OBJECTIVE: The history, diagnosis, and therapy of idiopathic intracranial hypertension (IIH) (pseudotumor cerebri) are reviewed. Theories of pathogenesis are considered, the clinical presentation is described, and potential diagnostic and therapeutic challenges are explored.

METHODS: An extensive literature review of IIH and related conditions (secondary pseudotumor syndromes) was performed. The history of and rationale for the diagnosis and medical and surgical approaches to treatment are reviewed. Available outcome studies are presented.

RESULTS: Diagnosis of IIH requires that the modified Dandy criteria be satisfied. Multiple potential contributing causes of intracranial hypertension must be identified or excluded. The clinical presentation most often includes headaches and papilledema, but many other findings have been described. The most important goal of therapy is to prevent or arrest progressive visual loss. Medical therapies include alleviation of associated systemic diseases, discontinuation of contributing medications, provision of carbonic anhydrase inhibitors, and weight loss. Surgical therapies include lumboperitoneal shunting, ventriculoperitoneal shunting, and optic nerve sheath fenestration. On the basis of the advantages and disadvantages of these treatment modalities, a suggested treatment paradigm is presented.

CONCLUSION: Idiopathic intracranial hypertension is the term to be adopted instead of pseudotumor cerebri. IIH remains an enigmatic diagnosis of exclusion. However, prompt diagnosis and thorough evaluation and treatment are crucial for preventing visual loss and improving associated symptoms.

KEY WORDS: Headache, Idiopathic intracranial hypertension, Lumboperitoneal shunt, Optic nerve sheath fenestration, Papilledema, Venous sinus thrombosis, Ventriculoperitoneal shunt
TABLE 1. Modified Dandy criteria for idiopathic intracranial hypertension

<table>
<thead>
<tr>
<th>Criterion</th>
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</thead>
<tbody>
<tr>
<td>Symptoms of increased ICP (headaches, nausea, vomiting, transient visual obscurations, or papilledema)</td>
</tr>
<tr>
<td>No localizing findings in neurological examinations (except for false localizing signs such as abducens or facial palsies)</td>
</tr>
<tr>
<td>Awake and alert patient</td>
</tr>
<tr>
<td>Normal CT/MRI findings without evidence of dural sinus thrombosis</td>
</tr>
<tr>
<td>ICP of &gt;250 mm H₂O with normal cerebrospinal fluid</td>
</tr>
<tr>
<td>No other cause of increased ICP found</td>
</tr>
</tbody>
</table>

Adapted from Reference 44. ICP, intracranial pressure; CT, computed tomographic; MRI, magnetic resonance imaging.

(44) emphasized, these modified Dandy criteria must be met for a condition to be called IIH (167, 188, 189). Increased ICP attributable to other causes, such as choroid plexus papilloma, venous sinus thrombosis, or venous hypertension attributable to obstructive sleep apnea, do not meet the modified Dandy criteria and are better referred to as secondary pseudotumor syndromes (see below).

EPIDEMIOLOGICAL CHARACTERISTICS

IIH occurs most commonly among women. The prevalence is approximately 1 case/100,000 women but increases to 13 cases/100,000 women of ages 20 to 44 years who are 10% above ideal body weight and 19 cases/100,000 women of ages 20 to 44 years who are obese (>20% above ideal body weight) (47). Despite the age specificity, large proportions of patients in virtually all series were obese (39, 44, 53, 82, 195). Most studies demonstrated an age of onset between 11 and 58 years, with a mean of approximately 30 years (47, 133, 134, 189).

Men are affected less frequently. The incidence is 0.3 cases/100,000 men but increases to 1.5 cases/100,000 obese men (>20% above ideal body weight). Female-to-male ratios are approximately 4.3:1 to 8:1 (44).

IIH may also be observed in the pediatric population. A Canadian study of children demonstrated equal incidences among boys and girls, of approximately 1 case/100,000 individuals (2). No racial predilection has been noted. Isolated familial cases (54, 81, 142, 149, 158, 181) raise the possibility of a genetic component in the disorder, but no linkage studies have been performed to date.

PATHOGENESIS

Many theories have been advanced to explain the pathogenesis of IIH. According to the Monro-Kellie rule (115), anything added to the blood, CSF, or brain volume or anything impeding CSF or venous egress would be expected to increase ICP. A first possibility is that the CSF volume could be increased because of excess CSF production. Quincke (132) suggested that hypersecretion of CSF accounted for the syndrome but, except for rare cases of choroid plexus papilloma (49), no clear evidence exists for elevated CSF production as an etiological factor in intracranial hypertension (46).

A second possibility is an increase in cerebral blood volume or brain water content. The original hypothesis proposed by Dandy (39) was that the cerebral blood or CSF volume might be increased. Foley (53) proposed a similar hypothesis of increased cerebral blood flow underlying elevated ICP. Raichle et al. (136) demonstrated with positron emission tomography that patients with IIH have little change in cerebral blood flow but exhibit markedly increased cerebral blood or water volumes. Other investigators focused on increased brain water content. Saha and Joynt (147) provided histological evidence of edema in brain biopsy specimens obtained at the time of subtemporal decompression for treatment of IIH, although this was challenged by later observations (190). More recent studies using magnetic resonance imaging (MRI) among patients with IIH demonstrated increased water apparent diffusion coefficients and increased white matter water signals (60, 119, 168, 169). The authors suggested that this might result from convective transependymal flow causing interstitial brain edema and increased brain water content (168).

