Low Cerebrospinal Fluid Pressure Headache

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Opinion statement

- Alterations in cerebrospinal fluid (CSF) pressure lead to neurologic symptoms, the most common clinical manifestation of which is headache. Typically, the headache is orthostatic and related to traction on pain-sensitive intracranial and meningeal structures, distention on periventricular pain-sensitive areas, and direct pressure on pain conveying cranial nerves.
- Low CSF headache is a distinct and familiar syndrome that is seen most frequently following lumbar puncture. In this clinical scenario, the diagnosis and proposed plan of treatment are obvious.
- Over the past decade, however, an emerging syndrome of spontaneous intracranial hypotension (SIH) is being recognized with increasing frequency. Most of these patients are found to have spontaneous CSF leaks and have unique, clinically distinct imaging findings, which confirm the diagnosis leading to appropriate treatment.
- Spontaneous intracranial hypotension is a relatively benign and usually self-limiting syndrome of orthostatic headache in association with one or more of numerous symptoms including nausea, vomiting, horizontal diplopia, unsteadiness or vertigo, altered hearing, neck pain/stiffness, interscapular pain, and occasionally visual field cuts.
- The headache itself, while often orthostatic, may initially be non-positional, may lose its orthostatic features, or rarely or never be orthostatic. It may be gradual, subacute, or thunderclap in onset. There may be a history of minor, antecedent trauma.
- By very definition, the opening CSF pressure is low, below 60 mm H_2O, and often a "dry" tap is encountered. However, the pressure may be normal, especially with intermittent leaks and may vary tap to tap. Fluid analysis is normal.
- Brain (and occasionally spinal) MRI studies, with gadolinium enhancement should be undertaken. In patients with SIH, studies typically reveal diffuse pachymeningeal enhancement, frequently in association with "sagging"of the brain, tonsilar descent, and posterior fossa crowding. Spinal MRI is an up and coming investigational technique, which may be helpful even in the case of a normal brain MRI.
- Computed tomography myelography is the diagnostic study of choice and may follow radiocisternography, which often shows absence of activity over the convexities and early appearance of activity in the renal/urinary tract.
- Although conservative measures are often undertaken first, epidural blood patch (EBP) is the treatment of choice. For those who fail EBP, surgery may need to be undertaken in those cases with clearly identified leaks.

Introduction

ETIOLOGY

The production, absorption, and flow of cerebrospinal fluid (CSF) play key roles in the dynamics of intracranial pressure. Alterations in CSF pressure lead to neurologic symptoms, the most common clinical manifestation being headache. The International Headache Society [1, Class III] classifies a low CSF pressure headache as one that "occurs or worsens less than 15 minutes after assuming the upright position and disappears or improves less than 30 minutes after resuming the recumbent position." Classification may be further based on etiology [2, Class III], for which categories include 1) post-lumbar puncture (LP), 2) spontaneous, 3) traumatic, 4) postoperative, and 5) associated with other medical conditions. The orthostatic headaches seen most often are those of the post-LP, spontaneous, and CSF shunt over-drainage syndromes.

In the intact craniospinal vault, the CSF supports the brain such that a brain weight of 1500 g in air is only 48 g in CSF [3, Class III]. As the CSF pressure decreases, there is a reduction in the buoyancy of the brain's supportive cushion. As the brain "sags" in the cranial cavity, there is traction on the anchoring and supporting structures of the brain [4–7, Class III]. Traction on pain-sensitive intracranial and meningeal structures, particularly cranial nerves V, VII, IX, and X, the upper three cervical nerves, and bridging veins is thought to cause headache and some of the associated symptoms [6, Class III]. In the upright position this traction is exaggerated, hence the postural component of the headache. Secondary vasodilatation of the cerebral vessels to compensate for the low CSF pressure may contribute to the vascular component of the headache by increasing brain volume [5, Class III]. Because jugular venous compression increases headache severity, it seems likely that venodilatation is a contributing factor in the headache.

