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Review

Hydrodynamic herniation: Pathophysiology of brain, spinal cord and nerve displacements associated with leakage or diversion of cerebrospinal fluid

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ABSTRACT

Leakage or diversion of cerebrospinal fluid (CSF) is associated with a variety of displacements of nervous tissue that may affect the brain, spinal cord and nerve roots. The displacements may be classified by the site of the leak - spinal canal or cranial cavity - and by whether the displacements are global, affecting wide regions of the nervous system, or local, affecting only nervous tissue adjacent to the leak. We propose a common pathophysiology for these displacements. A leak or a shunt results in an abnormal spatial pattern of CSF flow governed by abnormally directed hydrodynamic forces that act upon the submerged nervous tissue to propel it towards the site of the leak or the orifices of the shunt. We argue that the hydrodynamic mechanism causing displacement is distinct from the physical mechanisms responsible for other frequent manifestations of CSF leak, such as orthostatic headache, low recumbent CSF pressure, and dilation of dural veins. The existence of distinct mechanisms allows understanding of how the effects of CSF loss may differ in patients with spinal CSF leak and patients with ventricular shunts. It clarifies many variant cases where some of the characteristic manifestations of CSF leak may be absent. We discuss the roles of abnormal hydrodynamic forces in the variety of presentations subsumed under the term "slit ventricle syndrome" and consider the therapeutic implications of the proposed pathophysiological mechanism.

KEYWORDS: spinal CSF leak, cranial CSF leak, CSF shunts, brain herniation, slit ventricles, spinal cord herniation, encephalocele, transient radicular irritation syndrome, orthostatic headache, CSF hypotension

INTRODUCTION

Herniations of the brain caused by mass lesions in the context of increased intracranial pressure are well known to the neurologist and neurosurgeon. For example, herniation of the cerebellar tonsils through the foramen magnum [1] and uncal herniation through the incisura of the tentorium cerebelli [2] were both described early in the twentieth century. Less widely appreciated are displacements and herniations of nervous system tissue associated with leakage of cerebrospinal fluid (CSF), which occur in the context of low or normal intracranial pressure. In the present paper we will first classify these herniations and review the clinical settings in which they occur. We will then discuss the physical principles governing these displacements, which we call "hydrodynamic herniation" because they are the result of hydrodynamic forces associated with the abnormal flow patterns of CSF. Finally, we shall discuss the utility of the proposed pathogenesis including therapeutic implications.

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1. Classification

Herniations associated with CSF leakage or diversion may be classified according to the site of the leakage and according to whether the displacement or herniation of tissue is global or local. The site of the leak may be either the spinal canal or the cranial cavity. Global displacements involve widespread regions of the central nervous system (CNS) at a considerable distance from the site of leakage, whereas local herniations involve only tissue immediately adjacent to a dural defect where CSF is leaking. Each of these four types of herniation has a distinctive morphology and occurs in a distinctive clinical setting.

1.1. Global CNS displacement in spinal CSF leak

Global displacement of the brain in patients with a spinal CSF leak has a characteristic pattern [3]. The cerebral hemispheres and diencephalon are displaced caudally, and the basal subarachnoid cisterns are reduced or effaced. There is crowding of the posterior fossa; the belly of the pons abuts the clivus, effacing the prepontine cistern, and the cerebellar tonsils may herniate through the foramen magnum.

The displacement often occurs in the context of an acute syndrome that has its onset within a day or two of an event that disrupts the spinal dura. That event may be trauma, such as a fall on the buttocks [4]. The trauma may be iatrogenic, such as a diagnostic lumbar puncture [5, 6], a myelogram [7], spinal [8] or epidural [9] anesthesia, or spinal surgery. Spinal CSF leaks may also occur spontaneously [10-13]. Many of the “spontaneous” leaks may be caused by unrecognized mild trauma, precipitated by activities such as rapidly rising from bending forward, vigorous physical exertion, coughing, or straining [14]. Individuals with connective tissue disorders such as Marfan syndrome may have a weakened dura and be predisposed to injury from such minor trauma [14, 15].

The acute syndrome associated with spinal CSF leak has been extensively and recently reviewed [15, 16], and we will discuss only those aspects that bear on the pathophysiology of the brain displacement. The most characteristic and salient symptom is orthostatic headache. Usually, the opening CSF pressure on lumbar puncture is low; occasionally it is in the normal range. MRI of the brain typically shows smooth, non-nodular dural thickening and contrast enhancement [17, 18], often associated with underlying subdural collections that usually do not exert pressure on the cortical surface [19]. MRI of the spine typically shows a shrunken dural sac and an expanded extradural space, reflecting loss of CSF from the subarachnoid space into the epidural space. Dilated veins may be present at the anterolateral margins of the epidural space. The use of imaging, including radionucleide [7, 20], CT [21, 22] and MRI [23, 24] cisternography, to locate the site of the spinal CSF leak has been discussed elsewhere.

Treatment is directed to closure of the leak and is generally staged. Conservative measures include bed rest, oral hydration, caffeine, and an abdominal binder. If these fail, or if the situation is deemed more urgent, epidural blood patch (EBP) [25, 26] or epidural saline infusion [27, 28] is usually effective. Several attempts may be required, and a targeted EBP at the level of a localized leak may be more effective than an EBP far from the leak [29]. Injection of fibrin sealant at the site of the leak has also been successful after multiple EBPs have failed [30-32]. Surgery is reserved for intractable cases when the site of the leak can be identified.

Although orthostatic headache and low CSF pressure are common to all of the events causing spinal CSF leak, brain descent is frequent in cases of spontaneous spinal CSF leak [3], but is much less common in patients with acute trauma, whether external or iatrogenic. Brain descent also occurs in patients with chronic spinal intrathecal catheters [33-35]. These catheters divert CSF from the spinal subarachnoid space to another compartment of the body, which can be viewed as an intentional “leak” of spinal CSF. As patients with trauma generally come to medical attention sooner than those whose leaks are spontaneous or associated with intrathecal catheters, it appears that brain displacement typically takes more time to develop than orthostatic headache and other manifestations of the acute syndrome.

Focal symptoms related to displacement of the cerebrum, diencephalon and upper brainstem may be absent, or the patient may present with dementia [36, 37], chronic apathy with stereotyped behaviors

[38], subacute encephalopathy [39-41], or acute encephalopathy with or without pupillary asymmetry and extensor posturing [42, 43]. Focal symptoms related to caudal displacement of the brainstem and herniation of the cerebellar tonsils at the foramen magnum may also be absent, or the patient may present with suboccipital headache aggravated by Valsalva - which often replaces or augments the originally orthostatic headache - neck stiffness, gait ataxia, nausea and vomiting, bulbar dysfunction, and cardio-respiratory compromise [3, 44]. Like other conditions obstructing CSF flow at the foramen magnum [45], cerebellar herniation may result in syringomyelia that resolves with treatment [46-49]. Brain descent may also be associated with upper and lower cranial nerve palsies, a sixth nerve palsy being the most frequent of these [50].

Although we focus in this paper on acquired postnatal brain herniations, the presence of cerebellar and caudal brainstem herniation at birth in association with spinal meningomyelocele - the Chiari II malformation - is also relevant. A meningomyelocele can be viewed as an extreme CSF “leak” from the spinal subarachnoid space into the amniotic fluid, through which the majority of CSF drainage in the affected fetus occurs. Marked improvement or resolution of the hindbrain herniation after *in utero* surgical closure of the meningomyelocele has been reported [51-54].

