Spontaneous Spinal Cerebrospinal Fluid Leaks and Intracranial Hypotension

Wouter I. Schievink, MD

A patient presents with a new headache that occurs shortly after assuming an upright position and is relieved by lying down. Although such a positional headache pattern is well known following a diagnostic lumbar puncture, the spontaneous onset of an orthostatic headache is not well recognized and the patient may be diagnosed with migraine, tension headache, viral meningitis, or malingering. This has been a typical scenario for many patients experiencing spontaneous intracranial hypotension. The spontaneous form of intracranial hypotension was first described in 1938, and much has been learned about this syndrome, particularly since the early 1990s, but an initial misdiagnosis remains the norm. Unfamiliarity with spontaneous intracranial hypotension among physicians in general and the unusually varied spectrum of clinical and radiographic manifestations may all contribute to a delay in diagnosis that often is measured in months or even years and decades.

EVIDENCE ACQUISITION

The material covered in this review is based on a systematic review of journal articles in MEDLINE (1966-2005) and OLDMEDLINE (1950-1965) using the terms intracranial hypotension, CSF leak, low pressure headache, and CSF hypovolemia. Reference lists of these articles and ongoing investigations in this area were also used. Clinical trials were not available, and prospective studies were selected over retrospective studies. Selected articles were largely those published within the past 10 years and having adequate documentation and relevant clinical information, but older articles were also included if they were commonly referenced and highly regarded.

EVIDENCE SYNTHESIS

Epidemiology

Once considered an exceedingly rare disorder, recent evidence suggests that spontaneous intracranial hypotension is not that rare and has to be considered an important cause of new daily persistent headaches, particularly among young and middle-aged individuals. In the past, our knowledge regarding this disorder was limited to case reports and small series. However, recent studies have provided evidence that the incidence of spontaneous intracranial hypotension is higher than previously thought. For example, a study by Gudbjartsson et al. (2007) found an estimated incidence of 5 per 100,000 per year in young adults.

Context

Spontaneous intracranial hypotension is caused by spontaneous spinal cerebrospinal fluid (CSF) leaks and is known for causing orthostatic headaches. It is an important cause of new headaches in young and middle-aged individuals, but initial misdiagnosis is common.

Objective

To summarize existing evidence regarding the epidemiology, pathophysiology, diagnosis, and management of spontaneous spinal CSF leaks and intracranial hypotension.

Evidence Acquisition

MEDLINE (1966-2005) and OLDMEDLINE (1950-1965) were searched using the terms intracranial hypotension, CSF leak, low pressure headache, and CSF hypovolemia. Reference lists of these articles and ongoing investigations in this area were used as well.

Evidence Synthesis

Spontaneous intracranial hypotension is caused by single or multiple spinal CSF leaks. The incidence has been estimated at 5 per 100,000 per year, with a peak around age 40 years. Women are affected more commonly than men. Mechanical factors combine with an underlying connective tissue disorder to cause the CSF leaks. An orthostatic headache is the prototypical manifestation but other headache patterns occur as well, and associated symptoms are common. Typical magnetic resonance imaging findings include subdural fluid collections, enhancement of the pachymeninges, engorgement of venous structures, pituitary hyperemia, and sagging of the brain (mnemonic: SEEPS). Myelography is the study of choice to identify the spinal CSF leak. Treatments include bed rest, epidural blood patching, percutaneous placement of fibrin sealant, and surgical CSF leak repair, but outcomes have been poorly studied and no management strategies have been studied in properly controlled randomized trials.

Conclusions

Spontaneous intracranial hypotension is not rare but it remains underdiagnosed. The spectrum of clinical and radiographic manifestations is varied, with diagnosis largely based on clinical suspicion, cranial magnetic resonance imaging, and myelography. Numerous treatment options are available, but much remains to be learned about this disorder.

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Corresponding Author: Michael S. Lauer, MD

Author Affiliation: Maxine Dunitz Neurosurgical Institute, Cedars-Sinai Medical Center, Los Angeles, Calif.