POST-LUMBAR PUNCTURE HEADACHE

In 1891, Quinke [8, Class III] introduced the LP, and in 1898, Bier suffered and was the first to report post-LP headache [*see* 9]. Bier proposed that ongoing leakage of CSF through the dural puncture site was the cause of the headache. This belief is maintained today; it is supposed that leakage of CSF through the dural rent made by the LP needle exceeds the rate of CSF production, which results in low CSF pressure [10, Class III]. The reported incidence of post-LP headache ranges from 10% to 30% [9,10]. The typical individual who experiences a post-LP headache is a young woman with a low body mass index [11, Class III]. The incidence in women is twice that in men [9, Class III]. Children younger than 13 years and adults older than 60 are less likely to experience a post-LP headache [12, Class I; 13, Class III]. The amount of CSF removed at the time of LP has been shown not to influence the occurrence of headache [11, Class III]. Continued leakage of CSF has been shown to occur, whether or not headache develops [4, Class III]. Onset of the headache may be within minutes or after up to 12 day [3,4, Class III], however, more commonly it occurs within 12 to 24 hours of the LP. Without treatment, the headache typically lasts 2 to 14 days (on average of 4 to 8 days) [8, Class III].

Different methods have been proposed to reduce the incidence of post-LP headache. These include having patients lie supine or prone after the procedure, use of small-gauge needles (22 gauge or smaller), removal of the needle with the patient in the prone position, and hydration of the patient. However, the only proven method is the use of small-gauge needles, which in many cases is not practical [9,13, Class III].

SPONTANEOUS INTRACRANIAL HYPOTENSION

The clinical syndrome of spontaneous low CSF pressure or spontaneous intracranial hypotension (SIH) has been recognized for more than 55 years, although the exact cause is unknown. The syndrome was first proposed in 1938 by Schaltenbrand [15, Class III], who termed it *aliquorrhea,* and described a headache syndrome virtually identical to that following LP. He proposed the following pathophysiologic mechanisms to explain the symptoms: 1) decreased CSF production by the choroid plexus; 2) increased CSF absorption; and 3) CSF leakage through small tears. Today, the accepted etiology of spontaneous intracranial hypotension (SIH) is that of CSF leakage, which may occur in the context of rupture of an arachnoid membrane [16, Class III]. Most SIH leaks occur at the thoracic or cervicothoracic junction. Given the potential weakness of the thecal sac in some of these patients, theories have been put forth to suggest the possible association of connective tissue abnormalities. Marfanoid features, history of retinal detachment, and hypermobility of joints have been reported in some patients [17, Class III].

The other contributing factor is that of minor trauma or inciting event, including a fall, a sudden twist or stretch, sexual intercourse or orgasm, a sudden sneeze, sports activity, or "trivial trauma" [18••, Class III]. These relatively minor events may cause rupture of spinal epidural cysts (formed during fetal development) or of perineural (Tarlov) cysts or a tear in a dural nerve sheath [16], with resultant cryptic CSF leakage. Leakage of CSF into the petrous or ethmoidal regions or through the cribiform plate can also occur, and although overt CSF otorrhea and CSF rhinorrhea may result, it is not uncommon for the patient to swallow the fluid and be

unaware of the leak. Recently, it has been recognized that patients who have had CSF shunts placed for various neurosurgical indications may develop a syndrome identical to that of SIH.

CLINICAL EVALUATION

The headache caused by SIH may be of sudden or gradual onset. Often it is described as an intense, severe, throbbing, or dull pain that may be generalized or focal. Frontal pain is described by patients as often as is occipital and diffuse pain [18••, Class III]. Exacerbating factors include erect posture, head movement, coughing, straining, sneezing, and jugular venous compression. Relief is typically obtained with recumbency, usually within minutes. The headache is rarely relieved with analgesics. The headache may spontaneously resolve within 2 weeks [19, Class III]; but in some cases it may last months or, in rarer cases, years. In general, recurrences are rare [16, Class III].