1.2. Local herniations in spinal CSF leak

The spinal cord or a spinal nerve root may herniate through an adjacent defect in the spinal dura that is associated with a CSF leak. Such local herniations are much less frequent than the global displacements described above. Herniation of the spinal cord has been described in patients undergoing surgery on the cervical spine for myelopathy due to cervical spondylosis, intradural tumor, or spinal cord injury, in which the dura is opened but is incompletely closed. Herniation of a cauda equina nerve root has been described in patients undergoing lumbar laminectomy in which dural injury inadvertently occurs and is not repaired with a watertight closure. At a variable time after surgery, ranging from the immediate post-operative period [55, 56] to months [57, 58] or even years [59-61], progressive myelopathy or radiculopathy develops. In the few patients reported to date sensory symptoms appear to predominate. Imaging may reveal a fluid-filled extradural cyst posterior to the site of the initial surgery. At re-operation there is an opening in the ventral aspect of the cyst overlying the disrupted posterior dura that allows the fluid of the cyst to communicate with the spinal subarachnoid space (pseudomeningocele). The spinal cord or nerve root is herniated through this defect and is usually tethered to the wall of the defect by fibrous adhesions. Symptoms generally disappear after the spinal cord or nerve root is surgically restored to the subarachnoid space and the dural defect is repaired. Herniation of the spinal cord into a dural defect has also been reported in cases of spontaneous spinal CSF leak [62, 63]. These cases typically occur in the thoracic spine, and the dural defects are ventral. Patients usually present with progressive myelopathy, frequently a hemicord syndrome. Based on a review of imaging [64], it has been suggested that spinal CSF leak caused by injury to the ventral dura from osteophytes or herniated discs accounts for most cases of idiopathic thoracic spinal cord herniation [65, 66].

1.3. Local herniation in cranial CSF leak

Leaks from the intracranial CSF space occur most commonly at the base of the skull through defects in the bone and the adjacent dura. In some cases the brain herniates through the opening to form an encephalocele. Leaks in the anteromedial skull base may be associated with encephaloceles in the frontal sinus through defects in its posterior wall [67, 68]; in the sphenoid sinus, usually through defects in a lateral wall [69]; in the ethmoid sinuses from defects between the frontal and ethmoid bones [70]; and intranasally from defects in the cribriform plate. More posterior and lateral in the skull base, defects in the petrous portion of the temporal bone may be associated with herniation of a portion of the inferior temporal lobe, usually into the middle ear [71-74].

The events causing CSF leaks at the anteromedial skull base may be external trauma, a post-operative complication, or congenital bony defects. The leak may also occur spontaneously. The congenital and spontaneous types are often subclassified into those with pre-existing elevated

intracranial pressure and those with normal pressure. Originally, the group with elevated pressure was thought to consist primarily of patients with either intracranial tumors or hydrocephalus [75]. Recent clinical, epidemiological and radiographic evidence suggests that many "spontaneous" cases occur in patients with pre-existing pseudotumor cerebri, in whom the elevated CSF pressure erodes the thin bone at the roof of the ethmoid and the wall of the sella turcica [76, 77]. Leakage in the posterolateral skull base may also be a post-surgical complication, the result of external trauma, or due to congenital bony defects. In addition, it may occur as the result of bony erosion from either inflammatory disease or tumor [78, 79].

The clinical presentation of CSF leak from the skull base varies with the location of the leak. Leaks from the anterior portion of the skull base present most commonly as rhinorrhea but can also present with, or be complicated by recurrent meningitis. Headache may also occur but is generally not orthostatic and may be relieved by the nasal discharge of CSF. A level of 30 mg/100 cc or more of glucose and the presence of beta-2 transferrin in the nasal discharge confirm that it is CSF. Leaks from the posterolateral skull base into the middle ear typically present with conductive hearing loss, rhinorrhea from drainage through the Eustachian tube into the nose, and either middle ear effusion if the tympanic membrane is intact or otorrhea if either the eardrum is breached or the leak is directly into the external auditory canal. Recurrent meningitis and temporal lobe abscess may develop as life-threatening complications. The use of nasoendoscopy [80, 81] and of high-definition CT [82] to locate the site of leakage and the roles of CT and MR cisternography [83] have been reviewed elsewhere.

Treatment of intracranial CSF leaks depends on their etiology. Most traumatic leaks will cease within a few weeks with conservative measures such as restricted nose blowing, avoidance of straining, bed rest with the head elevated, and use of antitussives, antiemetics and stool softeners. Surgery is required for leaks that persist, including the majority of spontaneous, congenital and post-surgical cases. Surgical approaches to skull base CSF leak are discussed elsewhere and are beyond the scope of this paper [78, 80, 84-88].

Encephaloceles associated with CSF leaks at the skull base are generally asymptomatic. They tend to occur more commonly in the chronic, non-traumatic cases, again suggesting that the forces causing herniation are generally small and require time to effect the brain displacement. An encephalocele may be detected on MRI with contrast, which shows a non-enhancing mass that is isodense to brain, distinguishing the encephalocele from mucocele, tumor, and other masses in the paranasal sinuses and nasal cavity, and from cholesteatoma and other soft tissue masses in the middle ear.

1.4. Global CNS displacement in cranial CSF diversion

Diversion of CSF from the cranial cavity to an extracranial tissue compartment, most often a ventriculo-peritoneal shunt for hydrocephalus, can be viewed as a planned, i.e., intentional, cranial CSF "leak". A wide variety of acquired malformations due to displacements of skull and brain have been reported in patients with chronically indwelling ventricular shunts [89-93]. In infants shunted prior to the closure of the skull sutures, deposition of bone or cartilage in the skull sutures limits expansion of the skull, resulting in craniostenosis that takes the form of dolichocephaly, or, more rarely, brachycephaly. The skull is thickened and there is increased pneumatization of the sinuses. The spinal canal is narrowed [94]. Displacements of the brain include small slit-like ventricles associated with medial displacement of the basal ganglia and downward convex bending of the corpus callosum; marked thickening of the pachymeninges associated with shaggy gelatinous highly vascularized connective tissue on the inner surface of the dura; thickening of the cortical mantle because of diffuse infolding of the cortical surface; upward herniation of the cerebellum and brainstem through the tentorium; and narrowing of the aqueduct.

Clinical attention has focused on the slit-like ventricles. It has been estimated that up to 80% of successfully shunted hydrocephalic infants eventually develop slit ventricles, but only 12% of these will be symptomatic [95, 96]. Symptoms consist of intermittent headaches, nausea, vomiting, and lethargy. These symptoms may be caused by

intermittent shunt obstruction possibly because of coaptation of the ventricular wall with the perforations of the shunt catheter, or, in more posteriorly placed catheters, entry of choroid plexus into the perforations of the catheter [97]. The obstruction, which is associated with increased intracranial pressure, can be documented by imaging studies showing ventricular dilatation during a period of headache followed by a return to small ventricular size when the headache resolves [98]. In some patients with shunt obstruction the ventricles dilate little if at all, and the patient's symptoms may progress to coma and decerebration with extremely high intracranial pressure while ventricular size is still within the normal range [99]. In a second group of patients radionucleide washout studies ("shuntograms") demonstrate that the shunt is patent, the ventricles are not enlarging, but recordings of intracranial pressure show recurrent brief periods of increased pressure at the time of symptoms [98]. In a third group of patients the headaches are orthostatic, very much like those in the acute phase of spinal CSF leak. Orthostatic headaches in shunted patients are associated with markedly low intracranial pressure in the erect position and may occur with or without slit ventricles [100].