CLINICIAN’S CORNER

SPONTANEOUS SPINAL CEREBROSPINAL FLUID LEAKS AND INTRACRANIAL HYPOTENSION

PATIENT PRESENTS WITH A NEW HEADACHE THAT OCCURS SHORTLY AFTER ASSUMING AN UPRIGHT POSITION AND IS RELIEVED BY LYING DOWN. ALTHOUGH SUCH A POSITIONAL HEADACHE PATTERN IS WELL KNOWN FOLLOWING A DIAGNOSTIC LUMBAR PUNCTURE, THE SPONTANEOUS ONSET OF AN ORTHOSTATIC HEADACHE IS NOT WELL RECOGNIZED AND THE PATIENT MAY BE DIAGNOSED WITH MIGRAINE, TENSION HEADACHE, VIRAL MENINGITIS, OR MALINGERING. THIS HAS BEEN A TYPICAL SCENARIO FOR MANY PATIENTS EXPERIENCING SPONTANEOUS INTRACRANIAL HYPOTENSION. THE SPONTANEOUS FORM OF INTRACRANIAL HYPOVENTION WAS FIRST DESCRIBED IN 1938, AND MUCH HAS BEEN LEARNED ABOUT THIS SYNDROME, PARTICULARLY SINCE THE EARLY 1990S, BUT AN INITIAL MISDIAGNOSIS REMAINS THE NORM. UNFAMILIARITY WITH SPONTANEOUS INTRACRANIAL HYPOTENSION AMONG PHYSICIANS IN GENERAL AND THE UNUSUALLY VARIED SPECTRUM OF CLINICAL AND RADIOGRAPHIC MANIFESTATIONS MAY ALL CONTRIBUTE TO A DELAY IN DIAGNOSIS THAT OFTEN IS MEASURED IN MONTHS OR EVEN YEARS AND DECADES.

EVIDENCE ACQUISITION

THE MATERIAL COVERED IN THIS REVIEW IS BASED ON A SYSTEMATIC REVIEW OF JOURNAL ARTICLES IN MEDLINE (1966-2005) AND OLDMEDLINE (1950-1965) USING THE TERMS INTRACRANIAL HYPOTENSION, CSF LEAK, LOW PRESSURE HEADACHE, AND CSF HYPMOVLEMA. REFERENCE LISTS OF THESE ARTICLES AND ONGOING INVESTIGATIONS IN THIS AREA WERE ALSO USED. CLINICAL TRIALS WERE NOT AVAILABLE, AND PROSPECTIVE STUDIES WERE SELECTED OVER RETROSPECTIVE STUDIES. SELECTED ARTICLES WERE LARGELY THOSE PUBLISHED WITHIN THE PAST 10 YEARS AND HAVING ADEQUATE DOCUMENTATION AND RELEVANT CLINICAL INFORMATION, BUT OLDER ARTICLES WERE ALSO INCLUDED IF THEY WERE COMMONLY REFERENCED AND HIGHLY REGARDED.

EVIDENCE SYNTHESIS

EPIDEMIOLOGY

ONCE CONSIDERED AN EXCEEDINGLY RARE DISORDER, RECENT EVIDENCE SUGGESTS THAT SPONTANEOUS INTRACRANIAL HYPOTENSION IS NOT THAT RARE AND HAS TO BE CONSIDERED AN IMPORTANT CAUSE OF NEW DAILY PERSISTENT HEADACHES, PARTICULARLY AMONG YOUNG AND MIDDLE-AGED INDIVIDUALS. IN THE PAST, OUR KNOWLEDGE REGARDING THIS DISORDER WAS LIMITED TO CASE REPORTS AND SMALL SERIES. HOWEVER, RECENT STUDIES HAVE PROVIDED EVIDENCE THAT THE INCIDENCE OF SPONTANEOUS INTRACRANIAL HYPOTENSION IS HIGHER THAN PREVIOUSLY THOUGHT. FOR EXAMPLE, A STUDY BY GUDBJARTSSON ET AL. (2007) FOUND AN ESTIMATED INCIDENCE OF 5 PER 100,000 PER YEAR IN YOUNG ADULTS.

CONTEXT

SPONTANEOUS INTRACRANIAL HYPOTENSION IS CAUSED BY SPONTANEOUS SPINAL CEREBROSPINAL FLUID (CSF) LEAKS AND IS KNOWN FOR CAUSING ORTHOSTATIC HEADACHES. IT IS AN IMPORTANT CAUSE OF NEW HEADACHES IN YOUNG AND MIDDLE-AGED INDIVIDUALS, BUT INITIAL MISDIAGNOSIS IS COMMON.

OBJECTIVE

TO SUMMARIZE EXISTING EVIDENCE REGARDING THE EPIDEMIOLOGY, PATHOPHYSIOLOGY, DIAGNOSIS, AND MANAGEMENT OF SPONTANEOUS SPINAL CSF LEAKS AND INTRACRANIAL HYPOTENSION.

