of her symptoms less than 2 months later with headache and visual disturbance. Papilloedema had returned. DRCV with manometry was performed under general anaesthesia. Mean venous pressure in the SSS was 41 mmHg. The stenosis in the left transverse sinus was again seen. On the right side, the stent appeared to be patent. However, there had been some minor collapse of the stent along with the development of a stenosis at the proximal edge of the stent. Mean venous pressure above the stent was 37 mmHg which fell to 24 mmHg inside and 12 mmHg distal to the stent. Another overlapping stent was therefore deployed across the stenosis. This abolished the pressure

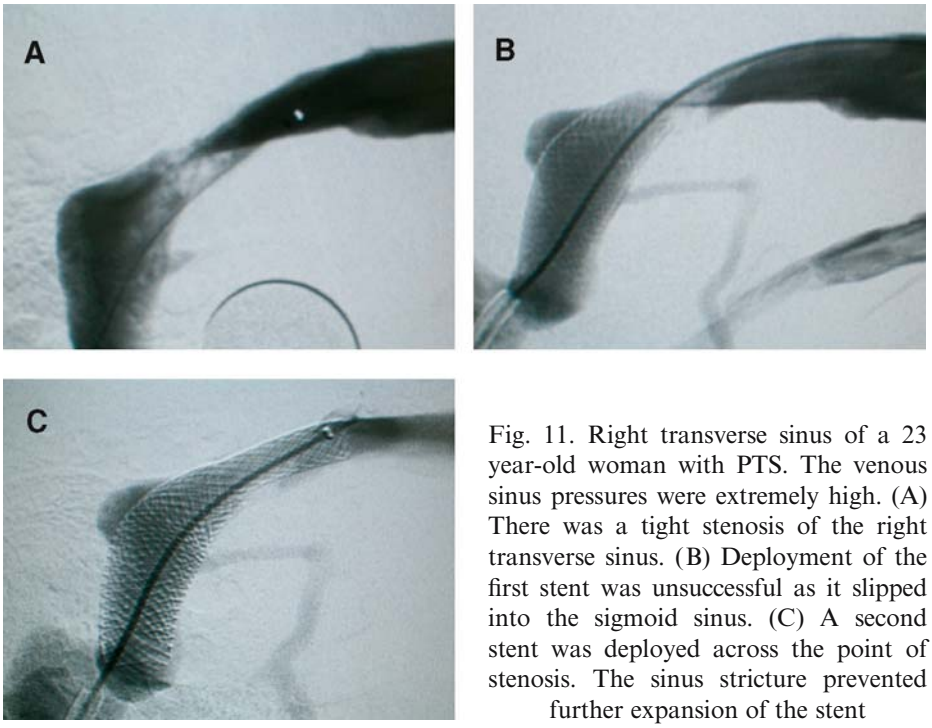

Fig. 11. Right transverse sinus of a 23 year-old woman with PTS. The venous sinus pressures were extremely high. (A) There was a tight stenosis of the right transverse sinus. (B) Deployment of the first stent was unsuccessful as it slipped into the sigmoid sinus. (C) A second stent was deployed across the point of stenosis. The sinus stricture prevented further expansion of the stent

gradient across the right transverse sinus. Mean venous pressure in the SSS was 17 mmHg compared to 15 mmHg in the right sigmoid sinus. Post-procedure, there was again remarkable clinical improvement. Her headache had resolved. There was some minor hearing disturbance which again resolved. Since then papilloedema had improved. She has now remained well for 12 months (Fig. 12). In the series of Higgins *et al.* [63], 2 patients required overlapping stents in a sinus to produce satisfactory reduction of the pressure gradient. We now recommend the use of balloon expandable stents rather than self expanding stents as these can be placed more precisely and with far less chance of stent migration and better initial expansion.

Paediatric PTS may also be related to venous sinus obstruction. In Sydney venography with manometry has been performed in 2 paediatric patients with PTS (both 9 years of age). In the first patient who had been treated first diagnosed at 3 years of age had undergone many suffered recurrent headaches and visual disturbance despite acetazolamide and had been controlled with repeated lumbar punctures. However there had been a slow worsening of symptoms and MRV demonstrated a dominant right transverse sinus with a hypoplastic left transverse sinus. There was a stenosis of the right transverse sinus at the junctions of the middle and distal thirds. Venography and manometry confirmed the stenosis and pressure gradient. A venous sinus stent was deployed across the stenosis with reso-

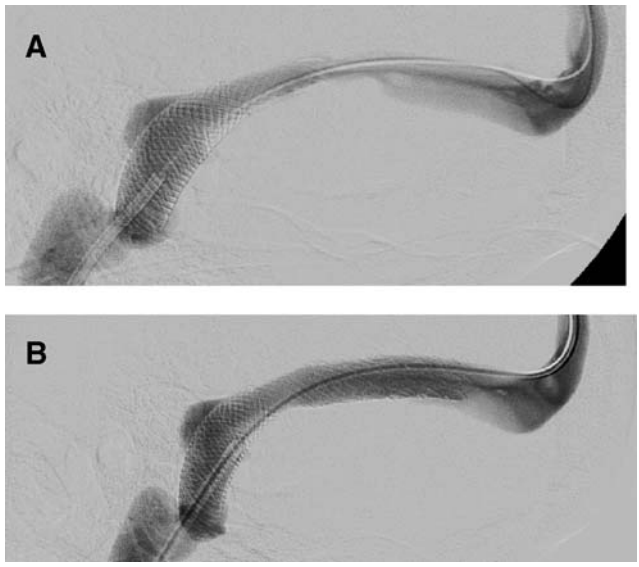

Fig. 12. Second procedure for recurrent PTS symptoms. (A) The stenosis of the right transverse sinus had recurred just proximal to the stents. (B) A third transverse sinus stent was deployed with dramatic resolution of symptoms and she remains well at 12 months

lution of the pressure gradient (Fig. 13). He remains well in early follow-up. A second patient did not have any pressure gradients although venous pressures were systemically high. He was subsequently treated with a lumbo-peritoneal shunt. In most cases of paediatric PTS there is spontaneous resolution and therefore medical treatment should always be trialled first. However there is a small group of patients that may require further treatment. In older children venous sinus stenting should be considered.

Technical Considerations

Once a patient is considered for venous sinus stenting, they are commenced on aspirin and clopidigrel several days before the procedure. Clopidigrel is omitted in children. The procedure is always performed under general anaesthesia. This is because the dura that constitutes the venous sinuses is sensitive to stretch and patients would not tolerated deployment of the stent if awake. A venogram is first performed to define the point of stenosis and the venous sinus pressures are checked. The diameter and the length of sinus to be stented are checked against a reference and appropriate stent is chosen. The stents used are uncovered stents and we prefer the slightly stiffer balloon expandable stents over self expanding stents for the reasons listed above.