A third possibility is obstruction of CSF or venous outflow as the cause of intracranial hypertension in IIH (82, 143). Many studies (5, 78, 84, 162) have suggested that the underlying mechanism involves disturbed CSF absorption secondary to increased sagittal sinus pressure (necessitating higher CSF pressure to drive bulk flow of CSF across the meninges). A recent study using pressure measurements during intracranial venography demonstrated elevated dural sinus pressures among patients with IIH (88). Although some of the patients in that study exhibited dural sinus thrombosis, venous pressures were elevated even among patients with no obvious evidence of dural sinus obstruction. Those authors hypothesized that the final common pathway for increased ICP in IIH involves elevated venous pressure, leading to increased resistance to CSF absorption and subsequently increased ICP (88). Indeed, among nine patients with IIH who were subjected to direct retrograde cerebral venography, Owler et al. (125) recently identified a subset (five of nine patients) with venous sinus obstruction that was treatable with endoluminal stenting. Direct measurements of the CSF production rate, CSF outflow resistance, and CSF pressure-volume index (an index of intracranial elastance) (159, 166) at various stages of the illness would improve our understanding of the mechanisms underlying IIH (51).

Because there is a female preponderance in IIH, endocrinological dysfunction has been hypothesized to contribute to the disease. Many theories of how obesity might be related to IIH have been proposed, including increased intra-abdominal...
Association with Medications

Obesity-associated sleep apnea may also lead to increased ICP (13, 79, 111). Recent weight gain may be associated with relapses of IIH (62). Treatment of obesity (175, 176) have been demonstrated to reduce papilledema and lower CSF pressures. Furthermore, treatment of obesity (94) and bariatric surgery (surgical treatment of obesity) (175, 176) have been demonstrated to reduce papilledema and lower CSF pressures. Interestingly, weight loss (94) and bariatric surgery (surgical treatment of obesity) (175, 176) have been demonstrated to subsequently increase central venous pressure (174, 175). The most convincing evidence involves tetracyclines and vitamin A and its derivatives. Many case reports have documented patients receiving vitamin A who developed increased ICP with papilledema; the papilledema resolved after withdrawal of the vitamin A source. Symptoms usually develop with doses of more than 50,000 international units among adults and 20,000 international units among children (44). Similarly, many case reports have documented the association between tetracycline and minocycline use and IIH, with resolution when the medication was discontinued (10, 25, 56, 61, 96, 114, 114a, 129).

Association with Systemic Diseases

Various systemic diseases have been associated with IIH, including systemic lupus erythematosus (22, 101, 127), underlying malignancies (193), anemia (21), Addison’s disease (32), hyperthyroidism and hypothyroidism (18, 74, 135), and uremia (23, 66, 123). Of these, the association with uremia is probably the strongest but is complicated by the fact that uremia may lead to hypervitaminosis A (66) and uremia itself can lead to optic neuropathy without papilledema (148).

Association with Venous Obstruction

Dural venous sinus thrombosis has long been recognized as being associated with intracranial hypertension (37, 59). Foley (53) and others (64, 178) reported on cases of “otic hydrocephalus” caused by transverse sinus thrombosis secondary to otitis and mastoiditis. This led some early investigators to consider dural sinus thrombosis as a cause of IIH (137). However, on the basis of the modern modified Dandy criteria, dural sinus thrombosis is best considered a secondary pseudotumor syndrome. Dural sinus occlusion leads to increased venous pressure and higher CSF pressures, with clinical findings of papilledema and headaches (37). Therefore, a specific evaluation for venous disease with imaging studies (especially magnetic resonance venography), to exclude the possibility of dural sinus thrombosis, may be advisable for atypical patients (e.g., nonobese patients) with suspected IIH, before the diagnosis of IIH is established (98).

Certain systemic conditions and medications may be associated with IIH via a hypercoagulable state leading to dural sinus thrombosis. These conditions include malignancies (193), systemic lupus erythematosus (22, 101, 127), protein C and S deficiencies (128), antithrombin III deficiency, Factor V Leiden mutations (104, 194), anticoagulopin antibodies (97, 116), oral contraceptive use (191), and pregnancy (19). Standard treatment of dural sinus thrombosis involves heparin or warfarin anticoagulation therapy or direct endovascular thrombolytic therapy (11). Other venous abnormalities that can elevate intracranial venous pressures, including dural arteriovenous fistulae (29) and carotid-cavernous fistulae (67), have been associated with

<table>
<thead>
<tr>
<th>TABLE 2. Clinical associations with idiopathic intracranial hypertension</th>
<th>Ref. no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>47</td>
</tr>
<tr>
<td>Obesity and weight gain</td>
<td>39, 44, 53, 62, 82, 195</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>13, 79, 111</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>18, 74, 135</td>
</tr>
<tr>
<td>Addison’s disease</td>
<td>32</td>
</tr>
<tr>
<td>Uremia</td>
<td>23, 66, 123</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>22, 101, 127</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
</tr>
<tr>
<td>Vitamin A and derivatives</td>
<td>117, 118, 121, 144, 170, 185, 186</td>
</tr>
<tr>
<td>Antibiotics (especially minocycline and tetracycline)</td>
<td>25, 61</td>
</tr>
<tr>
<td>Hormonal medications</td>
<td>68, 140, 177, 191</td>
</tr>
<tr>
<td>Corticosteroid withdrawal</td>
<td>122</td>
</tr>
<tr>
<td>Lithium</td>
<td>100, 150</td>
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</table>
IIH. Iatrogenic disruption of venous drainage, for example, after acoustic neuroma resection (184), radical neck dissection (91, 95, 106), or catheter-induced subclavian vein thrombosis (9, 95), has also been associated with elevated intracranial venous and CSF pressures. Venous sinus compression by tumors (e.g., meningiomas) has also been reported (107).