EVIDENCE ACQUISITION


EVIDENCE SYNTHESIS

SPONTANEOUS INTRACRANIAL HYPOTENSION IS CAUSED BY SINGLE OR MULTIPLE SPINAL CSF LEAKS. THE INCIDENCE HAS BEEN ESTIMATED AT 5 PER 100,000 PER YEAR, WITH A PEAK AROUND AGE 40 YEARS. WOMEN ARE AFFECTED MORE COMMONLY THAN MEN. MECHANICAL FACTORS COMBINE WITH AN UNDERLYING CONNECTIVE TISSUE DISORDER TO CAUSE THE CSF LEAKS. AN ORTHOSTATIC HEADACHE IS THE PROTOTYPICAL MANIFESTATION BUT OTHER HEADACHE PATTERNS OCCUR AS WELL, AND ASSOCIATED SYMPTOMS ARE COMMON. TYPICAL MAGNETIC RESONANCE IMAGING FINDINGS INCLUDE SUBDURAL FLUID COLLECTIONS, ENHANCEMENT OF THE PACHYMENINGES, ENHANCEMENT OF VENOUS STRUCTURES, PITUITARY HYPEREMIA, AND SAGGING OF THE BRAIN (MNEMONIC: SEEPS). MYELOGRAPHY IS THE STUDY OF CHOICE TO IDENTIFY THE SPINAL CSF LEAK. TREATMENTS INCLUDE BED REST, EPIDURAL BLOOD PATCHING, PERCUTANEOUS PLACEMENT OF FIBRIN SEALANT, AND SURGICAL CSF LEAK REPAIR, BUT OUTCOMES HAVE BEEN POORLY STUDIED AND NO MANAGEMENT STRATEGIES HAVE BEEN STUDIED IN PROPERLY CONTROLLED RANDOMIZED TRIALS.

CONCLUSIONS

SPONTANEOUS INTRACRANIAL HYPOTENSION IS NOT RARE BUT IT REMAINS UNDERDIAGNOSED. THE SPECTRUM OF CLINICAL AND RADIOGRAPHIC MANIFESTATIONS IS VARIED, WITH DIAGNOSIS LARGELY BASED ON CLINICAL SUSPICION, CRANIAL MAGNETIC RESONANCE IMAGING, AND MYELOGRAPHY. NUMEROUS TREATMENT OPTIONS ARE AVAILABLE, BUT MUCH REMAINS TO BE LEARNED ABOUT THIS DISORDER.
Regarding spontaneous intracranial hypotension was derived from case reports only, and no epidemiologic data were available. In a community-based study conducted in 1994, the prevalence of spontaneous intracranial hypotension was estimated at 1 per 50,000. In a more recent emergency department-based study (2003-2004), spontaneous intracranial hypotension was half as common as spontaneous subarachnoid hemorrhage, for an estimated annual incidence of 5 per 100,000.

Comprehensive population-based epidemiologic studies, however, are not yet available. In the past, spontaneous intracranial hypotension was probably more frequently underdiagnosed than it is now, and it is unlikely that there has been an actual increase in its incidence, although that possibility cannot be entirely excluded.

Spontaneous intracranial hypotension affects women more frequently than men, with a female-male ratio of approximately 2:1. Onset of symptoms typically is in the fourth or fifth decade of life, with a peak incidence around age 40 years, but children and elderly persons also may be affected.

**Etiology and Pathogenesis**

Spontaneous intracranial hypotension is caused by spontaneous spinal cerebrospinal fluid (CSF) leaks. Because spinal CSF leaks generally do not cause any local symptoms, they remain undetected unless actively

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**Figure 1.** Spinal Cord Anatomy and Intraoperative Photograph With Corresponding Line Drawing of a Complex Meningeal Diverticulum Arising From a Thoracic Nerve Root Sleeve in a 27-Year-Old Woman

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able as well, ranging from a minimal volume of the CSF leak is quite vari-

tional nerve root (FIGURE 1).11,16,20,21 The dural weakness predis-

group of disorders is heterogeneous, but there are no data to support such alternate mechanisms. It has been pos-

which is probably not CSF hypovolemia but rather an altered distribution of craniospinal elasticity due to spinal loss of CSF,41 and “spontaneous spinal CSF leak” is the preferred descriptive term.

Clinical Presentation

Positional Headache. The prototypical manifestation of spontaneous intracranial hypotension is an ortho-

tic fluid leak also have been described in neurofibromatosis type 131,32 and Lehman syndrome.33,34 Finally, some patients with spontaneous intracranial hypotension have a personal or family his-

SPONTANEOUS SPINAL CEREBROSPINAL FLUID LEAKS AND INTRACRANIAL HYPOTENSION

Box 1. Connective Tissue Disorders Associated With Spontaneous Spinal Cerebrospinal Fluid Leaks and Intracranial Hypotension

named Syndromes

Marfan syndrome

Ehlers-Danlos syndrome type II

Autosomal dominant polycystic kidney disease

Unnamed Syndromes/Associations

Isolated skeletal features of Marfan syndrome

Isolated joint hypermobility

Joint hypermobility with fascial thinning

Spontaneous retinal detachment

looked for in a patient suspected of spontaneous intracranial hypotension. Also, unlike CSF rhinorrhea or otor-

