Idiopathic intracranial hypertension (pseudotumor cerebri): Clinical features and diagnosis

INTRODUCTION — Idiopathic intracranial hypertension (IIH) is also commonly called pseudotumor cerebri. It is a disorder defined by clinical criteria that include symptoms and signs isolated to those produced by increased intracranial pressure (eg, headache, papilledema, vision loss), elevated intracranial pressure with normal cerebrospinal fluid composition, and no other cause of intracranial hypertension evident on neuroimaging or other evaluations. IIH primarily affects women of childbearing age who are overweight.

While once called “benign intracranial hypertension,” to distinguish it from secondary intracranial hypertension produced by a neoplastic malignancy, it is not a benign disorder. Many patients suffer from intractable, disabling headaches, and there is a risk of severe, permanent vision loss. Even patients with mild vision loss have an associated reduction in quality of life [1].

This topic will discuss the clinical features and diagnosis of IIH. The epidemiology and pathogenesis, as well as the prognosis and treatment of this disorder are discussed separately. (See "Idiopathic intracranial hypertension (pseudotumor cerebri): Epidemiology and pathogenesis" and "Idiopathic intracranial hypertension (pseudotumor cerebri): Prognosis and treatment".)

CLINICAL PRESENTATION — A typical presentation of idiopathic intracranial hypertension IIH is that of an obese woman of childbearing age who complains of headaches and is found to have papilledema on funduscopic examination. Other potential high risk groups are discussed separately. (See "Idiopathic intracranial hypertension (pseudotumor cerebri): Epidemiology and pathogenesis", section on 'Risk factors' and "Idiopathic intracranial hypertension (pseudotumor cerebri): Epidemiology and pathogenesis", section on 'Associated conditions'.)

Symptoms — In one case series and in the Idiopathic Intracranial Hypertension Treatment Trial, the most common symptoms of idiopathic intracranial hypertension (IIH) were [2,3]:

- Headache (84 to 92 percent)
- Transient visual obscurations (68 to 72 percent)
- Intracranial noises (pulsatile tinnitus) (52 to 60 percent)
- Photopsia (48 to 54 percent)
- Back pain (53 percent)
- Retrobulbar pain (44 percent)
- Diplopia (18 to 38 percent)
- Sustained visual loss (26 to 32 percent)

These symptoms, even as a cluster, are not specific for IIH. In one case-control study, these symptoms were as common in age and gender-matched controls who were recruited from hospital waiting areas; although the prevalence, severity, and frequency were lower in this group [4]. Pulsatile tinnitus was the most useful distinguishing feature.

Headache — Headache is the most common presenting symptom of IIH [2,3]. However, the features of
headaches in IIH patients are variable and are not specific to IIH. Many, but not all patients note that the pain is of unusual severity [2,5]. The headaches may be lateralized and throbbing or pulsatile in character. They may be intermittent or persistent, occur daily or less frequently. Associated nausea and vomiting are not infrequent. Some patients describe headache exacerbation with changes in posture and some may report that relief occurs with nonsteroidal anti-inflammatory medications and/or rest. Retrobulbar pain and pain with eye movement or globe compression are somewhat more specific features for IIH. In some patients, the pain follows a trigeminal or cervical nerve root distribution [5]. Neck stiffness and back pain are also commonly reported [2,6].

In most cases, the features of headache are consistent with other primary headache disorders including migraine and tension-type headache [7,8]. The often refractory nature of the headache may lead the patient to overuse analgesic medication, suggesting or even causing a superimposed rebound headache, further obscuring the diagnosis and making treatment challenging [9]. (See "Medication overuse headache: Etiology, clinical features, and diagnosis" and "Medication overuse headache: Treatment and prognosis".)

Rare patients present without headache [10,11]. Among younger children, headache is a less universal finding [6,12]; in one series, 29 percent of children with IIH did not have headache [13]. In one large case series, men were less likely to complain of headache than women [14]. In the absence of headache, the diagnosis is often suggested during a routine ocular examination when papilledema is incidentally discovered.