**CLINICAL PRESENTATION**

**Symptoms**

Headache is the most common symptom and is observed for nearly all patients (*Table 3*). IIH headaches are typically generalized, episodic, throbbing, and worse in the morning (1, 187). They are often aggravated by Valsalva maneuvers (straining or coughing) and may be associated with retroorbital pain (187). Neck, shoulder, and arm pain is often involved (62). The neck pain may be associated with electric shock-like sensations similar to Lhermitte's sign (31). In addition, transient visual symptoms (obscurations, blurring, and scotomata) and diplopia are frequently noted (62, 82, 146, 195). Pulsatile tinnitus is common (87% in one study [164]) and may be the initial complaint (8, 62, 163–165). The cause of tinnitus is thought to be turbulence resulting from higher-to-lower venous pressures around the jugular bulb, which can be auscultated in some patients (8, 112, 164). Other symptoms can include numbness, incoordination, decreased sense of smell, weakness, and dizziness (*Table 3*).

**Signs**

After recording of a complete history, specifically focusing on possible disease associations (as described above), the evaluation of a patient with potential IIH should continue with complete neurological and ophthalmological examinations. Papilledema, as a criterion for the condition, is observed for virtually all patients with IIH and is the most important sign (see below). However, there have been numerous case reports of patients with IIH for whom papilledema was not observed, and the absence of papilledema is thus not an exclusionary criterion (92, 102, 105, 108, 192, 198). Abducens palsy, a false localizing sign thought to be attributable to traction of the VIth cranial nerve resulting from intracranial hypertension, is observed in approximately 20% of cases (82, 146, 195). Facial palsy may also be observed (20, 28, 153). An afferent papillary defect may signal asymmetric optic neuropathy.

**Ophthalmoscopic Findings**

With the development of computed tomography and MRI, clinicians rely more heavily on imaging to support the clinical localization of disease. In cases of suspected IIH, however, an ophthalmoscopic examination is critical. Papilledema is usually the only objective finding in physical examinations for patients with IIH. The ophthalmoscopic appearance of IIH is most often characterized by bilateral optic nerve head swelling (*Fig. 1*). However, this can be quite subtle, and cases of IIH without papilledema have been reported (92, 102, 105, 108, 192, 198). Papilledema may be asymmetric or unilateral (99,

<table>
<thead>
<tr>
<th>TABLE 3. Symptoms of idiopathic intracranial hypertension</th>
<th>Approximate incidence (%)</th>
<th>Ref. no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papilledema</td>
<td>Virtually all cases</td>
<td>Case reports without: 92, 102, 105, 108, 192, 198</td>
</tr>
<tr>
<td>Headaches</td>
<td>92–94</td>
<td>62, 187</td>
</tr>
<tr>
<td>Transient visual obscurations</td>
<td>30–68</td>
<td>1, 62, 82, 195</td>
</tr>
<tr>
<td>Pulsatile tinnitus</td>
<td>Case reports, 64–87 in two small series</td>
<td>8, 62, 120, 146, 163, 164</td>
</tr>
<tr>
<td>Neck, shoulder, and/or arm pain</td>
<td>44–48</td>
<td>31, 62, 188, 189</td>
</tr>
<tr>
<td>Diplopia</td>
<td>20–38</td>
<td>1, 62, 82, 195</td>
</tr>
<tr>
<td>Numbness</td>
<td>24</td>
<td>62</td>
</tr>
<tr>
<td>Abducens palsy</td>
<td>20</td>
<td>82, 146, 195</td>
</tr>
<tr>
<td>Incoordination</td>
<td>14</td>
<td>62</td>
</tr>
<tr>
<td>Decreased smell</td>
<td>12</td>
<td>62</td>
</tr>
<tr>
<td>Weakness</td>
<td>10</td>
<td>62</td>
</tr>
<tr>
<td>Dizziness</td>
<td>9</td>
<td>86</td>
</tr>
<tr>
<td>Facial palsy</td>
<td>Case reports</td>
<td>20, 28, 153</td>
</tr>
</tbody>
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Optic Disc Edema versus Papilledema

It is important to distinguish the terms optic disc edema and papilledema. Optic disc edema is a general term used to describe any swelling of the optic disc. Its causes include increased ICP, structural diseases, vascular/circulatory diseases, hematological conditions, tumors, collagen vascular and inflammatory diseases, infections, demyelinating diseases, and metabolic and toxic conditions (Table 4). Papilledema refers only to optic disc edema caused by increased ICP.

Most cases of optic disc swelling are caused by optic neuritis, anterior ischemic optic neuropathy (AION), or papilledema. Optic neuritis and AION are usually unilateral, whereas papilledema is bilateral. Papilledema is often asymmetric, however, and optic neuritis and AION can occur bilaterally, creating the potential for diagnostic confusion.

Imaging Findings

Computed tomographic scans demonstrate that, for the vast majority of patients with IIH, ventricular size is either normal or small (138). Patients with IIH have traditionally been thought to have slit ventricles, but a review of computed tomographic findings for 35 patients with IIH demonstrated slit-like ventricles for only 11%; enlarged optic nerve sheaths (47%) and empty sella syndrome (46%) were more common (197). A quantitative analysis of ventricular volume by Jacobson et al. (77) noted no difference between patients with IIH and age-matched control subjects.

