Spontaneous Spinal Cerebrospinal Fluid Leaks and Intracranial Hypotension

Wouter I. Schievink, MD

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.1 The spontaneous form of intracranial hypotension was first described in 1938,2 and much has been learned about this syndrome, particularly since the early 1990s,3-15 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.1

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 re-

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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 monitored.

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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
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 otorrhea, there is no risk of meningitis because the CSF is directly absorbed into the sterile spinal epidural venous plexus or paraspinal soft tissues and is therefore not exposed to the external milieu.

The precise cause of spontaneous spinal CSF leaks remains largely unknown, but an underlying structural weakness of the spinal meninges generally is suspected. 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. The dural weakness predisposes to the formation of dural defects that allow CSF to leak into the epidural space. A wide variety of dural defects may be observed at the time of surgery, ranging from simple dural holes or rents to complex fragile meningeal diverticula or even complete absence of the dura that normally covers the spinal nerve root (Figure 1).

The volume of the CSF leak is quite variable as well, ranging from a minimal amount of seeping CSF only detectable when applying a Valsalva maneuver to large amounts of CSF spontaneously pouring out into the paraspinal soft tissues.

There is good evidence to suggest that a generalized connective tissue disorder plays a crucial role in the development of spontaneous spinal CSF leaks. First reported in 1994, this association has been confirmed by numerous subsequent studies. This group of disorders is heterogeneous, possibly affecting different components of the dural extracellular matrix (Box 1). Isolated joint hypermobility is found in approximately two fifths of patients with spontaneous intracranial hypotension and may be associated with attenuation of the dorsal muscular fascia, complicating surgical wound closure. Approximately one fifth of patients with spontaneous intracranial hypotension have subtle skeletal manifestations of Marfan syndrome, such as tall stature, arachnodactyly, highly arched palate, and joint hypermobility, but none of the other stigmata of the syndrome. These patients do not harbor mutations in the Marfan syndrome gene (FBN1) encoding fibrillin 1, but a defect of microfibrils, important components of the extracellular matrix associated with fibrillin, has been demonstrated. Less frequently, spontaneous intracranial hypotension occurs in well-characterized, generalized connective tissue disorders such as Marfan syndrome, Ehlers-Danlos syndrome type II, and autosomal dominant polycystic kidney disease. Spinal meningeal diverticula also have been described in neurofibromatosis type 1 and Lehmam syndrome. Finally, some patients with spontaneous intracranial hypotension have a personal or family history of spontaneous retinal detachment at an early age, suggesting the presence of a generalized connective tissue disorder affecting both dura and retina.

A distinct and uncommon cause of spontaneous intracranial hypotension not associated with a primary dural defect is the presence of osseous spinal pathology. A congenital osseous spur, as well as acquired degenerative disk disease piercing the dura, has been described.

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 postulated that a decrease in CSF volume, rather than in CSF pressure, may be the final common pathway in the pathophysiology of spontaneous intracranial hypotension. Therefore, “spontaneous CSF hypovolemia” has been introduced as an alternative term. However, this is an oversimplification. For example, loss of CSF volume also occurs with spontaneous CSF rhinorrhea or otorrhea, but the typical imaging and clinical features of spontaneous intracranial hypotension rarely, if ever, occur under those circumstances. The final common pathway is probably not CSF hypovolemia but rather an altered distribution of craniospinal elasticity due to spinal loss of CSF, and “spontaneous spinal CSF leak” is the preferred descriptive term.

**Clinical Presentation**

Positional Headache. The prototypic manifestation of spontaneous intracranial hypotension is an orthostatic headache. Such a headache generally occurs or worsens within 15 minutes of assuming the upright position, as reflected by the revised International Classification of Headache Disorders criteria (Box 2). But in some patients this lag period may be as long as several hours. Improvement of the headache after lying down is less variable and occurs within 15 to 30 minutes. The headache may be diffuse or localized to the frontal, temporal, or—most commonly—the occipital or sub-
occipital regions. The headache may be throbbing or nonthrobbing 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.