In 1825, Magendie [20, Class III] described vertigo and unsteadiness in a patient following the removal of CSF. Today, the list of reported associated symptoms is varied and extensive. Commonly, patients may experience nausea, vomiting, anorexia, vertigo, dizziness, diaphoresis, neck stiffness, blurred vision, and photophobia [18••, Class III]. Others have also reported the occurrence of tinnitus [8,18••, Class III], bilateral hyperacusis [7, Class III], unsteadiness or staggering gait [10, Class III], diplopia [3, Class III], transient visual obscuration [3, Class III], hiccups, and dysgeusia [18••, Class III]. Rarer symptoms including galactorrhea, stupor, ataxia, parkinsonism, and coma, as a result of compression of the pituitary stalk, diencephalon, posterior fossa, and midline structures, respectively, have been reported [21••, Class III].

Neurologic examination is typically normal. Frequently, mild neck stiffness is noted [19, Class III]. Unilateral or bilateral abducens palsies have been reported, as have visual field defects [3, Class III]. A slow pulse, or vagus pulse, has also been described [5, Class III].

The incidence of SIH is unknown, but previous to the advancement of MRI imaging and its specific findings in SIH, the diagnosis was often missed. Headache is a common ailment, and SIH patients typically present with normal neurologic examination; thus, the syndrome has been under recognized.

INVESTIGATIONS

Cerebrospinal fluid analysis In cases of post-LP headache, the clinical history usually suffices for diagnosis; however, a LP may be necessary to document low CSF pressure, especially in suspected cases of SIH. To obtain an accurate measurement of the opening pressure, it is recommended that the measurement be performed with the patient in the lateral decubitus position. To ascertain correct placement of the spinal needle, CSF flow should be observed either spontaneously, with gentle aspiration, or with Valsalva's maneuver [8, Class III]. Lumbar punctures on these patients are not uncommonly recorded as difficult; sometimes, repeated attempts are made, and traumatic blood-tinged fluids are not rare. So-called dry taps may sometimes be encountered, and in some patients, cisternal taps have been done to collect the fluid. In rare instances when the CSF pressure is negative (below that of atmospheric pressure), a sucking noise may be heard when the stylet is removed from the LP needle. An opening pressure consistent with a diagnosis of SIH has been reported to range from 0 to 70 mm H_20 [4, Class III]. However, in some cases of proven spontaneous SIH, the opening pressure is sometimes in the range of normal, especially if the measurement is made after a period of recumbency or if the leak is intermittent. Even within the same patient, the CSF pressure may vary tap to tap.

Typically the fluid is clear and colorless, with normal microbiologic and cytologic studies. Common CSF abnormalities include a moderate pleocytosis (up to 50 cells per mm^3), the presence of red blood cells, and elevated protein (commonly up to 100 mg/dL) [17, Class III]. The elevated protein may be related to lowered CSF pressure leading to disruption of normal hydrostatic and oncotic pressure across the venous sinus and arachnoid villi, resulting in the passage of serum protein into the CSF [19, Class III]. Pleocytosis likely reflects a reactive phenomenon secondary to hydrostatic pressure changes [19, Class III].

Magnetic resonance imaging As a result of CSF volume depletion, numerous MRI abnormalities are now commonly recognized in SIH patients. Diffuse pachymeningeal enhancement (DME), first noted by Mokri *et al.* [22, Class III] is typically supra and infratentorial, bilateral, non-nodular without skip lesions, and often thick in dimension. Diffuse pachymeningeal enhancement has been observed to improve or resolve with resolution of the headache. A second finding of interest is downward displacement of the brain [23, Class III]. Findings include cerebellar tonsilar herniation, descent of the brain stem, flattening of the basis pontis, and bowing of the optic chiasm over the pituitary gland, all of which are believed to contribute to the associated symptoms of low pressure headache. These abnormalities diminish or resolve when the patient is asymptomatic. Spontaneous intracranial headache has been misdiagnosed as Chiari type I malformation [24, Class III]. Subdural hematomas have been observed on MRI in association with low intracranial pressure syndromes [3,20, Class III]. The cause of the subdural hematomas is presumably rupture of the bridging veins as the CSF volume decreases and the brain sags pulling away from the dura (Figs. 1 and 2) [20, Class III].