The MRI findings in IIH are generally reported as unremarkable, but in fact abnormalities are usually present. The abnormalities include a partially empty sella, flattening of the posterior sclera, dilatation and tortuosity of the optic nerve sheath, and sometimes gadolinium enhancement of the optic disc (Fig. 2) (14, 57). However, the findings are often too subtle and nonspecific to allow the diagnosis of increased ICP on the basis of MRI scans alone. Ophthalmoscopic examinations must be performed to identify patients with increased ICP. A common error in the treatment of patients with headaches and normal MRI results is making the diagnosis of migraine without an adequate ophthalmoscopic examination.

Lumbar Puncture Findings

If the findings on standard MRI scans do not provide compelling evidence of ICP elevation, then a lumbar puncture, with direct measurement of the lumbar subarachnoid pressure, should be performed in cases of suspected papilledema (Fig. 3). A pressure of greater than 250 mm H2O (measured with the patient relaxed, in the lateral decubitus position) is one of the modified Dandy criteria mentioned above. However, it is important to recognize that 42% of asymptomatic obese female patients have opening pressures of greater than 250 mm H2O (69). Conversely, a pressure of less than 250 mm H2O is consistent with papilledema in some cases. ICP monitoring with intraparenchymal pressure monitors may occasionally be necessary if diagnostic doubt persists.

CLINICAL COURSE

The most significant sequela of IIH is blindness or permanent visual impairment caused by prolonged papilledema, with secondary optic atrophy. Because visual loss is usually insidious, patients may be nonchalant regarding vision testing and follow-up monitoring until irreversible damage to the optic nerve occurs. The best corrected Snellen visual acuity should be recorded at each office visit. However, because papilledema affects peripheral vision first, central acuity can be the last to be affected among patients with papilledema. As in glaucoma, the optic disc can sustain substantial and irreversible damage before central visual acuity fails.

Testing of the visual fields with finger confrontation is notoriously insensitive. Wall and George (189) observed Snellen acuity loss in 22% of patients among a cohort of 50 patients with IIH. Only 32% of patients demonstrated abnormal visual fields with confrontation testing, but 92% of patients demonstrated abnormal visual fields with quantitative testing methods. This discrepancy emphasizes that confrontation visual field testing is inadequate for detection of visual field loss among patients with IIH.

Therefore, all patients with a suspected diagnosis of IIH should undergo regular testing of the visual fields with quantitative perimetry. The tangent screen and Goldmann perimetry tests have poor reproducibility and are barely adequate for this purpose. The best method is automated perimetry (Humphrey perimetry), because it allows more accurate measurement of retinal thresholds throughout the visual field. In addition to visual acuity and visual field testing, it is helpful to obtain stereophotographs of the optic discs, to document their appearance over time. These assessments (automated perim-
<table>
<thead>
<tr>
<th>General causes of optic disc edema</th>
<th>Specific causes</th>
</tr>
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<tbody>
<tr>
<td>Increased ICP</td>
<td>Brain tumors</td>
</tr>
<tr>
<td></td>
<td><em>Idiopathic intracranial hypertension</em></td>
</tr>
<tr>
<td></td>
<td>Dural sinus obstruction/thrombosis</td>
</tr>
<tr>
<td></td>
<td>Carotid-cavernous fistulae</td>
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<td></td>
<td>AVMs (dural or parenchymal)</td>
</tr>
<tr>
<td>Structural</td>
<td>Optic disc drüsen</td>
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<td>Glial remnants</td>
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<td>Vascular/circulatory</td>
<td>Hypertension</td>
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<td></td>
<td>Nonarteritic AION</td>
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<td>Arteritic AION (temporal arteritis)</td>
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<td></td>
<td>Congestive heart failure</td>
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<td>COPD/empysema</td>
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<td>Congenital heart disease</td>
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<td></td>
<td>Pickwickian syndrome/obstructive sleep apnea</td>
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<td>Hypoxia</td>
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<td></td>
<td>Ocular ischemia</td>
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<td>Central retinal vein occlusion</td>
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<td></td>
<td>Papillophlebitis</td>
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<td>Radical neck dissection</td>
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<td>Hematological</td>
<td>Anemia</td>
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<td>Acute hemorrhage/acute hypotension</td>
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<td></td>
<td>Polycythemia vera</td>
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<td><em>Idiopathic</em> thrombocytopenic purpura</td>
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<td>Hyperviscosity syndrome</td>
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<td>Waldenström’s macrogloblinemia</td>
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<tr>
<td>Tumors</td>
<td>Meningiomas</td>
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<td>Gliomas</td>
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<td>Hemangiomas</td>
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<td>Hemangiopericytomas</td>
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<td>Metastases</td>
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<td>Orbital tumors</td>
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<td>Spinal tumors, especially parangliomas</td>
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<tr>
<td>Infiltrative tumors</td>
<td>Lymphomas/leukemia</td>
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<tr>
<td></td>
<td>Multiple myeloma</td>
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<td>Polynepath, organomegaly, endocrinopathy, monoclonal gammapathy, skin changes</td>
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<tr>
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<td>Meningeal carcinomatosis</td>
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<td>Hemangioblastomas</td>
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<td>Astrocytomas</td>
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<tr>
<td>Collagen vascular disease</td>
<td>Systemic lupus erythematosus</td>
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<tr>
<td></td>
<td>Polyarteritis nodosa</td>
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</tbody>
</table>

*ICP, intracranial pressure; AVM, arteriovenous malformation; HIV, human immunodeficiency virus; CMV, cytomegalovirus; HSV, herpes simplex virus; EBV, Epstein-Barr virus; COPD, chronic obstructive pulmonary disease; AION, anterior ischemic optic neuropathy; MEWDS, multiple evanescent white dot syndrome.*
etry and optic disc photographs) usually require collaboration with an ophthalmologist.