The optimal treatment of symptomatic patients with slit ventricles is still uncertain, but is based on the presumed pathophysiology of the symptoms. Approximately half of symptomatic patients with slit ventricles do not require surgical intervention, and can be observed or treated medically. Patients with orthostatic headaches may respond to daily periods of supine or head-down rest. Those with patent shunts but paroxysmal increased intracranial pressure may respond to avoidance of activities that can produce cerebral vasodilation, such as exercise in hot weather. They may also respond to drugs that lower the intracranial pressure such as acetazoleamide, diuretics or to propranolol and a variety of other medications used for migraine prophylaxis [95, 101]. If conservative measures fail, patients with either orthostatic "low pressure" headaches [100, 102], patients with intermittent shunt obstruction [98], and patients with shunt failure without increase in ventricular size usually respond to shunt revision in which an obstructed catheter - if present - is replaced, and the valve is upgraded to one that either has a higher opening pressure, or whose opening pressure is programmable, along with insertion of an "antisiphon" valve that closes in the erect posture. Patients whose headaches are not clearly indicative of intracranial hypertension or of orthostatic intracranial hypotension may benefit diagnostically from externalizing the distal portion of the ventricular catheter and monitoring intracranial pressure. A significant minority will be found to have normal intracranial pressure even with occlusion of the ventricular catheter. These patients are no longer shunt-dependent, and the shunt apparatus can be removed [103]. In patients with patent shunts who have paroxysmal elevated intracranial pressure, surgical treatment depends on intracranial volume. Patients with small intracranial volume due to craniostenosis can be treated with subtemporal decompressive craniectomy and, if that is unsuccessful, with a procedure to expand the calvarium. Patients with normal skulls can be treated first with shunt revision as above [104]. Subtemporal decompressive craniectomy may be effective if shunt revision is not [105, 106]. In patients with non-communicating hydrocephalus endoscopic third ventriculostomy, although technically difficult in patients with small ventricles, may be effective when other measures fail [107]. Adding a lumbo-peritoneal shunt to a functioning ventriculo-peritoneal shunt may reduce intracranial pressure and relieve symptoms in patients who have remained symptomatic despite multiple ventricular shunt revisions [108]. In patients with communicating hydrocephalus or whose non-communicating hydrocephalus can be made communicating by third ventriculostomy, conversion of a ventriculo-peritoneal shunt to a lumbo-peritoneal shunt has been reported to greatly decrease the number of obstructions due to occlusion of the proximal catheter [109].

2. Pathophysiology of displacements associated with CSF leak - hydrodynamic herniation

The varying patterns of herniation and displacement reviewed above share a common thread: A primary alteration in the spatial pattern of CSF flow caused by leakage or intentional diversion of CSF results over time in the displacement of tissue towards the site of the leak or shunt. In the

case of a spinal CSF leak the CSF flows caudally to exit through the dural defect. In turn, the brain is displaced caudally. The cerebral hemispheres descend towards the tentorial opening, and the brainstem and cerebellum also move caudally with herniation of the inferior cerebellum and at times of the caudal brainstem through the foramen magnum. The spinal cord is driven towards the site of an adjacent cervical or thoracic spinal CSF leak, and a nerve root of the cauda equina is driven towards an adjacent lumbar spinal CSF leak. In the case of a cranial CSF leak, the herniation (encephalocele) occurs at the site of CSF leakage at the base of the skull. In the patient with a chronic indwelling ventricular shunt the brain collapses towards the source of CSF diversion, the opening of the ventricular catheter. The ventricles decrease in size, the basal ganglia move medially, the brainstem is displaced upwards, and the corpus callosum and cerebral mantle are displaced downwards. For convenience we shall refer to this constellation of displacements simply as “slit ventricles”.

We propose that the altered spatial pattern of CSF flow in each case creates abnormal hydrodynamic forces that cause the herniation. The hydrodynamic forces are of three types: a) pressure gradients associated with spatial differences in CSF flow velocity (Bernoulli forces), b) pressure gradients required to overcome fluid viscosity and produce flow, and c) shear drag that is proportional to fluid viscosity.

According to Bernoulli’s law of energy conservation, in a fluid with steady flow, a region with high flow velocity will have lower pressure than a region with low velocity if the fluid heights are the same. If the volume of flow is constant, the velocity increases and the pressure falls wherever there is a decrease in the cross-sectional area through which the fluid flows. One such region may be the site of a fluid leak. At a circumscribed region where fluid is removed from a system - a fluid sink - the fluid velocity is generally higher than elsewhere in the fluid and the pressure is therefore lower. If a solid is submerged in a flowing liquid, the fluid velocity near the surface of the solid will generally be greatest at that part of the surface closest to the fluid sink. The pressure at that portion of the surface will therefore be lower than at other parts of the surface of the solid (Figure 1). This difference in pressure is a force moving the submerged solid towards the fluid sink. We propose that the site of a CSF leak is a fluid sink, and the pressure gradients induced by the Bernoulli forces drive the submerged brain, spinal cord, or nerve root towards the source of the leak.

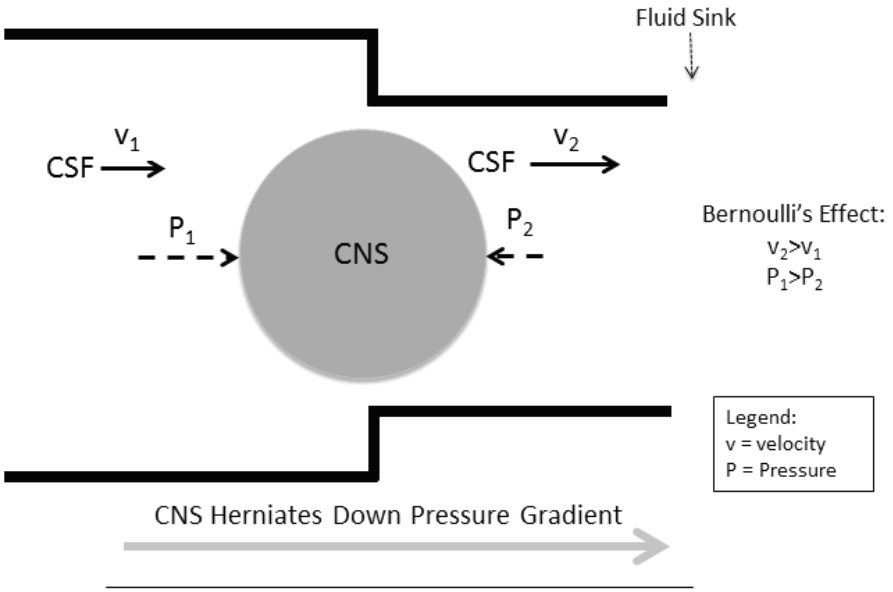

Figure 1. Bernoulli forces generate a pressure gradient contributing to hydrodynamic herniation.

Whereas Bernoulli forces apply even to "ideal" - i.e., frictionless - fluids; the existence of fluid friction (viscosity) creates additional forces tending to push or drag a submerged solid towards a fluid sink. Because of fluid viscosity, a pressure gradient in the fluid is required for CSF to flow even when the velocity is spatially uniform. This pressure gradient exists throughout the flowing fluid, unlike the Bernoulli forces, which exist only at regions of change in the cross-sectional area through which the fluid flows. The pressure gradient due to viscosity, acting perpendicular to the surface of a submerged solid, is a force driving it down the gradient towards the fluid sink (Figure 2).

Another force caused by fluid viscosity is shear drag. This refers to a force parallel to the surface of a body in contact with a flowing liquid. It arises from the velocity gradient between the motionless fluid at the surface of the solid and the moving fluid just off the surface and is proportional to the fluid viscosity. The effect of shear drag is to displace a submerged solid in the direction of the fluid flow. A CSF leak or diversion causes CSF to flow towards the site of leakage and drags the submerged nervous tissue in the same direction (Figure 3).