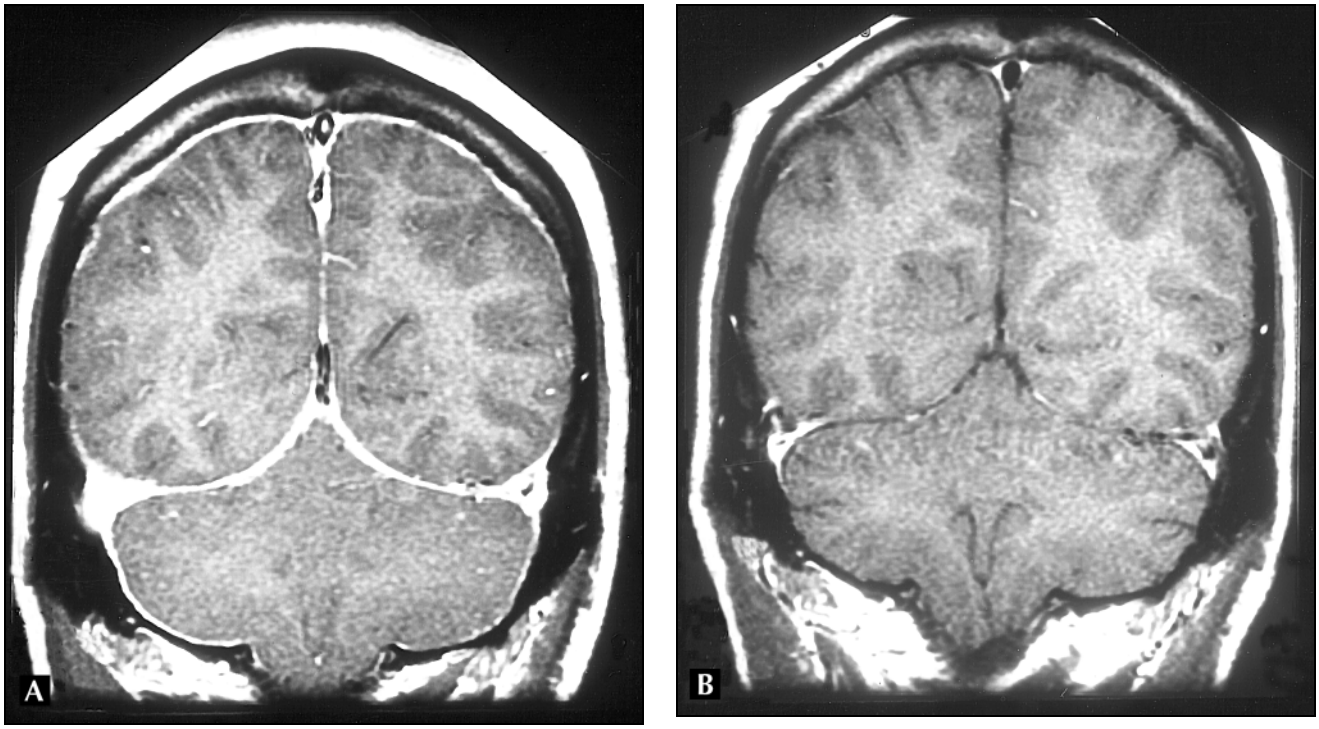

Figure 1. A, MRI coronal views demonstrating contiguous meningeal enhancement involving the convexity, falx, and tentorium. **B,** Resolution of meningeal enhancement following surgical repair of lumbar cerebrospinal fluid leak. (From Lay *et al.* [18••]; with permission.)