**Visual symptoms** — Transient visual obscurations occur in about two-thirds of patients with papilledema. These last seconds at a time and can be bilateral or unilateral [2]. The frequency is variable, ranging from rare or isolated episodes to those occurring several times a day. Some patients note that these can be precipitated by changes in position (usually standing, but sometimes lying down or bending over), Valsalva, bright light, or eye movement (ie, gaze-evoked) [2]. The frequency is variable, ranging from rare or isolated episodes to those occurring several times a day. Some patients note that these can be precipitated by changes in position (usually standing, but sometimes lying down or bending over), Valsalva, bright light, or eye movement (ie, gaze-evoked) [2,4]. The occurrence of transient visual obscurations does not appear to correlate with the degree of intracranial pressure elevation or the extent of disc swelling, and is not predictive of future visual loss [4,15].

Photopsias, brief sparkles or flashes of light, can also occur in patients with IIH and, similar to visual obscurations, can be provoked by positional changes and Valsalva [4].

A subset of individuals with IIH have a more malignant or fulminant course with rapid development of vision loss within a few weeks of symptom onset [16-19]. This is generally apparent at presentation. To limit the severity of permanent vision loss, more aggressive treatment measures are considered at the outset, after the diagnosis is established. (See "Idiopathic intracranial hypertension (pseudotumor cerebri): Prognosis and treatment".)

**Intracranial noise (tinnitus)** — Pulsatile tinnitus (also called pulse synchronous tinnitus) is common in IIH and in the setting of headache, is very suggestive of IIH [4,9,20]. Patients often describe hearing rushing water or wind. This symptom can be persistent or intermittent and is believed to represent vascular pulsations transmitted by cerebrospinal fluid under high pressure to the venous sinuses [21].

**Diplopia** — Patients with IIH may report intermittent or continuous horizontal diplopia. This is typically due to a unilateral or bilateral sixth cranial nerve palsy or divergence insufficiency from increased intracranial pressure. Rarely, other causes of diplopia can occur in IIH (eg, other cranial neuropathies, decompensated phoria) [22]. (See 'Other cranial nerve deficits' below.)

**Examination** — The most common signs in IIH are:

- Papilledema
- Visual field loss
- Sixth nerve palsy

**Papilledema** — Papilledema is the hallmark sign of IIH (picture 1A-B). Papilledema is described in detail separately. (See "Overview and differential diagnosis of papilledema".)
While typically bilateral and symmetric, papilledema may be asymmetric or frankly unilateral [22-25]. In one series, 10 percent of 478 IIH patients had highly asymmetric papilledema with greater visual loss in the eye with higher grade of papilledema [23]. In the IIHTT, asymmetric papilledema was noted in 7 percent [3]. Such patients may also have a relative afferent pupillary defect.

Papilledema can be graded in severity. We use the Frisén scale for grading papilledema (table 1 and picture 1A-F). Patients with more severe papilledema are at higher risk of permanent visual loss [23]. It is helpful to take photographs of both optic discs and grade the severity of papilledema at the initial visit and each follow-up. (See "Idiopathic intracranial hypertension (pseudotumor cerebri): Prognosis and treatment", section on 'Treatment goals and monitoring'.)

Other findings on funduscopic examination may include macular exudates and macular edema, choroidal folds across the macula (usually resulting from flattening of the globes from increased intracranial pressure), choroidal neovascularization, and serous retinal elevation around the nerve head [26].

Patients with headaches and elevated opening pressure on lumbar puncture but no papilledema have been described but are rare [8-10,27-31]. This has been speculated to be due to anatomic differences, or to early presentation prior to the development of papilledema [32]. It is also possible that these patients may not have the same IIH syndrome as those who present with papilledema. Opening pressures may not have been recorded correctly (See 'Lumbar puncture' below.) It has been noted that opening pressures tend to be lower (perhaps only borderline elevated) in such patients. Importantly, patients without papilledema are at lower risk for vision loss as compared to typical patients with IIH with papilledema [8,31,33].

Ophthalmologic evaluation is advised to confirm the presence of papilledema and to evaluate those patients with questionable or subtle papilledema [34]. (See 'Ophthalmologic evaluation' below.)