A distinct and uncommon cause of spontaneous intracranial hypotension not associated with a primary dural de-

Before precise imaging was able to detect the underlying spinal CSF leak, some authors speculated that spontaneous intracranial hypotension resulted from decreased CSF secretion or generalized CSF hyperabsorption, but there are no data to support such alternate mechanisms. It has been pos-

The precise cause of spontaneous spinal CSF leaks remains largely unknown, but an underlying structural weakness of the spinal meninges generally is suspected.13 A history of a more or less trivial traumatic event preceding the onset of symptoms can be elicited in about one third of patients, suggesting a role for mechanical factors as well.11,18,19 The dural weakness predis-

The prototypi-

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occipital regions. The headache may be throbbing or nonth throbbing and is rarely unilateral. Some patients use descriptive terms for their headaches, such as the feeling of "an ice cube in an empty glass" or a "pulling sensation from my head down to my neck," offering a clue to the diagnosis. Additional clues may be the patient’s recumbent position in the physician's office or a pillow they carry along to allow them to lie down comfortably. The initial onset of headache generally is gradual or subacute, reaching maximal intensity in several minutes to hours, but it may be instantaneous. Patients with such a "thunderclap" headache often will be suspected of having a subarachnoid hemorrhage and may undergo invasive testing, such as cerebral angiography. The severity of the headache varies widely; many mild cases probably remain undiagnosed, whereas other patients are incapacitated and unable to engage in any useful activity while upright.

The headache is a direct result of the downward displacement of the brain due to loss of CSF buoyancy, causing traction on pain-sensitive structures, particularly the dura. An alternative mechanism involves compensatory dilation of the pain-sensitive intracranial venous structures.

It should be noted that not all orthostatic headaches are caused by spontaneous spinal CSF leaks, and other diagnoses should be considered.44-45

Other Headache Patterns. Although a postural headache is the clinical hallmark of spontaneous intracranial hypotension, it is well known that the posture-related component often, but not invariably, becomes less prominent or even disappears over time when the underlying spinal CSF leak remains untreated.11 Rarely, the reverse occurs with a nonpositional headache preceding a typical orthostatic headache. Some patients have no posture-related component to their headache from the onset, while others report exertional headaches, headaches that mainly occur at the end of the day, or even paradoxical headaches that worsen when lying down.49,50 Intermittent headaches, presumably caused by intermittent spinal CSF leaks, may occur at intervals of weeks, months, or even years. Finally, some patients deny having any headache, usually when other symptoms of spontaneous intracranial hypotension predominate the clinical picture.

Because of the wide variety of headache patterns, magnetic resonance imaging (MRI) should be considered for all patients with unexplained headaches, presumably caused by unexplained spinal CSF leaks, to evaluate for spontaneous intracranial hypotension. A differential diagnosis of headache due to spontaneous intracranial hypotension is provided in the TABLE.

Miscellaneous Symptoms. In addition to headaches, a wide variety of other symptoms have been reported in spontaneous intracranial hypotension. Posterior neck pain or stiffness, nausea, and vomiting are the most common, being reported by approximately 50% of patients, and suggest meningeal irritation, particularly when photophobia or phonophobia also is present.11,12 The next most common symptom is a change in hearing, which may be described as "echoing" or as "being underwater" and may be associated with tinnitus or a disturbed sense of balance. These symptoms may be explained by direct transmission of the abnormal CSF pressure to that in the perilymph.31 Alternatively, downward displacement of the brain may cause stretching of the eighth nerve complex (cochlear and vestibular nerves). This latter mechanism may also explain other manifestations of spontaneous intracranial hypotension, such as visual blurring or visual field defects (optic nerve or chiasm), diplopia (abducens or, rarely, trochlear and oculomotor nerves), facial numbness or pain (trigeminal nerve), facial weakness or spasm (facial nerve), and dysgeusia (chorda tympani or glossopharyngeal nerve).31,12,32-35 Distortion of the pituitary stalk has been implicated as a cause of hyperprolactinemia and galactorrhea associated with spontaneous intracranial hypotension.56 Severe displacement of the brain may even result in a decreased level of consciousness due to diencephalic herniation. Although uncommon, numerous well-documented cases have now been reported from around the world, and spontaneous intracranial hypotension should be considered in the differential diagnosis of stupor and coma, par-

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**Box 2. Diagnostic Criteria for Headache Due to Spontaneous Spinal CSF Leak and Intracranial Hypotension According to the International Classification of Headache Disorders, 2nd Ed**42