The appearance of papilledema can be deceptive. The swelling may decrease among patients with papilledema due to progressive optic atrophy. Therefore, it is difficult to interpret the appearance of the optic disc in cases of chronic papilledema; optic nerve function is most important.

For some patients, IIH is a self-limiting condition that spontaneously remits before significant damage to the optic nerve occurs (52). However, Corbett et al. (36) emphasized that severe visual loss is not infrequent. In a follow-up study of 57 patients, 5 to 41 years after the initial diagnosis, blinding or severe visual impairment was noted for one or both eyes of 14 patients (24.6%). That finding is similar to a 17.6% occurrence of optic atrophy and permanent loss of visual acuity noted in an earlier study (139). Of the 12 patients (of 14 patients) who consented to repeat lumbar punctures, 10 exhibited persistent pressure elevation (220–550 mm H2O). That finding emphasizes the need for aggressive management of visual loss resulting from papilledema. Visual loss is usually gradual, but patients with severe papilledema can rapidly become blind. For patients with papilledema, decreased visual acuity, and frequent transient obscurations, vision should be monitored extremely closely and surgical intervention should be performed before it is too late. Visual function can decline rapidly in a matter of hours, creating the potential for a neurological emergency.

**TREATMENT**

**Medical Treatment**

Carbonic anhydrase inhibitors (e.g., acetazolamide) are the only effective medications for treatment of papilledema. Acetazolamide was originally demonstrated by Rubin et al. (145) to variably decrease CSF production by 6 to 57% among human subjects. A standard dosage is a 500-mg time-release capsule twice daily. Acetazolamide has teratogenic effects in animals (Pregnancy Category C), including limb malformations and cortical dysgenesis (6, 151, 161). Although adequate controlled trials have not been performed, case reports have documented neonatal metabolic acidosis and electrolyte abnormalities (113, 126). Therefore, acetazolamide should be avoided, if possible, among pregnant women. Furosemide is also a diuretic but has little effect on CSF production; it may be used for patients who cannot tolerate acetazolamide. The role of corticosteroids in the treatment of papilledema is controversial. A short course of high-dose corticosteroid therapy may be helpful for patients with acute visual loss resulting from fulminant papilledema (103). However, corticosteroids should not be used chronically for treatment of papilledema.

Weight loss can be beneficial for patients with papilledema resulting from IIH. Professional dietary counseling and weight loss programs may be recommended. It is difficult to prove that weight loss improves papilledema in IIH because 1) acetazolamide administration is often initiated concurrently (80), 2) few patients lose enough weight to test the theory, and 3) the disease can remit spontaneously. However, a history of recent weight gain often accompanies the initial presentation of IIH. Interestingly, Sugerman et al. (175) demonstrated dramatic decreases in CSF pressure and symptoms among obese patients treated with gastric stapling.

Because certain medications, such as vitamin A, vitamin A derivatives, and tetracycline, have been associated with intracranial hypertension (see above), these medications should be
discontinued if possible to assess the clinical response. For pediatric patients receiving all-trans-retinoic acid as chemotherapy for leukemia (121, 185, 186), it may be preferable to treat the secondary pseudotumor syndrome, rather than discontinuing the medication. It is not necessary to discontinue oral contraceptives in women with IIH.

Some neurologists advocate serial lumbar punctures (e.g., twice weekly) as an alternative to surgery for patients with papilledema that cannot be controlled medically. However, serial lumbar punctures are a poor approach because 1) most obese patients with chronic papilledema are difficult to treat with lumbar punctures and 2) patients generally dislike serial lumbar punctures. At best, lumbar puncture and drainage of a large volume of CSF are useful emergency measures for patients with severe papilledema and sudden extinction of vision. In some cases, it is necessary to hospitalize patients with lumbar subarachnoid drains until surgery can be scheduled. This is a good strategy if lumbo-peritoneal (LP) shunting is planned, although it may increase the risk of infection. Optic nerve sheath fenestration is easier to perform when the sheath is turgid; therefore, the drain should be removed or clamped before surgery.

**Surgical Treatment**

Surgical intervention is required as soon as medical treatment fails. A common management error is to delay too long before recommending surgery. Corbett (33) emphasized that “there is no ‘acceptable’ level of visual field or acuity loss which one should wait for—visual loss which continues despite optimum medical therapy is sufficient reason to turn to decompression” (33, p 228). Surgery should also be considered for patients who are unlikely to return for follow-up visits or who are unable to cooperate with medical therapy. Surgery should be considered not only for treatment of visual loss but also for treatment of intractable headaches.

**History of Surgical Treatment of Papilledema**

Optic nerve sheath fenestration, which was introduced by de Wecker (43), was the first treatment devised for the surgical relief of papilledema. The operation involved insertion of a guarded neurotome into the orbit to slit the optic nerve sheath via a conjunctival incision. However, subtemporal decompression, which was introduced by Dandy (39) in 1937, became the operation of choice for papilledema. Dandy performed a right subtemporal craniectomy for decompression and reported excellent initial results in alleviating headaches and preventing visual loss. However, the longer-term efficacy was uncertain and morbidity and complications were significant, including seizures, infections, focal brain damage, cosmetic disfigurement, intracranial hematomas, and further visual deterioration (65).

**LP Shunting**

Subtemporal decompression rapidly became obsolete after the introduction of intracranial shunting procedures by Ingraham et al. (75) and Matson (109). However, the ventriculoperitoneal (VP) shunts devised by those pioneers were difficult to insert among patients with IIH, because the ventricles were often small. The development of LP shunting circumvented this problem. Vander Ark et al. (183) published the first description of LP shunting for patients with IIH. Soon thereafter, Spetzler et al. (171) developed a method for percutaneous insertion of the shunt into the lumbar sac, greatly facilitating placement of LP shunts.