**Visual loss** — Loss of vision is the major morbidity in IIH and may be present on initial evaluation [2,15]. Vision loss is usually gradual but can be abrupt. Such patients have a more fulminant course and more significant permanent vision loss. (See "Idiopathic intracranial hypertension (pseudotumor cerebri): Prognosis and treatment", section on 'Prognosis'.)

Visual acuity is less than 20/20 in 10 to 29 percent of patients on presentation [2,3,35-37]. However, visual acuity is an insensitive measure of vision loss in IIH. Visual field loss occurs before loss of acuity; confrontation visual fields are abnormal (nasal loss, temporal loss, visual blurring) in up to 32 percent at presentation, but are often unreliable [2,37]. Perimetry gives a more accurate and detailed assessment of visual field abnormalities and is an essential feature of the evaluation of a patient with IIH. (See 'Ophthalmologic evaluation' below.)

The visual field loss is typically peripheral with predominate nerve fiber bundle type defects. Central visual field can be involved late in the course or earlier if there is concomitant macular pathology (serous detachment, macular hemorrhage, or edema), choroidal folds, or choroidal neovascular membrane.

**Abducens palsy** — A sixth cranial nerve (abducens) palsy may be unilateral or bilateral in patients with IIH [3,10]. This reflects a nonlocalizing effect of elevated intracranial pressure on the sixth nerve, which has a long intracranial course before exiting the skull.

**Other cranial nerve deficits** — Other cranial nerve deficits that resolve with IIH treatment are noted in case reports. Some of these may be more common in prepubertal children than in older patients [35,38]:

- Olfactory [39-42]
- Oculomotor [22,33,43,44]
- Trochlear nerve [33,45]
- Trigeminal nerve [22,43,46]
- Facial nerve [6,13,43,47]
- Auditory nerve [20,48,49]
Other neurologic signs — Patients with IIH do not usually have overt cognitive deficits. However, in one cohort of 31 patients with IIH who underwent neuropsychological testing, deficits in reaction time and processing speed were noted that persisted on retesting at three months despite improvement in measured ICP and in headache [50]. Patients were not on medications potentially affecting cognition at the time of initial testing. This result is difficult to interpret due to the similar effects of chronic headache on these measures.

EVALUATION — Increased intracranial pressure should be suspected in a patient with headache and papilledema. Urgent neuroimaging is required to exclude secondary causes of intracranial hypertension. If the neuroimaging study reveals no structural etiology for intracranial hypertension, a lumbar puncture (LP) is performed to document an opening pressure and to exclude other conditions. Ophthalmologic evaluation is required to document the severity of optic nerve involvement and monitor response to treatment.

The diagnosis of IIH may be suspected prior to the evaluation, on the basis of a history and examination that reveals conditions or medications that are associated with IIH; neuroimaging and LP are still required to exclude other conditions. (See "Idiopathic intracranial hypertension (pseudotumor cerebri): Epidemiology and pathogenesis", section on 'Associated conditions'.)

In addition, all patients with bilateral optic disc edema should have a measurement of the systemic blood pressure as optic neuropathy related to malignant hypertension can mimic papilledema and can also produce headache and other symptoms that might be mistaken for IIH. (See "Moderate to severe hypertensive retinopathy and hypertensive encephalopathy in adults".)

Some also suggest that all patients with IIH have a complete blood count to exclude anemia that may be causative or contributory to the patient's condition [51].

Magnetic resonance imaging — In a patient with headache and papilledema, the primary purpose of neuroimaging is to exclude secondary causes of increased intracranial pressure. (See 'Secondary intracranial hypertension' below.)

Magnetic resonance imaging (MRI) with MR venography (MRV) is the preferred test. A CT scan may be necessary for patients with contraindications to MR imaging (eg, pacemakers, metallic clips in head, metallic foreign bodies) and some morbidly obese or claustrophobic patients. The use of contrast enhancement increases the sensitivity of the study particularly for subtle intracranial masses (eg, gliomatosis cerebri) and meningeal-based pathologies [52].