- **A.** Diffuse and/or dull headache that worsens within 15 minutes after sitting or standing, fulfilling criterion D and with ≥1 of the following:
  1. Neck stiffness
  2. Tinnitus
  3. Hypacusia
  4. Photophobia
  5. Nausea

- **B.** At least 1 of the following:
  1. Evidence of low CSF pressure on MRI (eg, pachymeningeal enhancement)
  2. Evidence of CSF leakage on conventional myelography, CT myelography, or cisternography
  3. CSF opening pressure <60 mm H2O in sitting position
  4. No history of dural puncture or other cause of CSF fistula
  5. Headache resolves within 72 hours after epidural blood patching

Abbreviations: CSF, cerebrospinal fluid; CT, computed tomography; MRI, magnetic resonance imaging.
particularly in otherwise healthy young and middle-aged adults.67-62 Other rare manifestations of spontaneous intracranial hypotension include parkinsonism, ataxia, and cerebellar hemorrhage.50,63 Dementia is a rare complication of spontaneous intracranial hypotension, but subtle cognitive deficits are not rare and often are not recognized until cognition improves following successful treatment of the spinal CSF leak. Spinal manifestations include interscapular pain or, rarely, local back pain at the site of the CSF leak; quadriplegia; and radicular symptoms due to stretching of cervical spinal nerve roots or dilation of the epidural venous plexus.

**Diagnosis**

Cranial MRI. Magnetic resonance imaging has revolutionized the understanding of spontaneous intracranial hypotension and has greatly facilitated the ability to arrive at the diagnosis with confidence without having to resort to invasive procedures, such as spinal puncture or intracranial pressure monitoring. Recognition of the MRI features probably is the most important factor responsible for the ever-increasing number of patients diagnosed with spontaneous intracranial hypotension since the early 1990s. On the other hand, an incomplete understanding of the variability of MRI findings has resulted in the diagnosis of spontaneous intracranial hypotension being erroneously excluded in patients with normal findings.

The 5 characteristic imaging features of spontaneous intracranial hypotension visible on MRI are (1) subdural fluid collections, (2) enhancement of the pachymeninges, (3) engorgement of venous structures, (4) pituitary hyperemia, and (5) sagging of the brain (mnemonic: SEEPS) (FIGURE 2).

A relationship between subdural hematomas and intracranial hypotension has long been debated in the literature, and accumulation of subdural fluid was the first recognized imaging feature of spontaneous intracranial hypotension.65-71 Subdural fluid collections are common in spontaneous intracranial hypotension, occurring in approximately 50% of patients.71 Most of these subdural fluid collections represent hygromas and are thin, bilateral, located over the cerebral convexities, and do not cause any appreciable mass effect. They may also be seen in the posterior fossa, particularly over

**Table.** Differential Diagnosis of Headache Due to Spontaneous Spinal Cerebrospinal Fluid Leak and Intracranial Hypotension*

<table>
<thead>
<tr>
<th>Headache Disorder</th>
<th>Typical Age at Onset, y</th>
<th>Female-Male Ratio</th>
<th>Connective Tissue Disorders†</th>
<th>Headache Features</th>
<th>Thunderclap Headache</th>
<th>Associated Features</th>
<th>Confirmatory Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
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<tr>
<td>New daily persistent headache</td>
<td>15-50 (Mean, 35)</td>
<td>2:1</td>
<td>No</td>
<td>Bilateral more common than unilateral Migraine or tension-type dominant</td>
<td>No</td>
<td>Nausea, fatigue, preceding viral illness</td>
<td>None</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Spontaneous intracranial</td>
<td>20-60 (Mean, 40)</td>
<td>2:1</td>
<td>Yes</td>
<td>Bilateral much more common than unilateral Improved with recumbency, but variable</td>
<td>Yes</td>
<td>Visual/aural changes, meningismus, cranial nerve dysfunction</td>
<td>MRI, LP, myelogram</td>
</tr>
<tr>
<td>intracranial hypotension</td>
<td></td>
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<tr>
<td>Subarachnoid hemorrhage</td>
<td>&gt;20 (Mean, 50)</td>
<td>1.5:1</td>
<td>Yes</td>
<td>Bilateral more common than unilateral Onset instantaneous in most, but may be gradual</td>
<td>Yes</td>
<td>Meningismus, cranial nerve dysfunction, seizure</td>
<td>CT, LP</td>
</tr>
<tr>
<td>Carotid/vertebral artery dissection</td>
<td>20-70 (Mean, 45)</td>
<td>1:1</td>
<td>Yes</td>
<td>Unilateral much more common than bilateral Often with neck pain</td>
<td>Yes</td>
<td>Horner syndrome, cranial nerve dysfunction, pulsatile tinnitus</td>
<td>Angiography</td>
</tr>
<tr>
<td>Cerebral venous sinus thrombosis</td>
<td>Any age</td>
<td>3:1</td>
<td>No</td>
<td>Bilateral more common than unilateral (but unilateral when headache is only sign)</td>
<td>Yes</td>
<td>Seizure, papilledema, visual changes, cranial nerve dysfunction</td>
<td>MRI/MRV, angiography</td>
</tr>
<tr>
<td>Benign intracranial hypertension</td>
<td>20-40 (Mean, 50)</td>
<td>8:1</td>
<td>No</td>
<td>Bilateral much more common than unilateral Worse in recumbancy</td>
<td>No</td>
<td>Papilledema, visual changes, abducens nerve palsy</td>
<td>LP</td>
</tr>
<tr>
<td>Posttraumatic headache</td>
<td>Any age</td>
<td>1:1</td>
<td>No</td>
<td>Bilateral much more common than unilateral Tension-type, often after mild head injury</td>
<td>No</td>
<td>Dizziness, neuropsychological symptoms</td>
<td>None</td>
</tr>
<tr>
<td>Meningitis</td>
<td>Any age</td>
<td>1:1</td>
<td>No</td>
<td>Bilateral</td>
<td>Yes</td>
<td>Fever, meningismus, systemic illness</td>
<td>LP</td>
</tr>
</tbody>
</table>