After the introduction of LP shunting, few studies documenting its efficacy for the treatment of papilledema were published. Anecdotal reports of success suggested that it was a curative procedure, as long as the shunt functioned properly. In 1981, Johnston et al. (85) published a major review of 134 cases of IIH treated between 1942 and 1979, with a mean follow-up period of 11.6 years. Fourteen patients received shunts (six VP shunts and eight LP shunts). Of the six patients who received VP shunts, four demonstrated resolution of all symptoms within 6 months. One patient developed a shunt obstruction that necessitated revision, and another patient experienced a shunt infection that necessitated removal. Of the eight patients who received LP shunts, all demonstrated improvement within 1 month. One patient experienced a shunt infection, and one patient exhibited severe low-pressure symptoms as a result of overshunting. In a follow-up study, Johnston et al. (83) reported on 36 patients who received shunts for treatment of IIH. The patients required a total of 86 shunting procedures, with a complication rate of 52% and a failure rate of 48%; the lowest revision and complication rates were associated with LP shunts.

A multicenter review of the outcomes of shunting for 37 patients was performed in the late 1980s (141). In that study, 37 patients received a total of 73 LP shunts and 9 VP shunts, and only 14 patients remained “cured” after a single surgical procedure. Sixty-four percent of shunts lasted less than 6 months, with shunt failure (55%) and low-pressure headaches (21%) being the most common reasons for reoperation. The vision of most patients either improved (13 patients) or stabilized (13 patients) postoperatively. That report initially led to a resurgence of interest in optic nerve sheath fenestration among ophthalmologists. However, the finding that many optic nerve sheath fenestrations fail within 1 year, as well as mounting evidence of serious complications (see below), has restored LP shunting as the favored surgical treatment option.

Two major studies recently demonstrated the efficacy of LP shunting for treatment of IIH. Eggengerber et al. (48) conducted a retrospective study of 27 patients with IIH, who were monitored for a median of 47 months after shunting. Visual loss was the main reason for surgery for 14 patients; headaches were the reason for the remaining 13 patients. Vision improved or remained the same for all 14 patients, and headaches improved for all patients. There were no serious complications, except for shunt failure. Fifteen patients (56%) required shunt revision, sometimes more than once (range, 1–13 revisions). The average number of revisions per patient was 2.4, with one revision being performed every 2.6 years. The
authors concluded that LP shunting was a satisfactory treatment for the majority of patients.

Burgett et al. (17) reported data for 30 patients who underwent LP shunting for treatment of IIH. The mean follow-up period was 35 months. Of 14 eyes with impaired acuity, 10 eyes (71%) improved by at least two chart lines; only 1 eye experienced a decline in vision. Goldmann perimetry documented improvement for 64% of eyes with abnormal fields, and no eyes exhibited any worsening. Again, the only complication was frequent shunt obstruction. Twelve patients required no shunt revision. The remainder underwent a mean of 2.5 revisions/patient (excluding four patients who underwent exceptionally high numbers of revisions, i.e., 38, 29, 10, and 10).

Those two studies provided encouraging data regarding the efficacy of LP shunting; the operation seems effective, as long as the shunt remains patent. As in most large reviews (27, 83, 141), obstruction was the most common complication of LP shunts (accounting for 65% of revisions in the study by Eggenberger et al. [48]). In all patients with suspected shunt obstruction, lumbar subarachnoid pressure should be measured. Neuroimaging findings may not be revealing, because the ventricles are not enlarged in IIH (89). Technetium-99 shunt function studies can provide valuable data by demonstrating tracer flow into the abdomen and providing a halftime for radionuclide clearance (4, 73).

Other complications associated with LP shunting in those studies were less common (Table 5). Secondary intracranial hypotension caused by CSF overdrainage accounted for 15% of revisions in the study by Eggenberger et al. (48), and lumbar radiculopathy accounted for 4.5% of all revisions. Shunt infections occur in only approximately 1% of cases of LP shunting (154). Tonsillar herniation (acquired Chiari I malformation) (26, 196) and syringomyelia (50) are other recognized complications of LP shunting, but they only rarely necessitate revision (70). Tonsillar herniation may create a “new” headache syndrome. A problem common to all obese patients is technical difficulty with excessive subcutaneous abdominal fat, which necessitates large incisions. In this respect, the use of laparoscopic techniques for insertion of the peritoneal catheter is potentially advantageous.

LP shunt valve pressure mechanisms with external pressure control are now being developed. We currently prefer LP shunting with an inline horizontal-vertical valve, rather than stereotactic VP shunting. One commercially available system describes two pressure ranges, depending on ventricular size and/or body habitus. For each patient group, there is a fixed horizontal pressure setting (50–80 mm H$_2$O or 85–125 mm H$_2$O) and three different vertical pressure settings. For patients with IIH (small ventricles, large body habitus, and suspected intracranial hypertension), the senior author prefers to begin with the higher horizontal pressure setting (85–125 mm H$_2$O) and the midrange vertical pressure setting (265–365 mm H$_2$O).