Spinal MRI is an up and coming technique employed to help identify extra-arachnoid fluid collections, extradural fluid extravasation, diverticulae, spinal pachymeningeal enhancement, and epidural venous plexus engorgement [25, Class III]. Spinal MRI is not, at this point in time, a reliable technique to specifically identify the site of actual CSF leak.

Radioisotope cisternography A study particularly useful for identifying CSF leaks is radioisotope cisternography. Placement of numbered cotton pledgets in the nose for subsequent detection of radioactivity aids in detection and localization of CSF leakage through the paranasal sinuses. Normal CSF flow involves cephalad migration from the site of injection to the cerebral convexities and the sylvian fissures [5, Class III]. It is advisable to look for early accumulation within the bladder and kidneys, or leakage of isotope outside of the normal confines of the subarachnoid space (Fig. 3).

Computed tomographic myelography Computed tomography myelography is the best test to identify the site of the leak. Both early and delayed cuts should be obtained at each spinal level, because CSF leaks may be rapid or slow. In cases in which radiocisternography or spinal MRI has identified the site of the leak, focused cuts may be undertaken. Although CT myelography has a somewhat higher yield, the yield of both tests may be suboptimal.

CONCLUSIONS

Low CSF pressure headache following an LP rarely creates a clinical dilemma; however, SIH, if not considered, may result in extensive and unnecessary clinical investigation. The diagnosis is suggested by positional headache, with or without associated symptoms, perhaps in the setting of minor trauma. Although low opening CSF pressure is likely to be confirmed by LP, in some cases the pressure may be normal. It is reasonable to obtain a head imaging study and to hold off on further work-up unless the headache persists despite conservative treatment or epidural blood patch (EBP). If the MRI findings described previously are seen and if an adequate trial of bed rest and EBP have failed, radioisotope cisternography, or CT myelography should be considered. Repeated EBP, continuous epidural saline infusion, and, rarely, surgical repair of the defect may be needed.

Although the classic syndrome of orthostatic headache, low CSF pressure, and DME is typical, the clinical syndrome is evolving as cases are now being recognized that have nonorthostatic headache or normal CSF pressure or absent DME [29, Class III]. The independent variable in all case is CSF hypovolemia. Spontaneous intracranial pressure is being recognized with increasing frequency, and as it becomes more familiar, clinicians will gain more facility with its diagnosis and treatment.