Abbreviations: CT, computed tomography; LP, lumbar puncture; MRI, magnetic resonance imaging; MRV, magnetic resonance venography.

*The headache of spontaneous spinal cerebrospinal fluid leak and intracranial hypotension is best considered under the category of new daily persistent headache. Such headaches have an abrupt onset, often within minutes or hours but by definition within 3 days, and are present on most if not all days thereafter, typically in individuals without a prior history of headache. Including autosomal dominant polycystic kidney disease, Ehlers-Danlos syndrome, and Marfan syndrome.
the cerebellar convexities or in the retroclival space. Subdural hematomas with varying degrees of mass effect also are not uncommon in spontaneous intracranial hypotension and are about half as frequent as subdural hygromas (FIGURE 3).71 Fortunately, most of these subdural hematomas can be managed with treatment directed at the underlying spinal CSF leak without the need for craniotomy.71 Only rarely do the subdural hematomas require evacuation, and if the underlying CSF leak is left untreated, the risk of a recurrent subdural hematoma is high.68,69,71

Enhancement of the pachymeninges has become the most well-known imaging abnormality of spontaneous intracranial hypotension. The enhancement is diffuse, nonnodular, involves both supratentorial and infratentorial compartments, and spares the leptomeninges.72,73 Small, thin-walled dilated blood vessels in the subdural zone are the pathological substrate for the enhancement.12 The relation between the enhancement and spontaneous intracranial hypotension has been believed to be so close that the term “syndrome of orthostatic headache and diffuse pachymeningeal gadolinium enhancement” was coined.12 However, up to 20% of patients with spontaneous intracranial hypotension never develop enhancement, or any of the other abnormalities, on MRI.40,74,75

Engorgement of venous structures is most readily detected when it affects the dural venous sinuses or large cerebral veins.76-78 It is rarely the only or the most striking imaging feature of spontaneous hypotension and often is only detectable when pretreatment and posttreatment images are compared.

Pituitary hyperemia is a recently described imaging feature of spontaneous intracranial hypotension.79-82 The pituitary hyperemia may become quite striking and mimic a pituitary tumor or hyperplasia.

Sagging or downward displacement of the brain is a very specific imaging finding of spontaneous intracranial
hypotension and may be accompanied by ventricular collapse.\textsuperscript{6,7} Several features can be identified, such as effacement of perichiasmatic cisterns with bowing of the optic chiasm over the pituitary fossa; effacement of the pre-pontine cistern with flattening of the pons against the clivus; and descent of the cerebellar tonsils, which may mimic a Chiari type 1 malformation. Sagging of the brain in spontaneous intracranial hypotension may be attributed to coexisting subdural fluid collections, but the degree of sagging generally is out of proportion to any mass effect from the subdural fluid collections.

Most of the MRI features of spontaneous intracranial hypotension can be explained as compensatory changes related to the loss of CSF volume. According to the Monroe-Kellie hypothesis, the sum of the volumes of intracranial blood, CSF, and cerebral tissue must remain constant in an intact cranium.\textsuperscript{7} Thus, the loss of CSF from the spine can be compensated for by an increase of the vascular component, accounting for the pachymeningeal enhancement, engorgement of venous structures, and pituitary hyperemia; or by an increase in the intracranial CSF component, accounting for the subdural hygromas. Subdural hematomas may be caused by tearing of bridging veins or rupture of the dilated thin-walled blood vessels in the subdural zone. Sagging of the brain is caused by the loss of CSF buoyancy.