For patients with repeated LP shunt obstructions, the option of VP shunting should be considered. First, although the technique is more invasive, the long-term outcomes may be better (87). Second, technical innovations in stereotactic surgery enable accurate targeting of the lateral ventricle. A recent study of seven patients treated with stereotactic VP shunts (using a Cosman-Roberts-Wells frame) for IIH demonstrated successful uncomplicated shunt placement in all cases (182). Five of

| **TABLE 5. Complications of surgical procedures for treatment of papilledema** |
|---------------------------------|---------------------------------|
| **Optic nerve sheath fenestration** | **Lumboperitoneal shunt** |
| Central retinal artery occlusion | Obstruction |
| Branch retinal artery occlusion | Infection |
| Central retinal vein occlusion | Low-pressure headaches |
| Choroidal infarction | Radiculopathy |
| Traumatic optic neuropathy | Tonsillar herniation (acquired Chiari I malformation) |
| Hemorrhage (intrasheath or intraorbital) | Syringomyelia |
| Diplopia | Subdural hematoma |
| Pupil dilation resulting from sphincter denervation | Shunt migration |
| Anterior segment ischemia | |
| Compressive optic neuropathy resulting from orbital cyst | |
| Corneal delle formation | |
| Infection | |
the seven patients experienced resolution of papilledema and six of the seven experienced resolution of headaches postoperatively. Another study demonstrated the application of frameless stereotaxy and intraoperative fiberoptic endoscopy for precise ventricular catheter insertion (179). Those studies support the idea of routine stereotactic VP shunting in IIH, with either frame-based or frameless stereotaxy. Third, VP shunting may facilitate noninvasive assessment of shunt function, because it provides a reservoir for isotope shunt function testing; noninvasive analysis of LP shunt function has been limited to radiological findings (93).

**Optic Nerve Sheath Fenestration**

The failure rate associated with LP shunting renewed enthusiasm for optic nerve sheath fenestration among ophthalmologists in the 1980s. The procedure had continued to be performed by a few surgeons (7, 41, 42, 55, 90) but only sporadically. In 1988, three major reports appeared in the ophthalmological literature, describing the outcomes of optic nerve sheath fenestration for treatment of IIH in large series of patients (15, 35, 157). The results were surprisingly good; the operation seemed to provide effective treatment of papilledema and maintained or improved visual acuity for 85 to 100% of patients. However, the follow-up periods were short in those studies.

In a study of 53 patients (101 eyes), Spoor et al. (173) reported that optic nerve sheath fenestration improved visual function for 69 eyes with acute papilledema and 10 eyes with chronic papilledema. In a later report with longer follow-up periods, Spoor and McHenry (172) described the outcomes of optic nerve sheath fenestration for 75 eyes of 54 patients with IIH. After initial improvement in visual function, 24 eyes (32%) required repeat optic nerve sheath fenestration because of deteriorating visual function. Deteriorating vision was detected a mean of only 10.4 months after surgery, and 25% of eyes continued to lose vision even after repeat surgery.

In 1989, Sergott et al. (156) reported improved visual function for 12 of 14 patients with progressive nonarteritic AION who were treated with optic nerve sheath fenestration. In 1995, the National Eye Institute-sponsored Ischemic Optic Neuropathy Decompression Trial Research Group reported the results of a multicenter study of optic nerve sheath fenestration for treatment of AION (76). The study found no benefit of optic nerve sheath fenestration for treatment of AION, contradicting the study by Sergott et al. (156), and documented significant complications of the procedure, including optic nerve injury during surgery (Table 5). The incidence of catastrophic visual complications was 3 cases/115 patients, or 2.6%. Another study reported postoperative blindness for 3 of 200 patients (1.5%) (155). A 2% risk of outright blindness has discouraged patients and ophthalmologists. Plotnik and Kosmorsky (130) emphasized that the complication rate may be as high as 40%, including vascular compromise (11%, central retinal artery occlusion, branch retinal artery occlusion, or outer retinal ischemia), transient ocular motility disturbances (29%), and papillary dysfunction (11%). Although enthusiasm for optic nerve sheath fenestration has moderated, the procedure remains a viable option for the prevention of visual loss resulting from papilledema (3, 12, 63, 71).

**SUMMARY AND RECOMMENDATIONS**

We recommend LP shunting over optic nerve sheath fenestration as the initial surgical treatment for IIH for the following reasons. 1) LP shunting involves no direct risk to the eye. The 2% risk of devastating optic nerve or retinal vascular injury with optic nerve sheath fenestration is discouraging. 2) For most patients, surgical treatment of the optic nerve sheath of one eye improves papilledema in both eyes, but the benefit in the contralateral eye is usually less pronounced. For patients with severe papilledema, optic nerve sheath fenestration may be required for both eyes (two operations, with twice the risk of complications). Successful LP shunting needs to be performed only once. 3) Although shunt obstruction is a serious problem (almost 50% in the first 2 yr after shunt placement), the data reported by Spoor and McHenry (172) suggest that a similar number of optic nerve sheath fenestrations become closed by scarring over a similar period. 4) Many patients with visual loss resulting from papilledema also experience headaches attributable to increased ICP. After optic nerve sheath fenestration, ICP usually remains elevated (7, 16, 35, 72, 90), suggesting that optic nerve sheath fenestration works without producing major decreases in CSF pressure (as measured with lumbar punctures). The operation probably works by filtering small quantities of CSF into the orbit, which may produce a local pressure reduction within the subarachnoid space immediately behind the optic nerve head (152). It is true that optic nerve sheath fenestration can provide relief of headaches for some patients with papilledema (15, 35, 41, 55, 157). However, LP shunting is more effective for treating headaches and thus has the advantage of improving both papilledema and headaches. For many patients, headaches represent the main reason to operate. 5) Some patients with IIH exhibit diplopia resulting from abducens palsy. This usually resolves after LP shunting. In contrast, optic nerve sheath fenestration does not improve diplopia and can result in new diplopia as a postoperative complication. 6) LP shunting usually results in complete resolution of papilledema, as long as the shunt is functioning properly. After optic nerve sheath fenestration, some residual papilledema often persists. 7) Some patients cannot cooperate with vision testing. For those patients, it is difficult to monitor visual function after surgical treatment of papilledema. In such cases, objective proof of normal ICP in lumbar punctures is desirable. This option is not useful after optic nerve sheath fenestration, because pressure usually remains high.