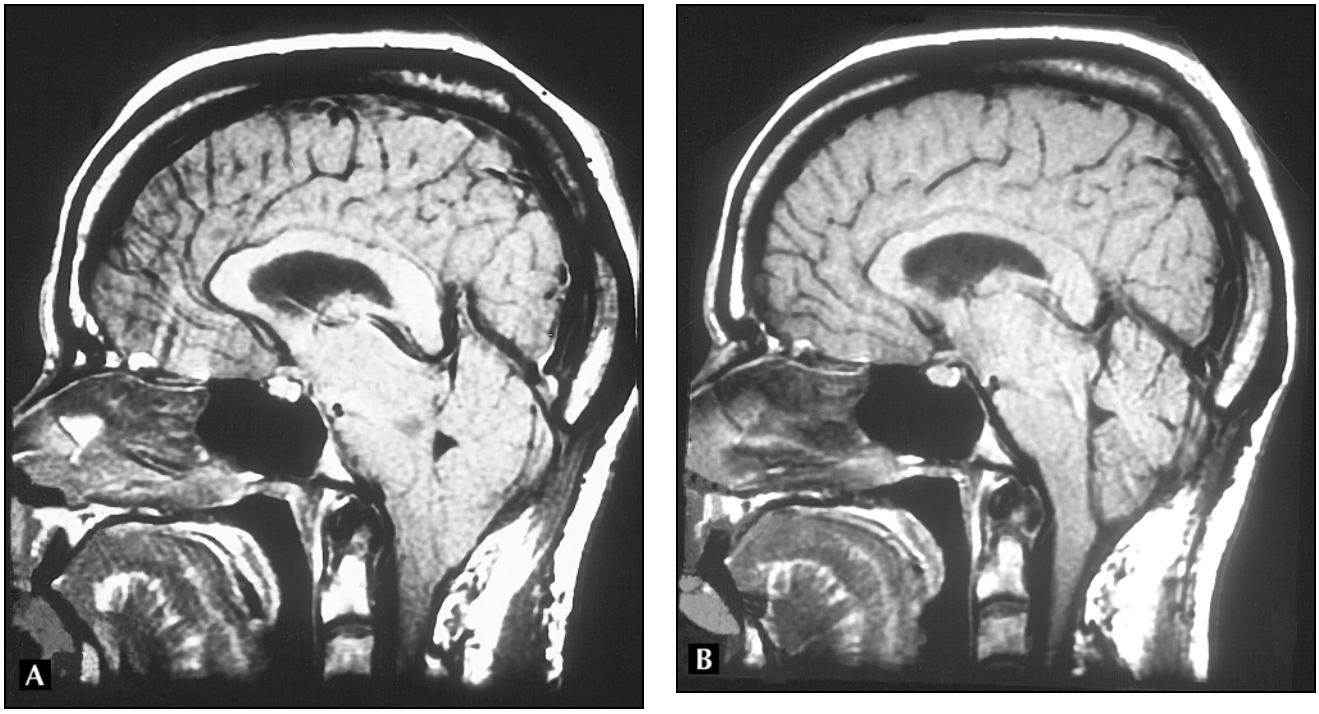

Figure 2. A, Same patient as shown in Figure 1. Magnetic resonance imaging sagittal view demonstrating descent of brain with crowding of the posterior fossa structures, resembling a Chiari type 1 malformation. **B,** Return to normal posterior fossa appearance with ascent of brain, following surgical repair of the cerebrospinal fluid leak. (From Lay *et al.* [18••]; with permission.)

Treatment

- Given enough time, a low-pressure headache may resolve without treatment. However, in many instances intervention not only helps to speed recovery but also may be necessary for a full recovery. Unfortunately, few scientific clinical trials have evaluated the effectiveness of the various treatment strategies employed and, as such, no definitive treatment protocol has been established.

Diet and lifestyle

- The most conservative treatment for low-pressure headache is avoidance of the upright position, with strict bed rest and the possible addition of analgesics. Frequently, however, patients are unable to comply with strict bed rest. Use of an abdominal binder has also been proposed [5, Class III]. Strategies aimed at restoring CSF volume include oral or intravenous hydration, high oral caffeine intake, and high salt intake.

Pharmacologic treatment

- Although analgesics are often recommended as first-line treatment, generally, they provide little relief [4]. Anecdotally, steroids have been reported to be of some, but unproven benefit [21••, Class III]. Theophylline [9, Class