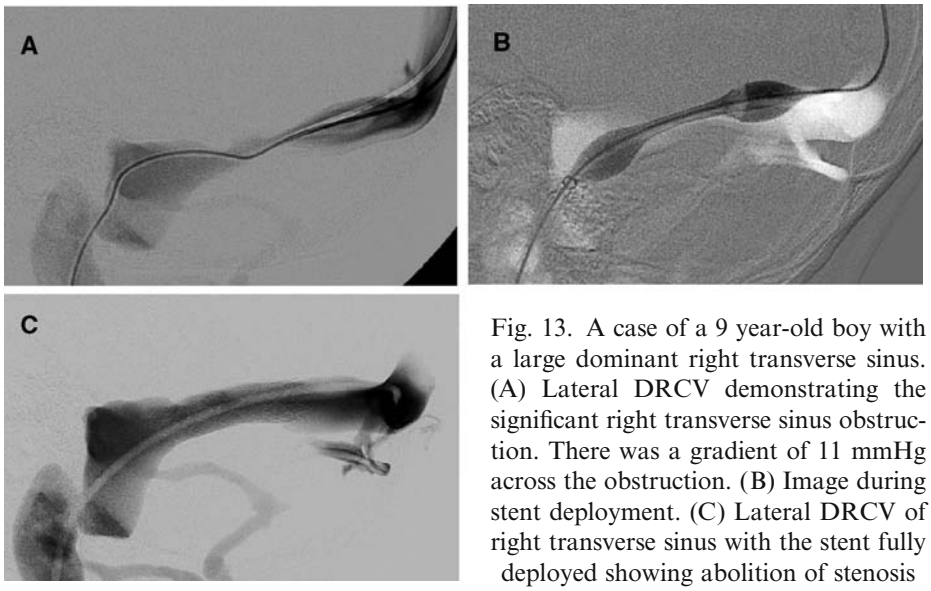

Fig. 13. A case of a 9 year-old boy with a large dominant right transverse sinus. (A) Lateral DRCV demonstrating the significant right transverse sinus obstruction. There was a gradient of 11 mmHg across the obstruction. (B) Image during stent deployment. (C) Lateral DRCV of right transverse sinus with the stent fully deployed showing abolition of stenosis

We prefer to deploy the stent via a sheath in the right femoral vein. It may be difficult to guide the stent through the jugular foramen and sigmoid sinus due to the tight curvature and stiffness of the catheter. Alternatively, the jugular vein may be used. Another group have deployed venous sinus stents into the transverse sinus via a frontal burr-hole over the SSS in order to overcome this problem (*Prof. Peter Reilly, Adelaide, Australia; personal communication*). Once the stent is situated over the point of stenosis the balloon is inflated and the stent is deployed. Several inflations of the balloon may be necessary in order to achieve the desired result. Care must be taken when withdrawing the delivery device as it may catch the edge of the stent, particularly with self expanding stents, and pull it along the sinus distally. Once the stent is deployed venography is performed to assess the position of the stent and resolution of the stenosis. Venous sinus pressures are also recorded to ensure that the pressure gradient has resolved.

At the present time it is our practice to recover the patient and have them observed in the neurosurgical high-dependency unit overnight. Heparin is either allowed to wear off or is continued for 24 hours. Aspirin is continued for at least six months. In adults, clopidigrel is given for one month.

Related Disorders

Dural AV Fistulas

The relationship between venous sinus stenosis and dural arteriovenous fistulae remains unresolved. There are several reports of dural AV fistulae

developing in association with transverse or sigmoid obstruction [1, 87, 106]. Although most case reports attribute the venous obstruction to thrombosis, there have been no case reports in which thrombosis has been clearly demonstrated. Kollar *et al.*'s [87] report of a dural AV fistula associated with a heterotopic brain nodule suggests that the pathology of venous obstruction causing PTS and dural AV fistula may have significant overlap. Stenting of the venous sinus has been used in an attempt to treat dural AV fistulas. There is one case report of a stent being deployed in the occipital sinus of a 13 year-old boy [106]. This patient had chronic venous thromboses at multiple sites associated with multiple dural AV fistulae. These were treated endovascularly with embolisation and a stent was subsequently deployed in the occipital sinus to re-establish cranial venous outflow. The stent was demonstrated to be radiologically patent at 3 months and the patient remained clinically well at 1 year. However, the author is aware of three unpublished cases that were stented in three different international centres all of which were associated with rapid restenosis of the stent and in at least one case, a poor outcome. The question of aetiology in these cases remains unanswered however venous sinus stenting must be used with great caution in cases of dural AV fistulae. One suggestion is that restenosis may be a reaction of the sinuses to continued high pressure inflow from feeding arteries.

Other Headache Disorders

Recently attention has also been given to the condition of idiopathic intracranial hypertension without papilloedema. These patients are characterised by chronic headache. Fundoscopy is normal and there is an absence of visual symptoms. Mathew *et al.* [114] performed lumbar punctures on 85 patients with chronic daily headache. Twelve of these patients had raised CSF pressure and responded to treatment with acetazolamide and frusemide. Quattrone *et al.* [136] examined patients with chronic daily headaches of at least six months. No patient had papilloedema. Of 114 consecutive patients 9.6% of patients had venous sinus abnormalities which consisted of marked irregular or absent flow in the distal portion of one or both transverse sinuses. While the authors considered these abnormalities to represent venous sinus thrombosis, the true nature of these flow gaps was not ascertained. A control group of 28 subjects had no flow gaps in the transverse sinuses on MRV. In contrast, Wang *et al.* [179] reported on 25 consecutive patients diagnosed with idiopathic intracranial hypertension without papilloedema. Pulsatile tinnitus (odds ratio 13) and obesity (odds ratio 4.4) in patients with chronic daily headaches were significant predictors of idiopathic intracranial hypertension without papilloedema. However, of the 6 patients that underwent MR venography none demonstrated