**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. 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. 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 headache 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. 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. 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). Distortion of the pituitary stalk has been implicated as a cause of hyperprolactinemia and galactorrhea associated with spontaneous intracranial hypotension. 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-
particularly in otherwise healthy young and middle-aged adults.\textsuperscript{37-62} Other rare manifestations of spontaneous intracranial hypotension include parkinsonism, ataxia, and cerebellar hemorrhage.\textsuperscript{50,63} Dementia is a rare complication of spontaneous intracranial hypotension,\textsuperscript{64} 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 intercapsular 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 dilatation 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.\textsuperscript{65-71} Subdural fluid collections are common in spontaneous intracranial hypotension, occurring in approximately 50% of patients.\textsuperscript{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

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**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>Primary</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New daily persistent headache</td>
<td>15-50</td>
<td>2:1</td>
<td>No</td>
<td>Bilateral more common than unilateral</td>
<td>No</td>
<td>Nausea, fatigue, preceding viral illness</td>
<td>None</td>
</tr>
<tr>
<td>Secondary</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous intracranial hypotension</td>
<td>20-60</td>
<td>2:1</td>
<td>Yes</td>
<td>Bilateral much more common than unilateral</td>
<td>Yes</td>
<td>Visual/aural changes, meningismus, cranial nerve dysfunction</td>
<td>MRI, LP, myelogram</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td>≥20</td>
<td>1.5:1</td>
<td>Yes</td>
<td>Bilateral more common than unilateral</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</td>
<td>1:1</td>
<td>Yes</td>
<td>Unilateral more common than bilateral</td>
<td>Yes</td>
<td>Homer 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 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</td>
<td>8:1</td>
<td>No</td>
<td>Bilateral much more common than unilateral</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 more common than unilateral</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).\textsuperscript{71} Fortunately, most of these subdural hematomas can be managed with treatment directed at the underlying spinal CSF leak without the need for craniotomy.\textsuperscript{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.\textsuperscript{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.\textsuperscript{72,73} Small, thin-walled dilated blood vessels in the subdural zone are the pathological substrate for the enhancement.\textsuperscript{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.\textsuperscript{12} However, up to 20% of patients with spontaneous intracranial hypotension never develop enhancement, or any of the other abnormalities, on MRI.\textsuperscript{40,74,75}

Engorgement of venous structures is most readily detected when it affects the dural venous sinuses or large cerebral veins.\textsuperscript{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.\textsuperscript{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.

![Figure 2. Pretreatment and Posttreatment Magnetic Resonance Imaging](https://jama.jamanetwork.com/fullarticle/2291)
bral tissue must remain constant in
of intracranial blood, CSF, and cere-
pothesis, the sum of the volumes
According to the Monroe-Kellie hy-
be explained as compensatory changes
collections.
mass effect from the subdural fluid
generally is out of proportion to any
collections, but the degree of sagging
attributed to coexisting subdural fluid
intracranial hypotension may be
Sagging of the brain in spontaneous
mimic a Chiari type 1 malformation.
the cerebellar tonsils, which may
pons against the clivus; and descent of
sagging caused by the loss of CSF
vessels in the subdural zone. Sagging
rupture of the dilated thin-walled blood
mas. 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 gen-
erally precedes that demonstrated on
MRI, and in some patients—particu-
larly those who have not received spe-
cific treatment for their CSF leak—
considerable clinical improvement is
shown over time, whereas the MRI ab-
normalities persist. Small subdural hy-
gromas resolve within days or weeks,
but large subdural hematomas may re-
main mild. Aggrava-
tion of symptoms is reported by only
approximately 5% of patients and is
generally mild.