In the CSF leaks that we have reviewed, the three hydrodynamic forces - Bernoulli pressure gradient, pressure gradient to overcome viscosity, and drag forces - all operate in the same direction, the direction of flow. There are no data that allow us to state their relative strengths. However, there is clinical literature to suggest that at least in one circumstance, the movement of fluid through a needle that has entered the subarachnoid space, the Bernoulli forces predominate. In routine lumbar puncture, contact of the needle with a nerve root of the cauda equina occurs frequently, as often as 13% in one large series [110]. The occurrence of brief "electric shock" radicular pain is evidence of such contact. As fluid is withdrawn the three hydrodynamic forces act co-operatively to draw the nerve roots towards the fluid sink at the needle. A similar syndrome occurs when a spinal anesthetic is injected *into* the lumbar subarachnoid space and is known in the literature as the transient radicular irritation syndrome (TRI) [111]. TRI is not rare; the frequency has varied in different series from 0-37%. Numerous studies have failed to demonstrate convincingly that the frequency of TRI depends upon the nature of the anesthetic [111], its concentration [112], or the position of the patient during surgery. It has

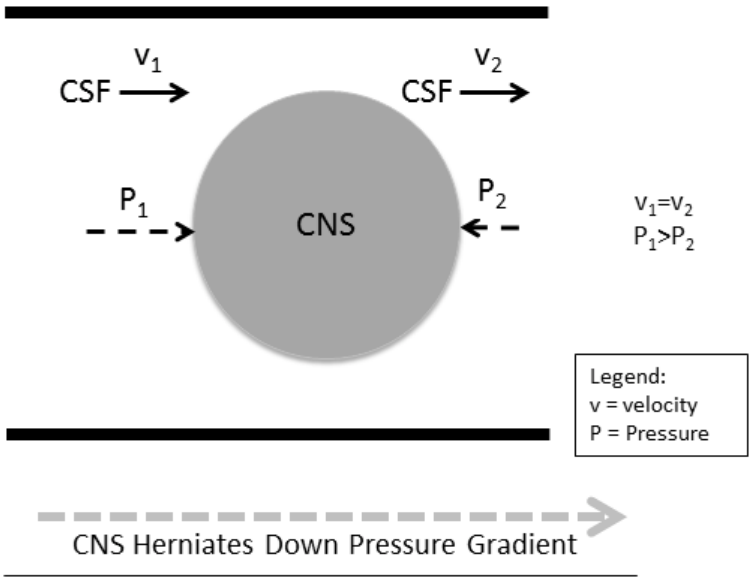

Figure 2. Flow of a fluid with viscosity requires a pressure gradient which acts on CNS tissue contributing to hydrodynamic herniation.

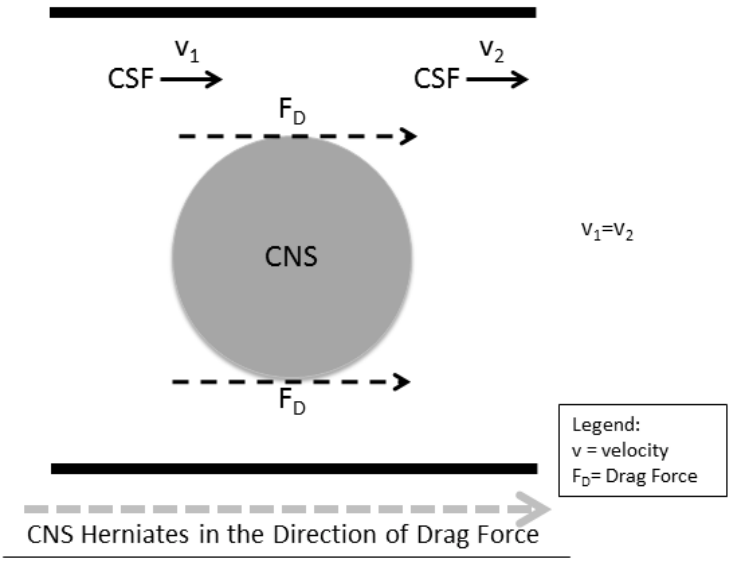

Figure 3. Drag force is exerted upon CNS tissue, contributing to hydrodynamic herniation.

in fact been reported during the intrathecal infusion of normal saline [113]. Case reports indicate that the radicular symptoms occur during the injection [114]. It is therefore likely that hydrodynamic forces driving the nerve root towards the needle are responsible for TRI. Here the Bernoulli forces continue to attract the adjacent nerve roots towards the fluid source at the mouth of the needle since the fluid velocity there is greatest. However, the flow is away from the needle and the other two hydrodynamic forces repel the adjacent nerve roots. We conclude that in this situation the Bernoulli forces overwhelm the viscosity induced pressure gradient and drag. As the Bernoulli forces depend strongly on the geometry of the fluid sink or fluid source, we cannot generalize this conclusion to other leaks with different geometry.

There are two qualifications to the hypothesis. First, we have discussed and illustrated the effects of the hydrodynamic forces as though the nervous system is a solid body impelled as a whole towards the site of a leak of its surrounding CSF. This simplification may suffice to understand the drifting of a nerve root or even of the spinal cord towards a rent in the adjacent dura. However, in the case of encephalocele or in the collapse of the cerebral mantle towards the opening of a ventricular catheter, the displacement involves primarily a distortion of tissue rather than the movement of a rigid, or even a flexible, solid body. The nervous system is not a simple solid but rather has the consistency of a viscoelastic gel. If forces operate over a sufficient time, the tissue will creep, showing flow characteristics resembling those of a liquid. The hydrodynamic forces produce such distortions by inducing creep of the nervous tissue down pressure gradients and in the direction of drag forces.

The second qualification concerns the Bernoulli forces, which we have thus far depicted as acting in the area of a leak, where velocity of CSF flow increases and pressure is thus depressed. However, the geometry of the CSF cisterns is complex. There are several regions along the neuraxis where there is a change in the cross-sectional area of the subarachnoid space through which CSF flows. An abnormal spatial pattern of CSF flow due to a leak thus creates opportunities for abnormal Bernoulli forces to develop at these sites away from the leak. For example, the cross-sectional area of CSF flow narrows in the transition from the posterior fossa cisterns to the spinal subarachnoid space at the foramen magnum. Any increase in the magnitude of CSF flow through the foramen magnum, whether the flow is steady in the caudal or rostral direction or whether it is pulsatile, will produce Bernoulli forces favoring

herniation of the cerebellar tonsils through the foramen magnum. In patients with spinal CSF leak the increased caudal net CSF flow across the foramen magnum towards the site of the spinal dural leak acts synergistically with the viscous forces induced by the leak to favor tonsillar herniation. The role, if any, of Bernoulli forces in other transitional areas, such as the tentorial incisura and the junction of the midbrain and pons, is unclear. More information is needed about the flow patterns of CSF at the foramen magnum and the other transitional regions in the various types of CSF leaks.

3. General discussion

This discussion will focus on the global herniations, because their clinical presentations are more varied and complex than the more straightforward clinical pictures in the local herniations. We will argue that the proposed mechanism of hydrodynamic herniation allows a better understanding of some hitherto puzzling variations in the pattern of symptoms associated with syndromes of CSF leakage, particularly spinal CSF leaks. The proposed mechanism also clarifies the development of slit ventricles in patients with indwelling ventricular shunts, explains some of the variation in the pattern of symptoms that these patients may develop, and makes predictions about the efficacy of treatments.

3.1. Multiple rather than unitary mechanisms in CSF leakage or diversion

Orthostatic headache, low CSF pressure, intracranial dural enhancement, and brain displacement occur frequently in patients with either spinal CSF leak or indwelling ventricular shunts. Until now the prevailing view has been that a single mechanism accounts for all of these clinical features. In the literature on spinal CSF leak the proposed unitary mechanism has been reduced CSF volume. The difficulty with this approach has been that variant cases occur in which one or more of the above clinical features are missing [19, 115, 116], and such variants are difficult to understand if all of the features derive from the same underlying mechanism. Plausible physical principles linking orthostatic headache and brain displacement to reduced CSF volume have not been forthcoming. It is claimed, for example, that reduced CSF volume leads to reduced buoyancy of the brain, causing the brain to sag, inducing headache from the stretch of pain sensitive veins. Yet brain descent is not evident in most patients with post-lumbar puncture headache [14, 117], and in patients with spontaneous spinal CSF leak brain descent often occurs and is most obvious only after the initial orthostatic headache has resolved.