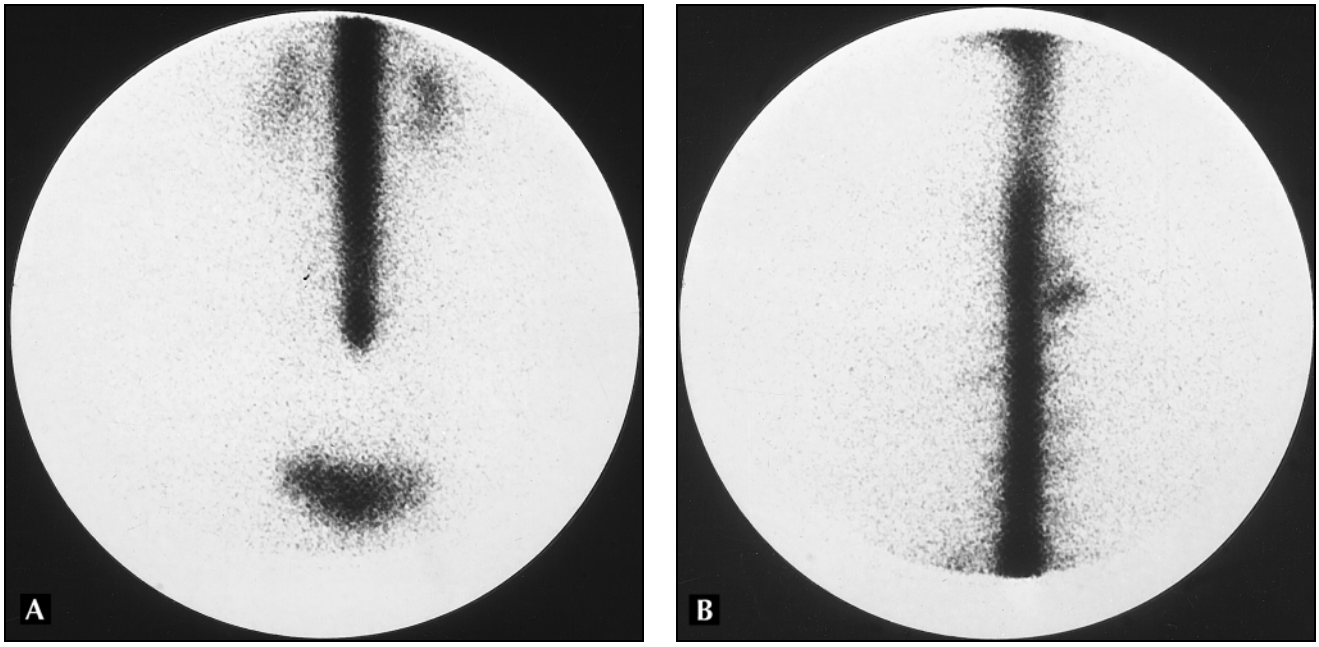

Figure 3. A, Posterior view scintiscan showing early accumulation of isotope in the kidneys and bladder after intrathecal administration. **B,** Extra-arachnoid leakage in the midthoracic region. (From Lay *et al.* [18••]; with permission.)

III] has also been used with some success to treat post-LP headache, as has intravenous caffeine sodium benzoate at 500 mg in 1L Ringer's lactate over 1 hour [18••, Class III].

Interventional treatment

- When conservative treatment fails, the treatment of choice is EBP. Epidural blood patch was first introduced by Gormley [5, Class III] in 1960 and involves the infusion of 10 to 20 cc of autologous blood into the epidural space. In the treatment of post-LP headache, it has a success rate of 97%, and is 85% to 100% effective in the treatment of spontaneous low-pressure headache [26]. The mechanism that accounts for the success of EBP is not completely understood. Presumably, it works by tamponade of a dural leak followed by fibrin deposition and eventual scar formation in 3 weeks' time [5, Class III]. Lumbar placement of the EBP can be effective even when the site of the leakage is unknown or is above the site of the patch. Mokri [21••, Class III] notes that up to 50% of patients with SIH require more than one patch and up to 4 to 6 patches may be required in some cases.
- Epidural patching with fibrin glue has been reported as successful, but is a fairly new technique and awaits consensus opinion [27, Class III].
- One method of restoring the intracranial CSF volume, and thereby reducing headache, is a continuous epidural infusion of saline or dextran [18••, Class III]. This method has limited success, but could be considered in patients who fail EBP and in whom the site of the leak cannot be identified.

Surgery

- Surgical repair of a CSF leak may be required in some cases, particularly if more conservative measures fail and for those patients with clearly identified site of leakage [28•,29•, Class III]. Because surgical treatment is not at all straight forward, it is best left in the hands of the experienced neurosurgeon.

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