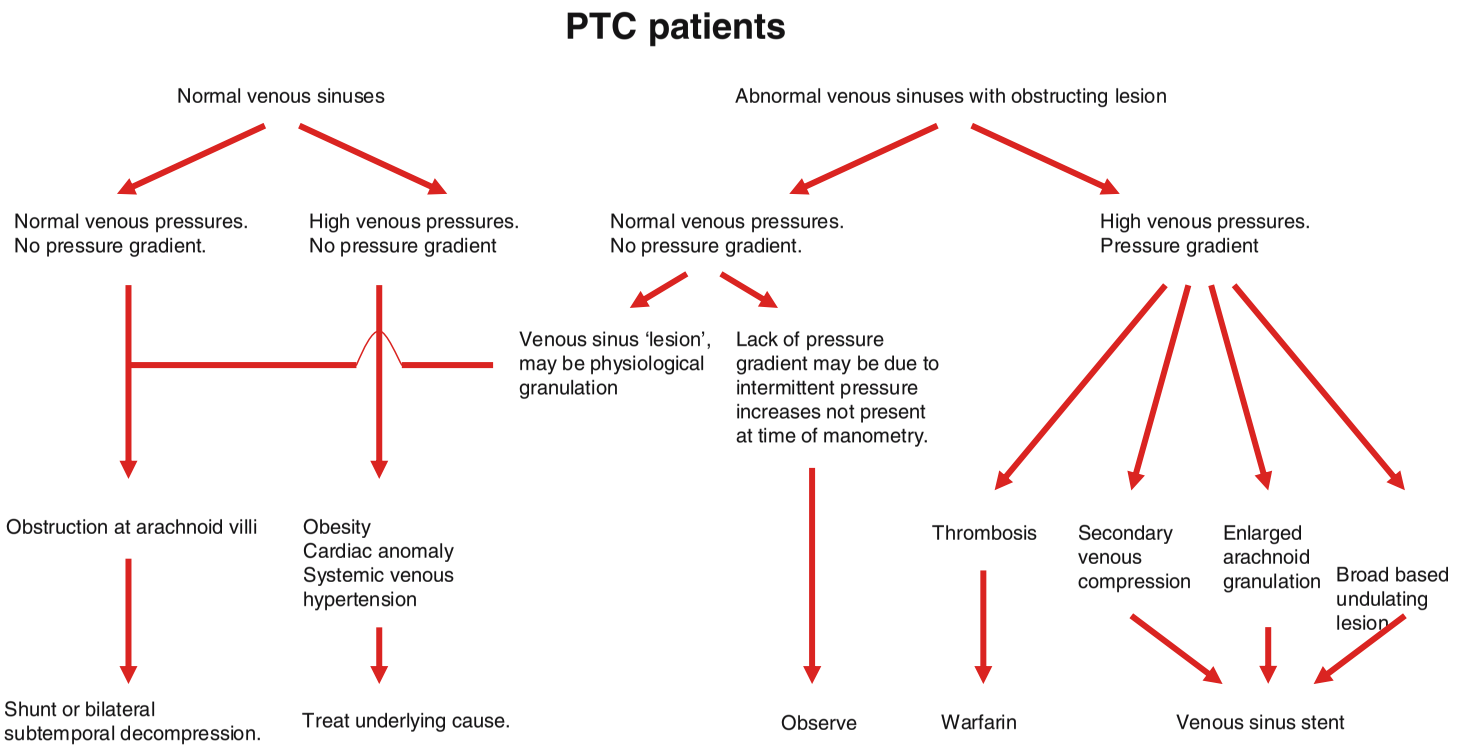

Fig. 14. Diagnostic and Therapeutic Scheme of patients with PTC based on DRCV and manometry

venous sinus occlusion. The more vexed question of prevalence of venous sinus obstruction in patients with chronic daily headache remains to be addressed.

Conclusions

Venous sinus obstruction in PTS is a more common factor in the pathogenesis of the condition than previously recognised. Venous sinus obstruction usually occurs around the junction of the middle and distal thirds of the transverse sinus and is often bilaterally symmetrical. Venous obstruction may be primary, that is, it is the underlying aetiological factor of PTS. Venous sinus obstruction may also be secondary to raised CSF pressure. The latter may exacerbate problems with intracranial compliance and raised CSF pressure. Venous sinus obstruction does not only occur in thin patients but occurs across the spectrum of PTS patients including young overweight females.

In the investigation of PTS, the index of suspicion for venous sinus obstruction should be high. Examinations should not only exclude thrombotic obstruction but should also focus on detecting venous sinus obstruction, especially in the region of the transverse and sigmoid sinuses. Static MR and contrast-enhanced MR venography are the most useful non-invasive investigations for this purpose and should be performed in all patients with PTS. Patients with PTS should preferably undergo DRCV with manometry. This should be performed in all patients who are considered for non-medical therapy whether or not an obstruction has been demonstrated on MR imaging. Venography with manometry will also diagnose systemic venous hypertension.

Treatment for cases of PTS with venous sinus obstruction should be medical initially. In cases where clinical PTS and raised CSF pressure persist or if vision is threatened, consideration should be given to other treatments. Figure 14 provides a useful scheme for the interpretation of venographic and manometric studied and may be used as a guide to therapy. Venous sinus stenting should be considered as a first-line option in cases of venous sinus obstruction with associated pressure gradients, especially where the obstruction appears to intrinsic. For patients with extrinsic compression, venous sinus stenting may still be effective, especially in the instance of disordered feedback loops and should be considered as a viable treatment alternative to other forms of surgical management including CSF shunting.

References

1. Alexander M, Rajaratanam S, Singh S, Korah IP, Gnanamuthu C, Seshadri MS (1999) Acquired dural fistulae in benign intracranial hypertension: a short case report. Acta Neurol Scand 99: 318–321

2. Amaral JF, Tsiaris W, Morgan T, Thompson WR (1987) Reversal of benign intracranial hypertension by surgically induced weight loss. Arch Surg 122: 946–949
3. Angeli SI, Sato Y, Gantz BJ (1994) Glomus jugulare tumors masquerading as benign intracranial hypertension. Arch Otolaryngol Head Neck Surg 120: 1277–1280
4. Arjona A, Delgado F, Fernandez-Romero E (2003) Neurological Picture: Intracranial hypertension secondary to giant arachnoid granulation. J Neurol Neurosurg Psychiatry 74: 418
5. Bastin M, Sinha S, Farrall A, Wardlaw J, Whittle I (2003) Diffuse brain oedema in idiopathic intracranial hypertension: a quantitative magnetic resonance imaging study. J Neurol Neurosurg Psychiatry 74: 1693–1696
6. Beaumont G, Hearn J (1948) A case of reversible papilloedema due to heart failure. BMJ 1: 50
7. Becht F (1920) Studies on the cerebrospinal fluid. Am J Physiol 51: 1
8. Beck D, Russell D (1946) Experiments on thrombosis of the superior longitudinal sinus. J Neurosurg 3: 337–347
9. Beck DW, Kassell NF, Drake CG (1979) Glomus jugulare tumor presenting with increased intracranial pressure. Case report. J Neurosurg 50: 823–825
10. Bedford T (1942) The effect of variations in the subarachnoid space pressure in the superior longitudinal sinus and in the torcular of the dog. J Physiol 101: 362–368
11. Beller A (1964) Benign post-traumatic inttracranial hypertension. J Neurol Neurosurg Psychiatry 27: 149–152
12. Benveniste R, Patel A, Post K (2004) Management of cerebral venous sinus thrombosis. Neurosurg Q 14: 27–35
13. Bergquist E, Willen (1974) Cavernous nodules in the dural sinuses. J Neurosurg 40: 330–335
14. Bergui M, Bradac G (2003) Clinical picture of patients with cerebral venous thrombosis and patterns of dural sinus involvement. Cerebrovasc Dis 16: 211–216
15. Bering E, Salibi B (1959) Production of hydrocephalus by increased cephalic-venous pressure. Arch Neurol Psychiatry 81: 693–698
16. Bloomfield G, Ridings P, Blocher C, Sugerman H (1997) A proposed relationship between increased intra-abdominal, intrathoracic, and intracranial pressure. Crit Care Med 25: 496–503
17. Bortoluzzi M, Di Lauro L, Marini G (1982) Benign intracranial hypertension with spinal and radicular pain. Case report. J Neurosurg 57: 833–836
18. Bousser M, Russell R (1997) Cerebral venous thrombosis. Major problems in neurology, vol 33. In: Warlow C, Van Gijn J (eds) W. B. Saunders, London
19. Brooks DJ, Beaney RP, Leenders KL, Marshall J, Thomas DJ, Jones T (1985) Regional cerebral oxygen utilization, blood flow, and blood volume in benign intracranial hypertension studied by positron emission tomography. Neurology 35: 1030–1034