MRV, particularly with contrast administration, is a more sensitive test than standard MRI for the detection of cerebral venous thrombosis [53]. This potential cause of secondary intracranial hypertension can have a similar clinical presentation to IIH. (See "Etiology, clinical features, and diagnosis of cerebral venous thrombosis", section on 'Clinical aspects'.) It is our practice to include a postcontrast MRV with MRI when evaluating patients with suspected IIH. If a patient comes to us with a normal MRI without MRV, and there are no other risk factors for CVT (including no oral contraceptive use), and the patient has a typical risk profile for IIH (an obese woman of childbearing age), we may defer MRV unless there is rapid clinical progression or poor response to treatment.

While the brain parenchyma and ventricles appear normal on MRI or CT in patients with IIH, other MRI abnormalities may be seen and suggest IIH [54-60]:

- Flattening of the posterior sclera (43 to 80 percent)
- Distension of perioptic subarachnoid space (45 to 67 percent)
- Enhancement (with gadolinium) of the prelaminar optic nerve (7 to 50 percent)
- Empty sella (25 to 80 percent)
- Intraocular protrusion of the prelaminar optic nerve (3 to 30 percent)
- Vertical tortuosity of the orbital optic nerve (40 percent)

These findings are not, individually or in the aggregate, diagnostic of IIH; nor do their absence exclude the
diagnosis [54,61-63]. Other abnormalities reported in a few cases include tonsillar ectopia, narrowing of the Meckel’s cave and cavernous sinuses, meningoceles, and widening of the foramen ovale [64-67].

There are many reports of cerebral venous abnormalities on magnetic resonance venography (MRV) in patients with IIH. In particular, narrowing of the transverse venous sinus is common in IIH and suggests increase intracranial pressure [68]. Depending on the MR technology utilized, this finding is reported in 65 to 90 percent of patients with IIH [59,69,70]. Although very common in IIH, transverse sinus stenosis is not specific of IIH.

**Lumbar puncture** — Elevated opening pressure on lumbar puncture (LP) is an essential element of the diagnosis of IIH; however, there are some pitfalls in accurate measurement and interpretation.

For accurate pressure recording, the patient should be relaxed and lying in the lateral decubitus position with legs extended [52]. Other positions (prone, sitting) can give falsely elevated readings, as can anxiety and pain and the use of sedating medications [71]. Misleading low readings can be obtained after multiple LP attempts or in the setting of hyperventilation and treatment with intracranial pressure lowering medications. CSF pressures can vary, and a normal reading in a patient with IIH may reflect an atypically low reading for that patient. Repeating the LP may be required in a patient if suspicion for IIH remains high after one normal CSF reading [33,72]. In rare patients, CSF pressure monitoring may be required to document elevated CSF pressure, but this is exceptional [34,73,74].

Traditionally, the upper limit of normal for opening pressure in adults is 200 mmH\(_2\)O. Some believe that obese patients may have a higher upper limit of normal, with opening pressures that may normally approach 250 mmH\(_2\)O [75]. However, others have not correlated obesity with elevated intracranial pressure in the absence of IIH [76,77]. We and others consider pressures less than 200 mmH\(_2\)O to be normal, greater than 250 mmH\(_2\)O to be abnormal, and 200 to 250 mmH\(_2\)O to be equivocal [52,72,76]. When opening pressure measures are equivocal, we use the presence or absence of MRI findings described above to support the diagnosis of IIH.

In young children (< 8 years), higher upper limits of normal have been proposed, particularly in obese or sedated children [71,78]. In one case series of 197 pediatric patients without symptoms or other evidence for increased intracranial pressure, the authors determined the upper limit of normal (based upon the 90\(^{th}\) percentile) to be 280 mmH\(_2\)O, and 250 mmH\(_2\)O in children who were not sedated or obese [71]. In a follow-up study, only 1 of 36 children with IIH had a pressure lower than 280 mmH\(_2\)O (220 mmH\(_2\)O), while 16 of 40 control patients had an opening pressure greater than 200 mmH\(_2\)O (all were less than 280 mmH\(_2\)O) [78]. It seems reasonable to consider very elevated levels (>280 mmH\(_2\)O) to be unequivocally abnormal (in a properly performed procedure), while intermediate levels (200 to 280 mmH\(_2\)O) should be interpreted along with the preponderance of other clinical data that suggests a diagnosis of IIH [79].