After a surge in popularity between 1987 and 1993, outcome reports suggested that optic nerve sheath fenestration may be less effective than LP shunting for treatment of papilledema and may be more prone to complications. LP shunting is the better option but is limited by shunt obstruction. Stereotactic
VP shunts may offer reduced rates of shunt obstruction. All patients with IIH require close postoperative follow-up because there is a threat to vision even after surgery. A multicenter prospective trial comparing the efficacy of LP shunting versus optic nerve fenestration or LP shunting versus VP shunting would be useful for determination of the optimal roles for these surgical treatment modalities.

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COMMENTS

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The authors make a case for lumboperitoneal shunt as a treatment potentially superior to optic nerve sheath fenestration as initial treatment for idiopathic intracranial hypertension. There is rationale for this, such as treating the intracranial pressure rather than only the visual symptoms of papilledema and vision loss. This does not explain the reports of improvement of multiple cranial symptoms after optic nerve sheath fenestration. In addition, the rather frightening incidence of shunt obstruction after lumboperitoneal shunt and the possibility of other complicating deteriorations such as intracranial hypotension or brainstem traction are not well quantified. Indeed, both treatments are very poor at establishing a long-term treatment. It is safe to say that no treatment has been universally effective and that the search for further treatments, both medical and surgical, should continue. A much stronger case could be made than the authors do for stereotactic ventriculoperitoneal shunt placement because of the improved ability to regulate intracranial pressure and the decreased risk of foramen magnum compaction. The authors’ decision to recommend lumboperitoneal shunt is not supported by positive evidence in this article.

The discussion of idiopathic intracranial hypertension is interesting. The relationship of the syndrome to vitamin A is compelling and calls for further investigation as to pathogenesis. The authors do make an important point that patients with headaches and normal magnetic resonance imaging scans are commonly misdiagnosed as having a migraine variant. Further investigation, especially formal ophthalmological examination, should always be included in the

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evaluation of such patients. This is especially important because the normal range of intracranial pressure may vary widely in obese patients. Although the article covers the pitfalls of the treatment options discussed, I would recommend a more careful review of other treatment options, including weight loss, venous studies, and stereotactic ventricular shunting.

Robert J. Dempsey
Madison, Wisconsin

The authors have provided a thorough and practical review of idiopathic intracranial hypertension. The pathophysiology of idiopathic intracranial hypertension/pseudotumor cerebri is most likely related to cerebral venous hypertension. So-called secondary pseudotumor cerebri patients with dural sinus thromboses represent only the extreme of a spectrum. I think that more effort should be placed on addressing the primary problem, venous hypertension, both diagnostically and therapeutically. From a diagnostic viewpoint, magnetic resonance venography lacks sufficient sensitivity to detect hemodynamically significant dural sinus obstructions. As the availability and use of percutaneous retrograde venous sinus dynometry increases, an increasing number of “idiopathic” cases will instead be found to be secondary to sinus strictures (despite “normal” magnetic resonance venographic studies). The placement of dural sinus stents is still relatively new, and long-term follow-up will be required before we can determine their efficacy and safety. Bariatric surgery, which lowers the cardiac right atrial pressure and secondarily the dural sinus pressure, may be indicated in obese patients in whom a dural sinus pressure gradient (stricture) was not found by dynometry. It is hoped that cerebrospinal fluid diversion procedures, which can be quite problematic in these patients, will diminish in importance and frequency.

Marvin Bergsneider
Daniel F. Kelly
Los Angeles, California

The authors have provided an excellent review of a very controversial topic. They have adopted the term idiopathic intracranial hypertension in place of pseudotumor cerebri, and I would certainly support that change. I would disagree with their use of the term secondary pseudotumor syndrome to include the known causes of intracranial hypertension. Certainly, if a patient has elevated intracranial pressure from an obstructed venous sinus or from hypervitaminosis A, they have simply “intracranial hypertension” and no longer “idiopathic intracranial hypertension.” The term pseudotumor should be abandoned.

William F. Chandler
Ann Arbor, Michigan

The authors have reviewed the history, diagnosis, and therapy of intracranial hypertension. I agree with the authors’ statement that the term idiopathic intracranial hypertension should be adopted in place of pseudotumor cerebri. This is a nice review, and the authors have put into perspective some historical and contemporary concepts regarding the pathophysiology of and treatment options for this disorder.

Warren R. Selman
Cleveland, Ohio

This article comes from the neurosurgery and ophthalmology departments at the University of California, San Francisco. The authors present a workman-like review of intracranial hypertension. For neurosurgeons, the greatest value of the article may be the extensive list of medications and medical conditions that have been reported to be associated with idiopathic intracranial hypertension and the compilation of the results of optic nerve sheath decompression.

Robert G. Grossman
Houston, Texas

Spirit rover robot-generated image of the Martian landscape. An image taken on January 27, 2004, from Spirit’s PanCam looking west depicts the nearby hills named after the astronauts of the Apollo 1. The crew of Apollo 1 perished in a flash fire during a launch pad test of their Apollo spacecraft at Kennedy Space Center, FL, on January 27, 1967. Miniaturization and increased sophistication in robotic technology make possible the exploration of Mars; such miniaturization and sophistication fuel technology transfer from aerospace engineering to medical, and especially neurosurgical, robotics. (Courtesy, NASA/JPL/Cornell.)