20. Browder J, Kaplan H, Howard E (1973) Hyperplasia of Pacchionian granulations. Arch Path Lab Med 95: 315–316
21. Cameron A (1933) Marked papilloedema in pulmonary emphysema. Brit J Ophthalmol 17: 167–169
22. Chin S, Chen C, Lee C *et al* (1998) Giant arachnoid granulation mimicking dural sinus thrombosis in a boy with headache: MRI. Neuroradiol 40: 181–183
23. Cinalli G, Sainte-Rose C, Kollar E *et al* (1998) Hydrocephalus and craniosynostosis. J Neurosurg 88: 209–214
24. Connolly MB, Farrell K, Hill A, Flodmark O (1992) Magnetic resonance imaging in pseudotumor cerebri. Dev Med Child Neurol 34: 1091–1094
25. Corbett J, Digre K (2002) Editorial: Idiopathic intracranial hypertension: an answer to, ''the chicken or the egg?''. Neurology 58: 9–10
26. Corbett JJ, Mehta MP (1983) Cerebrospinal fluid pressure in normal obese subjects and patients with pseudotumor cerebri. Neurology 33: 1386–1388
27. Cremer PD, Thompson EO, Johnston IH, Halmagyi GM (1996) Pseudotumor cerebri and cerebral venous hypertension. Neurology 47: 1602–1603
28. Cronqvist S, Granholm L, Lundström N (1972) Hydrocephalus and congestive heart failure caused by intracranial arteriovenous malformation in infants. J Neurosurg 36: 249–254
29. Cure J, Key L, Goltra D, VanTassel P (2000) Cranial MR imaging of osteopetrosis. Am J Neuroradiol 21: 1110–1115
30. Cushing H (1902) Some experimental and clinical observations concerning states of increased intracranial tension. Am J Med Sci 124: 375
31. Dandy W (1937) Intracranial pressure without brain tumor, diagnosis and treatment. Ann Surg 106: 492–513
32. Dandy W, Blackfan K (1914) Internal hydrocephalus. An experimental and clinical and pathological study. Am J Diseases Childhood 8: 406–482
33. Davidoff L, Dyke C (1937) Hypertensive meningeal hydrops: syndrome frequently folling infection in the middle ear or elsewhere in the body. Am J Ophthalmol 20: 908–927
34. Davson H, Hollingsworth G, Segai M (1970) The mechanism of drainage of the cerebrospinal fluid. Brain 93: 665–678
35. de Lange S, de Vlieger M (1970) Hydrocephalus associated with raised venous pressure. Dev Med Child Neurol 12[Suppl] 22: 28–32
36. Digre KB, Corbett JJ (1988) Pseudotumor cerebri in men [published erratum appears in Arch Neurol 1989 Feb; 46(2): 172]. Arch Neurol 45: 866–872
37. Dixon W, Halliburton W (1914) The cerebrospinal fluid II. Cerebro-spinal pressure. J Physiol 48: 128–153
38. Drew J, Grant F (1945) Polycythemia as a neurosurgical problem. Arch Neurol 54: 25–36
39. Eaton H (1969) Chronic bovine hypo- and hypervitaminosis A and cerebrospinal fluid pressure. Am J Clin Nutrition 22: 1070–1080
40. Ecker A (1946) Linear skull fracture across the venous sinuses. N Y St J Med 46: 1120–1121

41. Emery J, Zachary R (1956) Hydrocephalus associated with obliteration of the longitudinal sinus. Arch Dis Childhood 31: 299–292
42. Evans M (1942) Bilateral jugular vein ligation following bilateral suppurative mastoiditis. Ann Otology, Rhinol Laryngol 51: 615–625
43. Farb R, Vanek I, Scott J *et al* (2003) Idiopathic intracranial hypertension. The prevalence and morphology of sinovenous stenosis. Neurology 60: 1418–1424
44. Fishman M, Hogan G, Dodge P (1971) The concurrence of hydrocephalus and craniosynostosis. J Neurosurg 34: 621–629
45. Foley J (1955) Benign forms of intracranial hypertension – "toxic" and "otitic" hydrocephalus. Brain 78: 1–48
46. Ford F, Murphy E (1939) Increased intracranial pressure. A clinical analysis of causes and characteristics of several different types. Bull Johns Jopkins Hospital 64: 369–398
47. Friedman WA, Mickle JP (1980) Hydrocephalus in achondroplasia: a possible mechanism. Neurosurgery 7: 150–153
48. Gardner W (1939) Otitic sinus thrombosis causing intracranial hypertension. Arch Otolaryngol 30: 253–268
49. Gibson J, Taylor A, Richardson A (1959) Congenital arteriovenous fistula with an aneurysm of the great cerebral vein and hydrocephalus treated surgically. J Neurol Neurosurg Psychiatry 22: 224–228
50. Gideon P, Sorensen PS, Thomsen C, Stahlberg F, Gjerris F, Henriksen O (1995) Increased brain water self-diffusion in patients with idiopathic intracranial hypertension. AJNR Am J Neuroradiol 16: 381–387
51. Giuseffi V, Wall M, Siegel PZ, Rojas PB (1991) Symptoms and disease associations in idiopathic intracranial hypertension (pseudotumor cerebri): a case-control study. Neurology 41: 239–244
52. Golabi M, Edwards M, Oussterhout D (1987) Craniosynostosis and hydrocephalus. Neurosurgery 21: 63–67
53. Goldsmith P, Burn D, Coulthard A, Jenkins A (1999) Extrinsic cerebral venous obstruction resulting in intracranial hypertension. J Neurol Neurosurg Psychiatry 1999: 550–551
54. Gomez D, Potts D, Deonarine V (1974) Arachnoid granulations of the sheep. Structural and ultrastructural changes with varying pressure differences. Arch Neurol 30: 169–175
55. Greenfield JJ, Tindall G (1965) Effect of acute increase in intracranial pressure on blood flow in the internal carotid artery of man. J Clin Investigation 44: 1343–1351
56. Greer M (1962) Benign intracranial hypertension. I. Mastoiditis and lateral sinus thrombosis. Neurology (Minneapolis) 12: 472–476
57. Guthrie T, Dunbar H, Karpell B (1970) Ventricular size and chronic increased intracranial venous pressure in the dog. J Neurosurg 33: 407–414
58. Guttierrez Y, Friede R, Kaliney W (1975) Agenesis of arachnoid granulations and its relationship to communicating hydrocephalus. J Neurosurg 43: 553–558