In the literature on chronic indwelling ventricular shunts the proposed unitary mechanism explaining both slit ventricles and orthostatic headache has been “overdrainage” brought about by “siphoning”. This explanation does not withstand close scrutiny. To understand the effects of siphoning on the CSF space one must consider two different types of fluid filled systems, which we shall call hydrostatically stable and hydrostatically unstable.

In a hydrostatically stable system the pressure difference between any two points of the enclosed fluid is uniquely determined by their relative vertical heights. Two points at the same height must be at the same pressure, and two points at different heights will differ in pressure by an amount proportional to the difference in their heights. If the CSF space connected by a shunt to the peritoneal cavity were hydrostatically stable, only minuscule amounts of extra fluid could move between the CSF space and the peritoneal cavity when their relative heights change. In such a situation, if a supine patient with an unvalved shunt were to sit or stand, a small amount of fluid would move from the intracranial to the peritoneal space, which would suffice to lower the intracranial pressure substantially. Once the intracranial pressure fell to a level equal to the peritoneal pressure minus the height of the hydrostatic column formed by the shunt tubing, fluid would cease to flow. If the patient were to resume the supine position the extra fluid would return from the peritoneal to the intracranial compartment, and there would be no net extra drainage beyond the small steady drainage in both postures that equals the rate of CSF production. In the presence of a typical valve in the shunt apparatus, which does not allow the flow of CSF until a given opening pressure is reached, the same considerations apply. If the patient were to sit or stand, only a small amount of fluid would flow from the

intracranial cavity, and flow would cease as soon as the intracranial pressure fell to a level equal to the peritoneal pressure plus the opening pressure of the valve minus the height of the hydrostatic column of the fluid filled shunt tubing. If the patient were to resume a recumbent posture, the valve would prevent reverse flow. As a result, no drainage would occur until additional CSF was produced, sufficient to raise CSF pressure to a level equal to peritoneal pressure plus the opening pressure of the valve. Thus in a hydrostatically stable system no excess drainage can occur.

In a hydrostatically unstable system enclosed fluid at two different heights is exposed to a common pressure, usually - but not necessarily - atmospheric pressure. In such a system fluid will flow in bulk from the higher to the lower level and will not cease as long as the common pressure affects the two levels. This is the principle of the siphon. For example, if a piece of rubber tubing filled with water is turned vertically, and the upper and lower ends are opened to the atmosphere, the fluid immediately drains completely from the lower end of the tube. If the CSF space connected by shunt tubing to the peritoneal space were a purely unstable system, such that the vertical level at which CSF pressure equals peritoneal pressure was located higher than the peritoneal cavity, fluid would flow massively from the CSF space to the peritoneal cavity when the patient assumed a sitting or standing posture.

In fact, the combined CSF and peritoneal spaces connected by a shunt (and for that matter the CSF space alone with a breach in the spinal dura) acts neither as a purely stable nor as a purely unstable system. Rather, it displays an intermediate behavior in which siphoning occurs but is self-limited. It is not purely stable because the lumbar CSF pressure is significantly higher than the peritoneal pressure at the same vertical level in the erect position. Connecting the two compartments via a shunt tube necessitates some bulk flow from the CSF space into the peritoneal cavity. It is not purely unstable because once the CSF flow commences, the pressure in the CSF space falls, so that eventually the vertical level at which CSF pressure equals peritoneal pressure descends to the height of the opening of the peritoneal catheter (plus the opening pressure of the valve), and flow ceases, so that the CSF compartment is not totally drained.

This limited siphoning is the proximate cause of reduced CSF volume in patients with CSF shunts. The hypothesis of overdrainage by siphoning in patients with shunts is identical to the hypothesis of reduced CSF volume in patients with spinal CSF leak, only expressed in different language. Like the reduced CSF volume hypothesis, the siphoning hypothesis fails as a unitary hypothesis, as it can explain neither orthostatic headache nor the brain displacements that are summarized by the term slit ventricles. Shunted patients with orthostatic headaches are as likely to have enlarged ventricles as small ones [100], so that overdrainage with reduced CSF volume is not necessary for orthostatic headache. It is also not sufficient, as the large majority of patients with reduced CSF volume associated with slit ventricles do not have orthostatic headache. Slit ventricles, while associated with reduced CSF volume, are not proximately caused by it, because reduced CSF volume occurs in patients with spinal CSF leak with a totally different pattern of brain displacement and occurs in patients with osmotic dehydration of the brain and no gross brain displacement at all.

We propose instead that each of the characteristic clinical features noted above has a distinct physical mechanism:

A. Brain displacements result from the hydrodynamic forces discussed above, which are the focus of this review.

B. Orthostatic headache is the result of altered hydrostatic - not hydrodynamic - forces. An injury to the spinal dura or the presence of a shunt terminating in the right atrium or peritoneal space can alter the distribution of compliance along the neuraxis by creating an asymmetry in which compliance of the caudal spinal CSF compartment increases relative to the rostral intracranial compliance. As a result of this asymmetry the hydrostatic zero point moves downward when the patient becomes erect, creating markedly subatmospheric pressure intracranially. This in turn leads to acute dilation of intracranial dural veins and sinuses over and above that in the recumbent position. Pain receptors in the walls of the large

veins are stimulated, leading to orthostatic headache. Evidence in support of this mechanism has been reviewed in detail elsewhere [6].

C. Low recumbent CSF pressure results from yet another mechanism - loss of CSF volume as a result of the limited siphoning discussed above. The CSF compartment in each individual is governed by a pressure-volume curve [118, 119], so that in a normal individual, CSF pressure and CSF volume determine one another. As volume is added to (withdrawn from) the craniospinal compartment, the intracranial pressure rises (falls) in a roughly exponential manner. The form of the curve incorporates the compensatory mechanisms for accommodating an increase or decrease of craniospinal volume, which include changes in absorption of CSF and brain water into the blood stream, alteration of the caliber of the intracranial dural veins and sinuses, and expansion or contraction of the spinal dura reciprocally with changes in caliber of the spinal epidural veins.

D. Enhancement of the intracranial dura on MRI is due to engorgement of the dural veins and is caused by increased transmural venous pressure - i.e., the difference between the pressure inside the dural veins and the intracranial CSF pressure - which is the force determining the caliber of a vein [120].

3.2. Comparison of CSF loss from spinal CSF leak and from ventricular shunt

Some insight into the variability of the symptom patterns in patients with CSF loss can be gained by comparing the presence and, if present, the effect of each of the above mechanisms in two groups of patients: those with spinal CSF leak and those with diversion of CSF through a ventricular shunt. In both cases the loss of CSF can result in reduced CSF volume and low recumbent CSF pressure. It is therefore not surprising that dural enhancement on MRI, which reflects the dilation of intracranial dural veins, is commonly reported in both groups.