Improvement of abnormalities on MRI can be expected within days to weeks of successful treatment of the CSF leak. Clinical improvement generally precedes that demonstrated on MRI, and in some patients—particularly those who have not received specific treatment for their CSF leak—considerable clinical improvement is shown over time, whereas the MRI abnormalities persist. Small subdural hygromas resolve within days or weeks, but large subdural hematomas may require up to 3 months to resolve.

### Cranial Computed Tomography

Although not as conclusive as MRI, computed tomography may suggest the diagnosis by showing subdural fluid collections or obliteration of subarachnoid cisterns and ventricular collapse.\textsuperscript{66,83,84} Computed tomography can thus be of important diagnostic value, particularly in the emergency department setting.

### Myelography

Myelography with iohexol contrast followed by thin-cut computed tomography of the entire spine (or with gadolinium fol-

### Radionuclide Cisternography

Radionuclide cisternography has been used extensively in the evaluation of spontaneous intracranial hypotension but is of relatively limited usefulness.\textsuperscript{11,86,87} Typical findings include early accumulation of tracer in the kidneys and bladder, slow ascent along the spinal axis, and a paucity of activity over the cerebral convexities. However, the exact site of the CSF leak remains obscure in as many as one third of patients.\textsuperscript{11} Radionuclide cisternography remains useful when the diagnosis of intracranial hypotension is in doubt and myelography results are normal.

### Spinal MRI

In the past, relatively scant attention was given to spinal MRI in the diagnosis of spontaneous intracranial hypotension and may be accompanied by ventricular collapse.\textsuperscript{6,7} Several features can be identified, such as effacement of perichiasmatic cisterns with bowing of the optic chiasm over the pituitary fossa; effacement of the pre-pontine cistern with flattening of the pons against the clivus; and descent of the cerebellar tonsils, which may mimic a Chiari type 1 malformation. Sagging of the brain in spontaneous intracranial hypotension may be attributed to coexisting subdural fluid collections, but the degree of sagging generally is out of proportion to any mass effect from the subdural fluid collections.

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Most of the MRI features of spontaneous intracranial hypotension can be explained as compensatory changes related to the loss of CSF volume. According to the Monroe-Kellie hypothesis, the sum of the volumes of intracranial blood, CSF, and cerebral tissue must remain constant in an intact cranium.\textsuperscript{7} Thus, the loss of CSF from the spine can be compensated for by an increase of the vascular component, accounting for the pachymeningeal enhancement, engorgement of venous structures, and pituitary hyperemia; or by an increase in the intracranial CSF component, accounting for the subdural hygromas. Subdural hematomas may be caused by tearing of bridging veins or rupture of the dilated thin-walled blood vessels in the subdural zone. Sagging of the brain is caused by the loss of CSF buoyancy.

Improvement of abnormalities on MRI can be expected within days to weeks of successful treatment of the CSF leak. Clinical improvement generally precedes that demonstrated on MRI, and in some patients—particularly those who have not received specific treatment for their CSF leak—considerable clinical improvement is shown over time, whereas the MRI abnormalities persist. Small subdural hygromas resolve within days or weeks, but large subdural hematomas may require up to 3 months to resolve.

### Cranial Computed Tomography

Although not as conclusive as MRI, computed tomography may suggest the diagnosis by showing subdural fluid collections or obliteration of subarachnoid cisterns and ventricular collapse.\textsuperscript{66,83,84} Computed tomography can thus be of important diagnostic value, particularly in the emergency department setting.

### Myelography

Myelography with iohexol contrast followed by thin-cut computed tomography of the entire spine (or with gadolinium fol-

### Radionuclide Cisternography

Radionuclide cisternography has been used extensively in the evaluation of spontaneous intracranial hypotension but is of relatively limited usefulness.\textsuperscript{11,86,87} Typical findings include early accumulation of tracer in the kidneys and bladder, slow ascent along the spinal axis, and a paucity of activity over the cerebral convexities. However, the exact site of the CSF leak remains obscure in as many as one third of patients.\textsuperscript{11} Radionuclide cisternography remains useful when the diagnosis of intracranial hypotension is in doubt and myelography results are normal.