59. Guyton A (1991) Textbook of medical phsyiology, 8th edn. W. B. Saunders Company, Philidelphia pp 5–7
60. Haar F, Miller C (1975) Hydrocephalus resulting from superior vena cava thrombosis in an infant. Case report. J Neurosurg 42: 597–601
61. Hannerz J, Greitz D, Ericson K (1995) Is there a relationship between obesity and intracranial hypertension? [see comments]. Int J Obes Relat Metab Disord 19: 240–244
62. Hayes K, McCombs H, Faherty T (1971) The fine structure of vitamin A deficiency. II. Arachnoid granulations and CSF pressure. Brain 94: 213–224
63. Higgins J, Cousins C, Owler B, Sarkies N, Pickard J (2003) Idiopathic intracranial hypertension: 12 cases treated with venous sinus stenting. J Neurol Neurosurg Psychiatry 74: 1662–1666
64. Higgins J, Gillard G, Owler B, Harkness K, Pickard J (2004) MR venography in idiopathic intracranial hypertension: unappreciated and misunderstood. J Neurol Neurosurg Psychiatry 74
65. Higgins J, Owler B, Cousins C, Pickard J (2002) Venous sinus stenting for refractory benign intracranial hypertension. Lancet 359: 228–230
66. Higgins J, Pickard J (2004) Lateral sinus stenoses in idiopathic intracranial hypertension resolving after CSF diversion. Neurology 62: 1907–1908
67. Hooper R (1961) Hydrocephalus and obstruction of the superior vena cava in infancy. Clinical study of the relationship between cerebrospinal fluid pressure and venous pressure. Pediatrics 28: 792–799
68. Hunt M, Lee A, Kardon R, Lesley W, Chaloupka J (2001) Improvement in papilloedema and visual loss after endovascular stent placement in dural sinus thrombosis. Neuro-Ophthalmol 26: 85–92
69. Ikkala E, Laitinen L (1963) Papilloedema due to iron deficiency anaemia. Acta Haematoligica 29: 368–370
70. Ikushima I, Korogi Y, Makita O *et al* (1999) MRI of arachnoid granulations within the dural sinuses using a FLAIR pulse sequence. Brit J Radiol 72: 1046–1051
71. Janny P, Chazal J, Colnet G, Irthum B, Georget AM (1981) Benign intracranial hypertension and disorders of CSF absorption. Surg Neurol 15: 168–174
72. Jicha G, Suarez G (2003) Pseudotumor cerebri reversed by cardiac septal defect repair. Neurology 60: 2016–2017
73. Johnston I, Hawke S, Halmagyi M, Teo C (1991) The pseudotumor syndrome. Disorders of cerebrospinal fluid circulation causing intracranial hypertension without ventriculomegaly. Arch Neurol 48: 740–747
74. Johnston I, Kollar C, Dunkley S, Assaad N, Parker G (2002) Cranial venous outflow obstruction in the pseudotumor syndrome: incidence, nature and relevance. J Clin Neurosci
75. Johnston I, Paterson A (1974) Benign intracranial hypertension. I. Diagnosis and prognosis. Brain 97: 289–300
76. Johnston I, Paterson A (1974) Benign intracranial hypertension. II. CSF pressure and circulation. Brain 97: 301–312
77. Johnston I, Rowan J (1974) Raised intracranial pressure and cerebral blood flow. 3. Venous outflow tract pressures and vascular resistances in experi-

mental intracranial hypertension. J Neurol Neurosurg Psychiatry 37: 392–402
78. Karahalios DG, Rekate HL, Khayata MH, Apostolides PJ (1996) Elevated intracranial venous pressure as a universal mechanism in pseudotumor cerebri of varying etiologies. Neurology 46: 198–202
79. Katznelson D (1978) Increased intracranial pressure in cystic fibrosis. Acta Paediatr Scand 67: 607–609
80. Keiper GL, Jr, Sherman JD, Tomsick TA, Tew JM, Jr (1999) Dural sinus thrombosis and pseudotumor cerebri: unexpected complications of suboccipital craniotomy and translabyrinthine craniectomy. J Neurosurg 91: 192–197
81. Kesler A, Ellis M, Reshef T, Kott E, Gadoth N (2000) Idiopathic intracranial hypertension and anticardiolipin antibodies. J Neurol Neurosurg Psychiatry 68: 379–380
82. Kim AW, Trobe JD (2000) Syndrome simulating pseudotumor cerebri caused by partial transverse venous sinus obstruction in metastatic prostate cancer. Am J Ophthalmol 129: 254–256
83. Kinal M (1966) Infratentorial tumors and the dural venous sinuses. J Neurosurg 25: 395–401
84. Kinal M (1967) Traumatic thrombosis of dural venous sinuses in closed head injuries. J Neurosurg 27: 142–145
85. King J, Mitchell P, Thomsen K, Tress B (2002) Manometry combined with cervical puncture in idiopathic intracranial hypertension. Neurology 58: 26–30
86. King JO, Mitchell PJ, Thomson KR, Tress BM (1995) Cerebral venography and manometry in idiopathic intracranial hypertension. Neurology 45: 2224–2228
87. Kollar C, Johnston I, Parker G, Harper C (1998) Dural arteriovenous fistula in association with heterotopic brain nodule in transverse sinus. AJNR Am J Neuradiol 19: 1126–1128
88. Kollar C, Parker G, Johnston I (2001) The endovascular treatment of cranial venous sinus obstruction resulting in pseudotumor syndrome. Report of three cases. J Neurosurg 94: 646–651
89. Kollar CD, Johnston IH (1999) Pseudotumour after arteriovenous malformation embolisation [letter]. J Neurol Neurosurg Psychiatry 67: 249
90. Kuker W, Mull M, Mayfrank L, Weis J, Schiefer J, Thron A (1997) A cystic lesion within the dural sinuses: a rare cause of increased intracranial pressure. Neuroradiology 39: 132–135
91. Lam BL, Schatz NJ, Glaser JS, Bowen BC (1992) Pseudotumor cerebri from cranial venous obstruction. Ophthalmology 99: 706–712
92. Lam C, Solomon R, Brent Clark H, Casey S (2001) Reversal of increased intracranial pressure with removal of a torcular epidermoid: case report. Neurosurgery 48: 929–932
93. Lamas E, Lobato R, Esparza J, Escudero L (1977) Dural posterior fossa AVM producing raised sagittal sinus pressure. J Neurosurg 46: 804–810