Both conditions may also be associated with orthostatic headache. In cases of spinal CSF leak, orthostatic headache typically occurs at the outset, because the dural injury opens the lumbar subarachnoid space to the epidural and paraspinal spaces, increasing the compliance of this combined space relative to the intracranial end of the neuraxis. With the passage of time the orthostatic headache often resolves, indicating either healing of the leak or tissue reaction that results in reduced epidural or paraspinal compliance. In patients with ventricular shunts, orthostatic headache occurs less commonly and at varying times after insertion of the shunt. In the series of Foltz and Blanks [100] all of the patients with orthostatic headache presented in adolescence or adulthood, at ages ranging from 14-70 years. Most had carried ventricular shunts for many years, and several had been shunted in the first year of life. The interval between shunt insertion and the onset of orthostatic headache varied from two weeks to thirty years. In a patient with a ventriculo-peritoneal shunt a column of CSF between the ventricle and the peritoneal cavity runs parallel to the normal column between the ventricle and the spinal subarachnoid space. The peritoneal cavity thus adds to the caudal spinal compliance, creating the possibility of asymmetry sufficient to cause orthostatic headache. For this to be the case the shunt column must be continuous, i.e. the valves must be open. It is therefore more likely that orthostatic headache will occur with valveless shunts or shunts with valves of low opening pressure. The compliance of the spinal epidural space is very low in pre-adolescent children and in the very elderly [121], and lumbar puncture headaches are rare in those age groups [8, 122], so that even the added caudal compliance from a shunt will often be insufficient to produce orthostatic headache. It is possible that with maturation and a natural increase in spinal compliance, a point is reached where the additional caudal compliance afforded by the terminus of the shunt suffices to create the asymmetry between caudal and rostral compliance needed for orthostatic headache. Alternatively, there may be a change in the compliance of the shunt terminus. Disconnection of the distal shunt tubing in the chest with free flow of CSF at the site of the disconnection through a fibrous tract into the peritoneal cavity has been reported as a cause of orthostatic headache [123]. At the cranial end of the neuraxis it is possible that reduced intracranial compliance caused by depletion of displaceable intracranial CSF and obstruction of intracranial venous outflow at the skull base in patients with

acquired craniostenosis further contributes to this asymmetry.

Both spinal CSF leaks and chronic ventricular shunts are associated with brain displacements, but they are very different in nature, because the hydrodynamic forces have a different spatial pattern in the two clinical situations. Spinal CSF leak is associated with brain descent, while ventricular shunt is associated with collapse of the cerebrum towards the ventricle and ascent of the cerebellum and brainstem.

The comparison of mechanisms operative in spinal CSF leak and chronic ventricular shunts allows a better understanding of other symptoms that may be either common to the two clinical situations or unique to one of them. Subdural hematoma is a common complication both in patients with spinal CSF leak and in patients with ventricular shunts and typically occurs shortly after the spinal dural injury or the insertion of a shunt. This suggests that lowered CSF recumbent pressure due to lowered CSF volume is the underlying mechanism, since both conditions share this mechanism in the acute phase. Altered distribution of compliance producing highly negative erect intracranial pressure is an unlikely mechanism, as it is typically a late development in patients with shunts. Brain displacement with traction on veins is unlikely, as the pattern of displacement is quite different in the two conditions and, being the result of the continued action of small hydrodynamic forces, is typically a late development in both clinical situations.

Dilated cervical spinal epidural veins occur in both situations as well. The epidural veins dilate as a result of increase in their transmural pressure that is attributable to low CSF pressure associated with reduced CSF volume. In rare patients with spinal CSF leak, cervical myelopathy occurs within weeks of onset of orthostatic headache and has been attributed to compression of the cervical spinal cord by dilated epidural veins [124, 125]. Progressive cervical myelopathy due to compression of the cervical spinal cord by dilated epidural veins has also been reported in patients with chronic indwelling shunts [126-129]. The existence of this syndrome in patients with ventricular shunts, where extradural CSF from a leak is not present, validates the syndrome in patients with spinal CSF leak, where the existence of extradural collections of leaked CSF - also capable of exerting mass effect - complicates attribution of the myelopathy to the mass effect produced by the dilated veins.

In contrast to conditions shared by patients with spinal CSF leaks and patients with ventricular shunts, encephalopathy, whether chronic progressive dementia [36, 37], subacute encephalopathy [39-41], or acute encephalopathy with coma and decerebration [42, 43], is unique to patients with spinal CSF leak and has not been reported in patients with ventricular shunts unless these are complicated by obstruction and elevated intracranial pressure. The encephalopathy can thus be attributed to brain descent, since that too is present only in patients with spinal CSF leak. Hydrodynamic induced descent of the midbrain and diencephalon through the tentorial incisura appears to be more likely to produce symptoms than hydrodynamic induced ascent of the brainstem and superior cerebellum through the same opening, which occurs in patients with chronic indwelling ventricular shunts.

3.3. Variant syndromes in patients with CSF leakage or diversion

With the existence of distinct physical mechanisms for different features of CSF loss, it is possible to understand variant cases where one or more clinical features associated with CSF loss are missing. In any particular clinical situation not all of the mechanisms may be operative and hence not all of the typical features need be present.

The first variant that we will consider is the patient with a spinal CSF leak who has orthostatic headache but normal recumbent CSF pressure. Such cases have been reported either after lumbar puncture [130] or with spontaneous spinal CSF leak [115]. A normal recumbent CSF pressure may occur because of an altered pressure-volume curve resulting from a breach in the spinal dura and accumulation of fluid in the epidural space. The epidural fluid collection will bend the dura inward, accentuating the shrinkage of the subarachnoid space, i.e. the loss of subarachnoid volume, at any given pressure. Stated differently, for a given loss of subarachnoid volume, the pressure in the subarachnoid space will be higher

in the presence of an epidural fluid collection than it would be for the same loss of subarachnoid volume in the absence of an epidural fluid collection. In addition to accounting for the significant minority of patients with spinal CSF leak who have normal CSF pressure, alteration of the pressure-volume curve also explains rebound intracranial hypertension, which may occur after epidural injection of blood or other substances to treat spinal CSF leak. Despite normal recumbent CSF pressure a patient with spinal CSF leak may still have orthostatic headache because of the increased compliance in the caudal CSF space resulting from the breach in the spinal dura. This increased compliance becomes evident when the patient's lumbar CSF pressure is measured in the sitting position, where it will be lower than the lumbar CSF pressure of a normal seated individual, even when the patient's recumbent CSF pressure is in the normal range [6].

A second variant is the patient with a ventricular shunt with low opening pressure of the valve, who may show reduced recumbent CSF pressure and intracranial dural enhancement but no orthostatic headache or brain sag [19]. Such patients are common in the population with shunts and are here considered "variant" only in the sense that some symptoms associated with CSF loss are not present. In these typically elderly patients with low spinal epidural compliance the additional caudal compliance afforded by the shunt is insufficient to create the asymmetry required for orthostatic headache, or the shunt has an "anti-siphon" valve so that the shunt terminus does not communicate with the intracranial compartment when the patient is upright. Orthostatic headache therefore does not occur. Brain sag does not occur because the CSF flow is rostral rather than caudal, towards the source of the shunt in the lateral ventricle. In patients with shunts who do experience orthostatic headache, caudal displacement of the brain, with rare exceptions [131], also does not develop [93]. The altered hydrostatic forces are present, but again CSF flow in the subarachnoid space is rostral rather than caudal, so that the brainstem ascends rather than sags.

Yet another variant is the patient with spinal CSF leak who has orthostatic headache but has no intracranial dural venous enhancement on MRI. Some of these have normal recumbent CSF pressure [132]. The absence of dural vein enhancement in these patients is readily understood since, assuming dural venous pressure to be unchanged, transmural pressure is not increased. Other patients with orthostatic headache and absent intracranial dural enhancement have low recumbent CSF pressure [133]. A possible explanation for the absent intracranial venous engorgement in these patients is that venous dilation to compensate loss of subarachnoid CSF is occurring primarily in the cervical spinal epidural veins rather than in the veins of the intracranial dura. For example, the patient of Clarot [134] developed orthostatic headache a few hours after lumbar puncture. MRI of the head with contrast showed no dural enhancement, but MRI of the cervical spine showed markedly dilated cervical epidural veins. In such a patient the orthostatic headache may be caused by further engorgement of the cervical spinal epidural veins on assuming the erect posture [6].