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intracranial hypotension, mainly because it is not particularly effective in localizing the CSF leak. However, numerous spinal manifestations of spontaneous intracranial hypotension have now been described, such as dilated epidural or intradural veins, dural enhancement, meningeal diverticula, extrathecal CSF collections, syringomyelia, and retrospinal C1-C2 fluid collections.88-94

Lumbar Puncture. Typically, CSF opening pressure is less than 60 mm H2O (reference range, 65-195 mm H2O) and can be unmeasurable or even negative.9 However, some patients have consistently normal CSF opening pressures.11 Examination of CSF often demonstrates abnormal results, showing a primarily lymphocytic pleocytosis (up to 200 cells/mm³), an elevated protein content (up to 1000 mg/dL), or xanthochromia that is probably due to increased permeability of dilated meningeal blood vessels and a decrease of CSF flow in the lumbar subarachnoid space.

Treatment and Outcome
Although data are lacking, it is often stated that many cases of spontaneous intracranial hypotension resolve spontaneously without any specific therapy. Fortunately, several options are avail-

Figure 4. Postmyelography Computed Tomography Scans—Demonstration of Spinal Cerebrospinal Fluid (CSF) Leaks


Figure 5. Postmyelography Computed Tomography Scans—Results of Treatment

able to treat patients with spontaneous intracranial hypotension who seek medical attention (FIGURE 5). However, none of the treatments have been evaluated by randomized clinical trials. A purely conservative approach consists of bed rest, oral hydration, a generous caffeine intake, and use of an abdominal binder. Given enough time, this treatment is probably effective in many patients. However, symptoms may be debilitating, and more timely results may be desired. Administration of steroids, intravenous caffeine, or theophylline all have been advocated as specific treatments for spontaneous intracranial hypotension, but their effectiveness is limited.

The mainstay of treatment is the injection of autologous blood into the spinal epidural space, the so-called epidural blood patch.95,96 Relief of symptoms often is instantaneous, thereby also serving a diagnostic purpose, and this is likely due to replacement of lost CSF volume with blood volume within the spinal canal. Initially, about 10 to 20 mL of blood is used, and this is effective in relieving symptoms in about one third of patients, presumably by forming a dural tamponade, thereby sealing the leak. Another mechanism of action may be restriction of CSF flow within the spinal epidural space, thereby interfering with CSF absorption. If the epidural blood patch is unsuccessful it can be repeated, and consideration should be given to a large-volume (20-100 mL) epidural blood patch. Given the potentially high volume of injected blood, a minimum of 5 days between blood patches is advised. The volume of blood that can be injected is mainly limited by local back pain or the development of radiculopathy. I prefer to place the blood patch at 2 separate sites, first at the thoracolumbar junction and then in the lower lumbar area, after which the patient is placed in the Trendelenburg position, either supine, prone, and/or lateral for 30 to 60 minutes, depending on the location of the CSF leak. This allows blood to travel over many spinal segments toward the site of the leak.

If epidural blood patches fail to provide relief, a directed epidural blood patch or percutaneous placement of fibrin sealant is recommended. These therapies require that the exact site of the CSF leak be known, and placement of fibrin sealant probably provides the best chance of alleviating symptoms. In my experience, about one third of patients for whom epidural blood patching has not been effective experience relief with the percutaneous placement of fibrin sealant, thereby avoiding surgery.97

Surgical treatment is reserved for those patients in whom these nonsurgical measures have failed. Surgical repair of CSF leak is safe and often succeeds in providing relief for those patients in whom a structural abnormality or focal CSF leak is identified.16,20,21 Leaking meningeal diverticula can be ligated with suture or a metal aneurysm clip, while dural rents, holes, or other defects are repaired either directly with suture or, more commonly, by placement of a muscle pledget along with gelfoam and fibrin sealant. Rarely, intradural exploration may be required.

Intrathecal infusion of saline or artificial CSF should not be expected to seal a CSF leak but may be required as an effective temporizing measure to restore CSF volume until the leak can be permanently repaired in patients who require urgent treatment, such as those with a decreased level of consciousness.98-99 A recurrence of headache following successful treatment of spontaneous intracranial hypotension may indicate a recurrent CSF leak,98 but if the pattern of headache has changed, rebound transient intracranial hypertension11 or dural venous sinus thrombosis99 should be considered.

Data on long-term outcomes are scarce, but in my experience, recurrence of a spinal CSF leak is seen in approximately 10% of patients, regardless of treatment. Outcome studies have shown that patients with abnormal brain MRI findings and a focal spinal CSF leak have an excellent prognosis, while those with normal initial MRI findings and a diffuse multilevel spinal CSF leak have a poor prognosis.100 Some patients have persistent symptoms following treatment, in spite of documented resolution of CSF leakage. Such patients may have residual altered CSF dynamics or small residual CSF leaks below the level of detection of current imaging techniques.

Author Contributions: Dr Schievink had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; administrative, technical, or material support; study supervision: Schievink.

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