94. Langfitt T, Weinstein J, Kassell N, Gagliardi L, Shapiro H (1966) Compression of the cerebral vessels by intracranial hypertension. I. Dural sinus pressures. Acta Neurochir (Wien) 15: 212–222
95. Le Gros Clark W (1920) On the pacchionian granulations. J Anatomy 55: 40–48
96. Leach J, Jones B, Tomsick T, Stewart C, Balko M (1996) Normal appearance of arachnoid granulations on contrast-enhanced CT and MR of the brain: differentiation from dural sinus disease. Am J Neuroradiol 17: 1523–1532
97. Lee G, Seex K, Scott G (2001) Pseudotumor cerebri due to a torcular epidermoid cyst. ANZ J Surg 71: 385–388
98. Leker RR, Steiner I (1999) Features of dural sinus thrombosis simulating pseudotumor cerebri. Eur J Neurol 6: 601–604
99. Leker RR, Steiner I (2000) Isolated intracranial hypertension as the only sign of cerebral venous thrombosis [letter; comment]. Neurology 54: 2030
100. Levine J, Povlishock J, Becker D (1982) The morphological correlates of primate cerebrospinal fluid absorption. Brain Res 241: 31–41
101. Levine S *et al* (1987) Cerebral venous thrombosis with lupus anticoagulants: report of 2 cases. Stroke 18: 801–804
102. Liedler, RabTA (1928) Otitic general septic infection with bilateral optic neuritis. J Laryngol Otology 43: 672–673
103. Loman J, Damashek W (1944) Increased intracranial venous and cerebrospinal fluid pressures in polcythemia. Trans Amer Neurol Assoc 70: 84–87
104. Luce J, Husebuy J, Kirk W, Butler J (1982) Mechanism by which positive end-expiratory pressure increases cerebrospinal fluid pressure in dogs. Am J Physiol
105. Lundar T, Blakke S, Nornes H (1990) Hydrocephalus in an achondroplastic child treated by venous decompression at the jugular foramen. J Neurosurg 73: 138–140
106. Malek A, Higashida R, Balousek P *et al* (1999) Endovascular recanalization with balloon angioplasty and stenting of an occludedd occiptal sinus for treatment of intracranial venous hypertension: technical case report. Neurosurgery 44: 896–901
107. Mamourian A, Towfighi J (1995) MR of giant arachnoid granulation, a normal variant presenting as a mass within the dural venous sinus. AJNR 16: 901–904
108. Marks M, Dake M, Steinberg G, Norbash A, Lane B (1994) Stent placement for arterial and venous cerebrovascular disease: preliminary experience. Neuroradiology 191: 441–446
109. Martin J (1955) Signs of obstruction of the superior longitudinal sinus following closed head injuries (traumatic hydrocephalus). Brit Med J 2: 467–470
110. Martins A, Kobrine A, Larsen D (1974) Pressure in the sagittal sinus during intracranial hypertension in man. J Neurosurg 40: 603–608
111. Martins AN (1973) Resistance to drainage of cerebrospinal fluid: clinical measurement and significance. J Neurol Neurosurg Psychiatry 36: 313–318

112. Massons J *et al* (1992) Cerebral venous thrombosis and hereditary protein C deficiency. Neurologia 7: 34–38
113. Mathew NT, Meyer JS, Ott EO (1975) Increased cerebral blood volume in benign intracranial hypertension. Neurology 25: 646–649
114. Mathew NT, Ravishankar K, Sanin LC (1996) Coexistence of migraine and idiopathic intracranial hypertension without papilledema [see comments]. Neurology 46: 1226–1230
115. McGonigal A, Bone I, Teasdale E (2004) Resolution of transverse sinus stenosis in idiopathic intracranial hypertension after L-P shunt. Neurology 62: 514–515
116. McLaughlin J, Loeser J, Roberts T (1997) Acquired hydrocephalus associated with superior vena cava syndrome in infants. Child's Nerv Syst 13: 59–63
117. Medlock MD, Olivero WC, Hanigan WC, Wright RM, Winek SJ (1992) Children with cerebral venous thrombosis diagnosed with magnetic resonance imaging and magnetic resonance angiography. Neurosurgery 31: 870–876; discussion 876
118. Mitchell D, Fisher J, Irving D, Gazzard BG, Guiloff RJ (1986) Lateral sinus thrombosis and intracranial hypertension in essential thrombocythaemia [letter]. J Neurol Neurosurg Psychiatry 49: 218–219
119. Mokri B, Jack CR, Jr, Petty GW (1993) Pseudotumor syndrome associated with cerebral venous sinus occlusion and antiphospholipid antibodies. Stroke 24: 469–472
120. Moser FG, Hilal SK, Abrams G, Bello JA, Schipper H, Silver AJ (1988) MR imaging of pseudotumor cerebri. AJR Am J Roentgenol 150: 903–909
121. Newton Pitt G (1890) An analysis of 57 fatal cases of ear disease and of the complication which led to death. BMJ 1: 643–647
122. Noggle JD, Rodning CB (1986) Rapidly advancing pseudotumor cerebri associated with morbid obesity: an indication for gastric exclusion. South Med J 79: 761–763
123. Nonne M (1904) Über Fälle vom Symptomkomplex "Tumor cerebri" mit Ausgang in Heilling (Pseudotumor cerebri): Über letal verlaufene Fälle von "Pseudotumor cerebri" mit Sektionsbefund. Dtsch Z Nervenheilk 27: 169–216
124. Norrell H, Wilson C, Howieson J *et al* (1969) Venous factors in infantile hydrocephalus. J Neurosurg 31: 561–569
125. Ogungdo B, Roy D, Gholkar A, Mendelow A (2003) Endovascular stenting of the transverse sinus in a patient presenting with benign intracranial hypertension. Br J Neurosurg 17: 565–568
126. Olivero W, Asner N (1992) Occlusion of the sagittal sinus in craniectomized rabbits. Child's Nerv Syst 8: 307–309
127. Osterholm J (1970) Reaction of the cerebral venous sinus system to acute intracranial hypertension. J Neurosurg 32: 654–659
128. Owler B, Allan R, Parker G, Besser M (2003) Pseudotumor cerebri, CSF Rhinorrhoea and the role of Venous Sinus Stenting in Treatment. Brit J Neurosurg 17: 79–83