The existence of distinct physical mechanisms for the different features of CSF loss also allows the prediction of variant cases that have yet to be reported. The patient who is dehydrated or who is given an osmotic diuretic may have low CSF volume and pressure. He will not have orthostatic headache because the distribution of compliance along the neuraxis has not been altered. There will be no brain displacement since the spatial pattern of CSF flow remains the same. Whether dural enhancement occurs will depend on the extent to which venous pressure is lowered along with CSF pressure. The patient with a CSF leak from the skull base will also have low recumbent CSF pressure. Orthostatic headache will usually not occur, because the point of leakage is too rostral for the necessary asymmetry of caudal and intracranial compliance to materialize. Brain displacement will consist primarily of encephalocele into the defect in the skull base, but there will be no descent of the brainstem. Intracranial dural enhancement may occur in the event that CSF recumbent pressure is sufficiently low if venous pressure has not changed.

3.4. Slit ventricles and the slit ventricle syndrome

We have proposed that the development of slit-like ventricles in patients with chronic indwelling

ventricular shunts is the result of the hydrodynamic forces that accompany altered patterns of CSF flow. These hydrodynamic forces move brain tissue toward the fluid sinks represented by the orifices of the shunt within the ventricle. It is therefore not surprising that - given enough time - the large majority of patients shunted as infants [95, 96] will develop small ventricles. In most of these patients the small ventricles are an incidental radiological finding with no obligatory symptoms or signs. In the minority of patients in whom symptoms occur, there are a variety of presentations that are often subsumed under the single term “slit ventricle syndrome”. In some of these presentations the hydrodynamic forces producing the slit ventricles are primarily responsible for the symptoms, whereas in others the relationship is less direct or even non-existent:

A. Intermittent obstruction of the ventricular catheter likely occurs because either the ependymal surface or the choroid plexus of the lateral ventricles is drawn toward orifices of the catheter by the same hydrodynamic forces that create the small ventricles. When the catheter becomes obstructed, CSF no longer flows through it, and the hydrodynamic force ceases. As CSF continues to be secreted into the ventricles, intraventricular pressure rises, and symptoms of headache, vomiting and lethargy develop. Usually the ventricles enlarge slightly, disengaging the obstructing tissue, and relieving the symptoms. With restoration of flow through the ventricular catheter, the cycle begins anew.

B. In some patients with shunt obstruction the ventricles dilate very slowly or imperceptibly despite significantly increased intracranial pressure. This is most likely related to reduced brain compressibility. On a time scale of minutes to hours there are two main sources of brain compressibility that allow accommodating an added intracranial volume such as dilation of the ventricles. First, CSF can be displaced from the intracranial subarachnoid space into either the bloodstream or the spinal subarachnoid space. Second, intracranial blood volume can be reduced as blood exits via the veins at the base of the skull. As a result of acquired craniostenosis patients with chronic indwelling shunts may have less CSF in the supratentorial intracranial compartment [135] relative to that in the brainstem cisterns and spinal compartments. If so, there will be diminished capacity to tolerate ventricular expansion by displacing intracranial subarachnoid CSF. In addition venous outflow obstruction may hinder the rapid reduction of intracranial blood volume. Patients with idiopathic craniostenosis involving multiple sutures frequently develop obstruction to venous outflow at the skull base [136]. Similar outflow obstruction is likely present in acquired ossification or cartilage deposition in the cranial sutures [98], which is associated with chronic intracranial shunts [135] placed during infancy. This venous outflow obstruction reduces the intracranial compressibility that derives from changes in intracranial blood volume. These two sources of reduced intracranial compressibility will hinder acute ventricular expansion. In order for the ventricles to dilate, a small difference in pressure must exist between the CSF in the ventricles and that in the subarachnoid space. To establish such a mini-gradient CSF pressure throughout the intracranial space must rise to a degree that is determined largely by brain compressibility [137]. When the brain is relatively incompressible, the rise in pressure needed to establish a mini-gradient between ventricle and subarachnoid space that is sufficient for prompt and perceptible ventricular dilation may be so high as to be incompatible with life.

Another mechanism for lack of ventricular dilation in patients with shunt obstruction may involve the original diagnosis for which the shunt was inserted. Infants may develop hydrocephalus from dural venous hypertension or from diffuse reduction in the absorptive capacity of the arachnoid villi, two conditions which in older children and adults cause pseudotumor cerebri rather than hydrocephalus. In such patients, once the sutures fuse, shunt obstruction might manifest itself as increased intracranial pressure with small rather than enlarging ventricles [138].

Thus failure of the ventricles to dilate acutely and significantly after catheter obstruction is not directly related to the small size of the ventricles except insofar as slit-ventricles are an index of reduced intracranial CSF volume and reduced brain compressibility.

C. Patients with slit ventricles who have recurrent episodes of increased intracranial pressure despite patent shunts may also be symptomatic because of diminished brain compressibility [139, 140]. Ordinarily, intracranial pressure varies from moment to moment, and a major source of this variation is changes in intracranial blood volume. The increase in intracranial pressure caused by an increase in cerebral blood volume is ordinarily mitigated by displacement of CSF into the bloodstream or into the spinal subarachnoid space. In the patients we are considering there is usually little available CSF in the intracranial subarachnoid space, and mitigation of the increased pressure is dependent on drainage of CSF through the ventricular catheter. However, in these patients it is frequently noted that the shunt reservoir fills slowly after being pumped, i.e., flow through the patent ventricular catheter is slowed. This suggests either that the shunt itself is partially obstructed or that the amount of CSF that can be drained promptly by the shunt catheter is too small. The CSF available for prompt drainage by the catheter may be limited to that in the ipsilateral slit ventricle, as narrowing or even obstruction of the opposite foramen of Munro and of the aqueduct of Sylvius have been described in patients with slit ventricles [141] - presumably from hydrodynamically induced brain displacements. Thus the hydrodynamic forces producing slit ventricles may play an important role in the reduced brain compressibility in these patients.

D. Patients with slit ventricles who present with orthostatic headache have developed a redistribution of craniospinal compliance such that the compliance of the caudal spinal component is increased relative to that of the intracranial component. As a result, the zero point of intracranial hydrostatic pressure is lower than normal in the upright position, leading to orthostatic intracranial hypotension, and additional venous dilation on sitting or standing with resultant headache [6]. This change in hydrostatic pressure is completely independent of the hydrodynamic mechanisms producing slit ventricles. Evidence for the independence of these mechanisms is that orthostatic headache does not require slit ventricles and may present in patients with ventricles that are small, normal or enlarged.