Radionuclide Cisternography. Ra-
dionuclide cisternography has been
used extensively in the evaluation of
spontaneous intracranial hypotension
but is of relatively limited useful-
ness. Typical findings include early
accumulation of tracer in the kidneys
and bladder, slow ascent along the spi-
nal axis, and a paucity of activity over
the cerebral convexities. However, the
exact site of the CSF leak remains ob-
scure in as many as one third of pa-
tients. Radionuclide cisternography re-
mains 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
hypothesis and may be accompanied
by ventricular collapse. Several fea-
tures can be identified, such as efface-
ment 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.

Most of the MRI features of sponta-
neous intracranial hypotension can be
explained as compensatory changes
related to the loss of CSF volume.
According to the Monroe-Kellie hy-
pothesis, the sum of the volumes of intracranial blood, CSF; and cere-
bral tissue must remain constant in
an intact cranium. Thus, the loss of
CSF from the spine can be compen-
sated for by an increase of the vascular
component, accounting for the pachy-
meningeal enhancement, engorge-
ment of venous structures, and pitu-
itary hyperemia; or by an increase in
the intracranial CSF component,
accounting for the subdural hygro-
mas. Subdural hematomas may be
cased 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 gen-
erally precedes that demonstrated on
MRI, and in some patients—particu-
larly those who have not received spe-
cific treatment for their CSF leak—
considerable clinical improvement is
shown over time, whereas the MRI ab-
normalities persist. Small subdural hy-
gromas resolve within days or weeks,
but large subdural hematomas may re-
quire up to 3 months to resolve.

Cranial Computed Tomography. Al-
though not as conclusive as MRI, com-
puted tomography may suggest the di-
agnosis by showing subdural fluid
collections or obliteration of subarach-
noid cisterns and ventricular col-
lapse. Computed tomography can
thus be of important diagnostic value,
particularly in the emergency depart-
ment setting.

Myelography. Myelography with
iodinated contrast followed by thin-
cut computed tomography of the
entire spine (or with gadolinium fol-
lowed by MRI) has been shown to be
the study of choice to accurately
define the location and extent of a CSF
leak (FIGURE 4). The leak may vary
from a small amount of contrast
tracking along a single nerve root to
 extensive bilateral collections of con-
trast within the paraspinal soft tis-
ues. Single or multiple meningeal
diverticula may be demonstrated, but
they are frequently below the level of
detection of myelography and not
uncovered until the time of surgery.
The majority of CSF leaks are found
at the cervicothoracic junction or
along the thoracic spine. Frequently,
multiple simultaneous CSF leaks are
demonstrated. Retrospinal collec-
tions of contrast at C1-C2 should not
be mistaken for the actual site of the
CSF leak. Delayed imaging may be
required to visualize slow or inter-
mittent leaks, and ultra-early (ie,
immediately following injection of
contrast) computed tomography may
be required to identify the site of
rapid high-volume leaks.

The fear of cerebral herniation caused
by performing a myelogram is entirely
theoretical and has never been docu-
mented. Not only is the dural hole made
by the lumbar puncture relatively small,
but CSF pressure is already low. Aggra-
vation of symptoms is reported by only
approximately 5% of patients and is
generally mild.

Radionuclide Cisternography. Ra-
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used extensively in the evaluation of
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but is of relatively limited useful-
ness. Typical findings include early
accumulation of tracer in the kidneys
and bladder, slow ascent along the spi-

FIGURE 3. Axial T2-Weighted Magnetic Resonance Image in a 39-Year-Old Man

A. Imaging shows subdural hygromas (arrowheads). B. The patient’s spinal cerebrospinal fluid leaks were left untreated and bilateral subdural hematomas developed (arrowheads).

2292 JAMA, May 17, 2006—Vol 295, No. 19 (Reprinted) ©2006 American Medical Association. All rights reserved.
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-
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 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, or/and 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 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 pledge 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.39,62 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 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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The universe is full of magical things patiently waiting for our wits to grow sharper.
—Eden Phillpots (1862-1960)