129. Owler B, Pena A, Green H, Donovan T, Carpenter A, Pickard J (2001) A study of benign intracranial hypertension using diffusion tensor imaging. In World Congress of Neurological Surgeons, Sydney
130. Owler BK, Parker G, Halmagyi GM *et al* (2003) Pseudotumor Cerebri Syndrome: Venous sinus obstruction and treatment with venous sinus stenting. J Neurosurg 98: 1045–1055
131. Pierre-Kahn A, Hirsch J, Renier D, Metzger J, Maroteaux P (1980) Hydrocephalus and Achondroplasia. A study of 25 observations. Child's Brain 7: 205–219
132. Plant G, Donald J, Jackowski A, Vinnicombe S, Kendall B (1991) Partial, non-thrombotic, superior sagittal sinus occlusion due to occipital skull tumors. J Neurol Neurosurg Psychiatry 54: 520–523
133. Powers JM, Schnur JA, Baldree ME (1986) Pseudotumor cerebri due to partial obstruction of the sigmoid sinus by a cholesteatoma. Arch Neurol 43: 519–521
134. Pritz MB (1984) Monitoring cardiac function and intravascular volume in neurosurgical patients. Neurosurgery 15: 775–780
135. Purves M (1972) The physiology of the cerebral circulation. Cambridge University Press, Cambridge
136. Quattrone A, Bono F, Oliveri R *et al* (2001) Cerebral venous thrombosis and isolated intracranial hypertension without papilloedema in CDH. Neurology 57: 31–36
137. Quattrone A, Bono F, Pardatscher K (2002) Manometry combined with cervical puncture in idiopathic intracranial hypertension. Neurology 59: 963
138. Quincke H (1893) Meningitis serosa. Samml Klin Votr, Leipzig 67. Inn Med 23: 655
139. Quincke H (1897) Ueber meningitis serosa und verwandte zustände. Dtsch Z Nervenheilk 9: 149–168
140. Raichle ME, Grubb RL, Jr, Phelps ME, Gado MH, Caronna JJ (1978) Cerebral hemodynamics and metabolism in pseudotumor cerebri. Ann Neurol 4: 104–111
141. Ray B, Dunbar H (1951) Thrombosis of the dural venous sinuses as a cause of ''pseudotumor cerebri''. Ann Surg 134: 376–385
142. Roche J, Warner D (1996) Arachnoid granulations in the transverse and sigmoid sinuses: CT, MR, and MR angiographic appearances of a normal anatomic variation. Am J Neuroradiol 17: 677–683
143. Rollins N, Booth T, Shapiro K (2000) MR venography in children with complex craniosynostosis. Pediatr Neurosurg 32: 308–312
144. Ropper AH, Marmarou A (1984) Mechanism of pseudotumor in Guillain-Barre syndrome. Arch Neurol 41: 259–261
145. Rosenberg A, O'Connell J, Ojemann R, Palmer W (1993) Giant cystic arachnoid granulations: a rare cause of lytic skull lesions. Human Pathol 24: 438–441
146. Rosman NP, Shands KN (1978) Hydrocephalus caused by increased intracranial venous pressure: a clinicopathological study. Ann Neurol 3: 445–450

147. Röther J, Waggie K, van Bruggen N, de Crespgny A, Moseley M (1996) Experimental cerebral venous thrombosis: evaluation using magnetic resonance imaging. J Cereb Blood Flow Metabolism 16: 1353–1361
148. Saggi B, Bloomfield G, Sugerman H *et al* (1999) Treatment of intracranial hypertension using nonsurgical abdominal decompression. The Journal of Trauma: Injury, Infection and Critical Care 46: 646–651
149. Sahs A, Hyndman O (1939) Intracranial hypertension of unknown cause: cerebral oedema. Arch Surg 38: 429–434
150. Sahs A, Joynt R (1956) Brain swelling of unknown cause. Neurol Minneapolis 6: 791–803
151. Sainte-Rose C, LaCombe J, Pierre-Kahn A, Renier D, Hirsch JF (1984) Intracranial venous sinus hypertension: cause or consequence of hydrocephalus in infants? J Neurosurg 60: 727–736
152. Shapiro K, Langfitt T, Weinstein J (1966) Compression of the cerebral vessels by intracranial hypertension. II. Morphological evidence for collapse of vessels. Acta Neurochir (Wien) 15: 223–233
153. Shulman K, Ransohoff J (1964) Sagittal sinus venous pressure in hydrocephalus. 169–173
154. Silbergleit R, Junck L, Gebarski SS, Hatfield MK (1989) Idiopathic intracranial hypertension (pseudotumor cerebri): MR imaging. Radiology 170: 207–209
155. Simpson T (1948) Papilloedema in emphysema. BMJ II: 639–641
156. Sindou M, Auque J (2000) The intracranial venous system as a neurosurgeon's perspective. Adv Techn Stand Neurosurg 26: 131–216
157. Sindou M, Mercier P, Bokor J, Brunon J (1980) Bilateral thrombosis of the transverse sinuses: microsurgical revascularization with venous bypass. Surg Neurol 13: 215–220
158. Sklar FH, Beyer CW Jr, Ramanathan M, Cooper PR, Clark WK (1979) Cerebrospinal fluid dynamics in patients with pseudotumor cerebri. Neurosurgery 5: 208–216
159. Soleau S, Schmidt R, Stevens S *et al* (2003) Extensive experience with dural venous sinus thrombosis. Neurosurgery 52: 534–542
160. Soler D, Cox T, Bullock P, Calver DM, Robinson RO (1998) Diagnosis and management of benign intracranial hypertension. Arch Dis Child 78: 89–94
161. Sorensen PS, Thomsen C, Gjerris F, Henriksen O (1990) Brain water accumulation in pseudotumour cerebri demonstrated by MR-imaging of brain water self-diffusion. Acta Neurochir (Wien) [Suppl] 51: 363–365
162. Sorensen PS, Thomsen C, Gjerris F, Schmidt J, Kjaer L, Henriksen O (1989) Increased brain water content in pseudotumour cerebri measured by magnetic resonance imaging of brain water self diffusion. Neurol Res 11: 160–164
163. Steinbok P, Hall J, Flodmark O (1989) Hydrocephalus in achondroplasia: the role of intracranial venous hypertension. J Neurosurg 71: 42–48
164. Stewart D, Johnson D, Myers G (1975) Hydrocephalus as a complication of jugular catheterisation during total parental nutrition. J Pediatric Surg 10: 771–777