3.5. Therapeutic implications

The hypothesis that hydrodynamic forces are responsible for displacements of nerve tissue in both spinal CSF leak and drainage of CSF by ventricular shunts has important therapeutic implications. It is already widely recognized in cases of spinal CSF leak that restoring a normal flow pattern is the best treatment. This is ordinarily accomplished by measures to repair the leak, such as epidural blood patch [25, 26], epidural saline infusion [27, 28], and, if necessary, surgical repair of the dural defect. There are two important exceptions to this approach: The first concerns the management of some patients with subdural hematoma, which, as previously discussed, may complicate spinal CSF leak. Most subdural fluid collections in patients with spinal CSF leak will regress with repair of the leak. Occasionally a subdural hematoma may be sufficiently large to exert mass effect and cause acute clinical deterioration. In this event emergency evacuation may be required before repairing the leak. The second exception involves management of the end stages of hydrodynamic brain descent. In this situation the midbrain-diencephalic junction may become impacted in the tentorial notch, separating the supratentorial and infratentorial CSF compartments into separate non-communicating compartments. Any reduction in the hydrostatic pressure of the infratentorial compartment, such as from a lumbar puncture or lumbar drainage, or any increase in hydrostatic pressure of the upper compartment will cause further impaction and acute clinical deterioration in the form of decline of consciousness, flexor or extensor posturing, and pupillary asymmetry. Such bi-compartmental hydrostatic herniation has been described in two clinical situations. The “sinking-brain” [142] or “brain sag” [43] syndrome after craniotomy is one of them. Komotar [43] reported 11 cases occurring within 1-4 days after craniotomy for clipping of a ruptured aneurysm, in which a lumbar catheter was used to drain CSF in order to relax the brain. Several features of these patients [43] explain the unusually rapid hydrodynamic descent of the brain that allowed impaction within a few days. Most of them had pre-operative cerebral edema, related to the subarachnoid hemorrhage, and varying degrees of

pneumocephalus, thus lessening the degree of descent required for impaction to occur. Also, many of them had intraoperative fenestration of the lamina terminalis to prevent hydrocephalus. This third ventriculostomy likely facilitated the caudal CSF flow towards the lumbar drain and thus increased the hydrodynamic forces driving the brain descent. The second clinical situation in which initial hydrodynamic brain descent culminates in bi-compartmental hydrostatic herniation is that of spontaneous spinal CSF leak that progresses to stupor and coma over a period of weeks or months. A recent review identified 22 such cases in the literature [143]. All cases demonstrated caudal displacement of the brain. It is important to note, however, that the degree of brain descent, as seen on MRI, does not correlate with the patient's mental state [144]. Rather, it appears that the rate of descent is more important, a faster rate being more likely to cause altered mental status. Cases with bi-compartmental hydrostatic herniation are best treated emergently with the head-down (Trendelenberg) position [43] and possibly with infusion of saline into the lumbar subarachnoid space before repair of the leak [41]. A minority of patients do not respond to the head-down position but respond dramatically to emergency epidural blood patch [145].

In contrast to the case of spinal CSF leak, the importance of altering the flow pattern of CSF has not been recognized in cases of slit ventricle syndrome. This is understandable in that the "leak" in the form of the ventricular catheter was created as a therapy rather than occurring as a pathological process such as a spinal dural tear, and there is no treatment in a shunt-dependent patient that will restore a completely normal pattern of CSF flow. Nevertheless, some treatments do not alter the spatial pattern of flow at all, whereas others do. Measures such as increasing the opening pressure of the shunt valve or adding an "antisiphon" device do not change the spatial pattern of CSF flow, and the present hypothesis predicts that any improvement in the sense of increasing ventricular size and thereby reducing the incidence of ventricular catheter obstruction is likely to be temporary. In a controlled study [146] slit ventricles developed in 48% of patients, and slit ventricle syndrome developed in 7% of patients shunted for infantile hydrocephalus; there was no difference between those shunted with a medium pressure flow-control valve and those shunted with a valve that incorporated an antisiphon device. "Antisiphon" valves, which close in the upright posture, should be useful in treating orthostatic headache by preventing profoundly subatmospheric hydrostatic pressure in the erect position but would not be expected to reverse or to prevent slit ventricles. Subtemporal decompressive craniectomy might be expected to increase intracranial compressibility and to mitigate the spikes of increased intracranial pressure and the associated headache in patients with patent shunts. However, the pattern of CSF flow towards the ventricular shunt remains the same, and the ventricles will either not dilate or dilate only temporarily. Linder *et al.* [147] reported that ventricular size decreased after subtemporal decompressive craniectomy in each of 4 patients, and Holness *et al.* [106] reported no ventricular enlargement after subtemporal decompressive craniectomy in 5 of 7 patients. In contrast, inserting a lumboperitoneal shunt in addition to, or as a replacement for, ventricular drainage does alter the flow pattern of CSF, and the present hypothesis predicts long-term changes in ventricular size. However, patients must be monitored for caudal displacement of the brain, particularly if the lumboperitoneal shunt is the only source of CSF drainage.

3.6. Terminology

We have reviewed a variety of situations in which displacements and herniations of brain, spinal cord and nerve roots occur as a result of abnormal spatial patterns of CSF flow. We have proposed that the mechanism for such displacements is the abnormal hydrodynamic forces exerted on the nervous system that is submerged in the abnormally flowing CSF. We have used the term "hydrodynamic herniation" to describe these displacements, although the term "flow-induced herniation" would serve as well. In contrasting these herniations with those caused by mass lesions in the context of increased intracranial pressure it is tempting to employ the term "low-pressure herniation" because such herniations typically occur with leakage or diversion of CSF in the context of low CSF pressure. However, this

term would be misleading if it led to the belief that low hydrostatic pressure in any way caused these displacements. By definition hydrostatic pressure in a single fluid-filled compartment cannot cause displacement of a submerged object. Only a difference of hydrostatic pressure between two non-communicating compartments separated by a flexible membrane can cause displacement, a situation we have termed “bi-compartmental hydrostatic herniation”. The latter can occur in the terminal phases of both hydrodynamic herniation and of herniation caused by mass lesions. It is thus independent of the level of hydrostatic pressure and depends only on the difference of hydrostatic pressure between the two compartments. When there is continuity between all of the CSF spaces - i.e., a single connected CSF compartment - displacement of the submerged nervous tissue can be caused only by altered flow patterns of CSF which engender hydrodynamic forces in the form of pressure gradients and drag forces that act on the submerged tissues.

CONCLUSION

We present our conclusions by describing, admittedly somewhat schematically, our view of the sequence of events that occurs when the dura enclosing the CSF space is breached, either by injury or by insertion of a draining catheter. We present the physical principles underlying each step and the main clinical consequences that result from them.

Prior to injury the CSF space can be viewed as a stable hydrostatic system. In the erect posture the CSF space forms a hydrostatic column like that of a closed vertical fluid-filled tube. This model is not entirely accurate, as CSF is flowing between its sites of production and absorption. Nevertheless, the CSF flow is quite small and can be neglected over a short interval of time such as that typically required in changing postures.

When the dura is first breached, the CSF space becomes hydrostatically unstable. As a consequence, there is relatively rapid bulk flow (“siphoning”) of CSF into the breach. The loss of CSF results in diminished CSF volume and pressure. Intracranial and/or cervical epidural veins dilate, partially compensating the lost volume, because of increased transmural venous pressure. Dilated intracranial veins and sinuses are the basis of the dural enhancement and engorged dural sinuses seen on MRI. Leakage of fluid from veins occurs, and veins may rupture to form subdural hematomas.

As CSF pressure continues to fall, a state is reached where the siphoning stops and hydrostatic stability returns. However, the structure of the system is now abnormal, either because of a persisting opening in the spinal dura connecting the CSF space to the epidural and paraspinal spaces or because of an intracranial ventricular catheter connecting the CSF space to another body compartment such as the peritoneum. The distribution of compliance along the cranio-spinal axis is altered. If the compliance of the caudal portion sufficiently exceeds the compliance of the cranial portion, intracranial pressure will fall dramatically on assumption of the erect posture, leading to additional acute venous dilation and consequent orthostatic headache [6].

From the outset, breach of the dura leads to an abnormal spatial pattern of CSF flow, which is directed towards the leak. This abnormal flow pattern begins during the initial period of hydrostatic instability and, if the leak persists, is maintained during the later period of recovered hydrostatic stability, in which steady-state flow of CSF, equal to its rate of production, continues in the direction of the leak. The flow of CSF is governed by hydrodynamic forces that also act on the submerged nervous tissue. These forces, which include Bernoulli and viscosity-induced pressure gradients and drag forces, result in a cumulative displacement of tissue towards the site of the leak, which we have called hydrodynamic herniation.

CONFLICT OF INTEREST STATEMENT

Neither of the authors has any conflict of interest to report.

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