165. Sugerman H, Felton W, Sismanis A *et al* (1999) Effect of externally applied negative abdominal pressure device (ABSHELL) on headaches and pulsatile tinnitus in patients with pseudotumor cerebri. Neurology 52 6 [Suppl] 2: A34–35
166. Sugerman HJ, DeMaria EJ, Felton WL, 3rd, Nakatsuka M, Sismanis A (1997) Increased intra-abdominal pressure and cardiac filling pressures in obesity-associated pseudotumor cerebri. Neurology 49: 507–511
167. Sugerman HJ, Felton WL, 3rd, Salvant JB, Jr, Sismanis A, Kellum JM (1995) Effects of surgically induced weight loss on idiopathic intracranial hypertension in morbid obesity. Neurology 45: 1655–1659
168. Sugerman HJ, Felton WL 3rd, Sismanis A, Kellum JM, DeMaria EJ, Sugerman EL (1999) Gastric surgery for pseudotumor cerebri associated with severe obesity. Ann Surg 229: 634–640; discussion 640–642
169. Sussman J, Leach M, Greaves M, Malia R, Davies-Jones GA (1997) Potentially prothrombotic abnormalities of coagulation in benign intracranial hypertension. J Neurol Neurosurg Psychiatry 62: 229–233
169a. Sussman J, Sarkies N, Pickard JD (1998) Benign intracranial hypertension. Adv Tech Stand Neurosurg 24: 261–305
170. Symonds C (1931) Otitic Hydrocephalus. Brain 54: 55–71
171. Taylor W, Hayward R, Lasjaunias P *et al* (2001) Enigma of raised pressure in patients with complex craniosynostosis: the role of abnormal intracranial venous drainage. J Neurosurg 94: 377–385
172. Tinney W, Hall B, Giffin H (1943) CNS manifestations of polycythemia vera. Proc Mayo Clin 18: 300–303
173. Tokiguchi S, Ando K, Tsuchiya T, Ito J (1986) Fat in the dural sinus. Neuroradiol 28: 267–270
174. Tokiguchi S, Kurashima A, Ito J, Takahashi H, Shimbo Y (1988) Fat in the dural sinus – CT and anatomical correlations. Neuroradiol 30: 78–80
175. Upton M, Weller R (1985) The morphology of cerebrospinal sluid drainage pathways in human arachnoid granulations. J Neurosurg 63: 867–875
176. Wall M, Dollar JD, Sadun AA, Kardon R (1995) Idiopathic intracranial hypertension. Lack of histologic evidence for cerebral edema. Arch Neurol 52: 141–145
177. Wall M, George D (1991) Idiopathic intracranial hypertension. A prospective study of 50 patients. Brain 114: 155–180
178. Wall M, Giuseffi V, Rojas P (1989) Symptoms and disease associations in pseudotumor cerebri: a case-control study. Neurology [Suppl] 39: 210
179. Wang S, Silberstein S, Patterson S, Young W (1998) Idiopathic intracranial hypertension without papilloedema: a case-control study in a headache center. Neurology 51: 245–249
180. Weed L, Flexner L (1933) The relations of the intracranial pressures. Am J Physiol 105: 266–272
181. Wright R (1938) Experimental observations on increased intracranial pressure. ANZ J Surg 7–8: 215–235
182. Yamada H (1981) Neurological manifestations of paediatric achondroplasia. J Neurosurg 54: 49–57

Patient demographics								
Case No.	Age (years)	Body mass index (kg/m^2)	Duration of symptoms (years)	Previous procedures	Symptoms		Papilloedema	CSF pressure (cms H_2O)
Cambridge Patients					Headache	Visual symptoms		
1	34	44	3	LPS × 6*	yes	blurring	absent	25
2	30	30	1.3	none	yes	sparkling	present	35
3	46	32	4	none	yes	decreased acuity	chronic	30
4	49	33	11	LPS	yes	obscurations, constricted fields	chronic	40
5	52	41	12	LPS, ONSF, BSTD, VPS*	yes	decreased acuity, constricted fields	absent	31 (before VPS)
6	32	45	5	LPS, VPS*	yes	poor vision	chronic	39 (before VPS)
7	33	30	0.4	none	yes	obscurations	present	46
8	24	31	0.7	none	yes	obscurations	present	30
9	21	29	1	none	yes	constricted fields	mild	30
10	19	43	3.5	LPS × 3*	yes	obscurations, constricted fields	present	refused LP

11	25	42	2.3	none	yes	blurring	absent	40
12	32	43	5	none	yes	blurring, constricted fields	absent	25
Sydney Patients								
1	17	38	3 months	Diamox, ONSF, Ext CSF drainage	yes	obscurations	present	48
2	27	25	1	Diamox, LP	yes	obscurations, pulsatile tinnitus	present	30
3	27	34	>5	Diamox, ONSF, LP shunt, subtemporal decompression	moderate	blurring	present	39
4	38	23	10	LP shunts, Anterior fossa repair	Yes, CSF Rhinorrhoea	blurring	minimal	N/A
Newcastle Patients								
1	37	–	5 months	–	yes	obscurations	present	40

* LPS lumboperitoneal shunt
* ONSF optic nerve sheath fenestration
* BSTD bilateral subtemporal decompressions
* VPS ventriculoperitoneal shunt

Summary of published cases of venous stenting for PTC

Venous pressures and clinical outcome								
Case	pressures prior to stenting (mm Hg)		pressures after stenting (mm Hg)		Pcsf after stenting cms H_2O (mmHg)	Clinical outcome		
	torcular	jugular bulb	torcular	jugular bulb		symptoms	papilloedema	follow-up (months)
Cambridge Patients								
1	45	8	23	8		no change	absent$^+$	26
2	29	8	13	7		improved	resolved	24
3	25	4	19	9		no change	no change	18
4	25	7	13	9		asymptomatic	improved	18
*5	23	11	16	12		no change	no change	14
*6	15	7	14	11		no change	absent$^+$	14
7	34	6	13	11		asymptomatic	resolved	12
8	29	7	12	8		asymptomatic	resolved	12
9	26	9	17	10		improved	resolved	14
10	24	13	17	11		asymptomatic	unknown	2
11	20	8	12	10		asymptomatic	absent$^+$	9
12	31	11	18	12		no change	absent$^+$	7

Sydney Patients								
1	35	11	–	–	15 (11)	improved	resolved	12
2	15	2	–	–	15 (11)	asymptomatic	resolved	11
3	36	9	–	–	16 (12)	modest headache	resolved	5
4	22	8	–	–	N/A	resolved	–	11
Newcastle Patients								
1	40	15	–	–	26 (19)	resolved	mild	6

[+] papilloedema resolved prior to stenting
* ventriculoperitoneal shunt in situ

Technical Standards