In addition to measuring the opening pressure, the cerebrospinal fluid (CSF) is analyzed for cell count and differential, glucose, and protein. Appropriate CSF studies for microbial agents, CSF cytology, and antigen testing (eg, CSF VDRL) may be indicated if the CSF content is abnormal or the clinical situation suggests additional testing. Cerebrospinal fluid composition (protein, cells, glucose) is normal in patients with IIH. (See "Lumbar puncture: Technique, indications, contraindications, and complications in adults".)

**Ophthalmologic evaluation** — Ophthalmological evaluation is essential for all patients with suspected IIH. A complete ocular examination should document formal visual field examination, dilated fundus examination, and optic nerve photographs. Orbital ultrasound and fluorescein angiography can be utilized if the presence of papilledema is subtle or questionable. (See "Overview and differential diagnosis of papilledema".)

Visual field testing is essential in IIH to assess the severity of optic nerve involvement and monitor response to treatment. Options include Goldmann kinetic perimetry and the computer-assisted static perimetry. While each has advantages and limitations, the latter is generally preferred, as it provides a more reliable measure for follow-up examinations [26].

The most common findings on perimetry in the Idiopathic Intracranial Hypertension Treatment Trial were a partial
arcuate defect with an enlarged blind spot (about three-fourths of the hemifields in the study eye and about half of the hemifields in the fellow eye) [3]. Generalized constriction is also common [2]. Less commonly, central, paracentral, arcuate, and altitudinal scotomas may occur [52].

The frequency of visual field loss and acuity loss with IIH is somewhat variable. Among various reports, visual field loss was noted in 71 to 100 percent of eyes using various forms of perimetry [2,3,12,36,80,81].

**DIAGNOSIS** — IIH is diagnosed according to the modified Dandy criteria; each of the following apply [72,82]:

- Symptoms and signs of increased intracranial pressure (eg, headache, transient visual obscurations, pulse synchronous tinnitus, papilledema, visual loss)
- No other neurologic abnormalities or impaired level of consciousness
- Elevated intracranial pressure with normal cerebrospinal fluid (CSF) composition
- A neuroimaging study that shows no etiology for intracranial hypertension
- No other cause of intracranial hypertension apparent

While revisions to these guidelines have been proposed, they do not substantially change the approach to diagnosis [31]. Because treatment trials have used the modified Dandy criteria, we believe that these remain the most appropriate criteria for making the diagnosis of IIH.

**DIFFERENTIAL DIAGNOSIS** — When papilledema is present, this suggests elevated intracranial pressure, which can have many etiologies in addition to IIH. There are also many etiologies of unilateral or bilateral optic disc swelling, which can have a similar appearance to papilledema.

**Secondary intracranial hypertension** — Any entity that increases intracranial pressure may lead to papilledema. These include:

- Intracranial mass lesions (tumor, abscess)
- Obstruction of venous outflow, eg, venous sinus thrombosis, jugular vein compression, neck surgery
- Obstructive hydrocephalus
- Decreased CSF absorption, eg, arachnoid granulation adhesions after bacterial or other infectious meningitis, subarachnoid hemorrhage
- Increased cerebrospinal fluid (CSF) production, eg, choroid plexus papilloma
- Malignant systemic hypertension

Most of the conditions are excluded by MRI. MR venography (MRV) is often required to exclude conditions causing venous outflow obstruction. In particular, cerebral venous thrombosis can have a very similar clinical presentation as IIH [83-85]. (See *Etiology, clinical features, and diagnosis of cerebral venous thrombosis*, section on ‘Clinical aspects’.)

Other unusual causes of obstructed venous outflow include transverse sinus septum causing sinus stenosis [86]; osteopetrosis of the jugular foramen [87-91]; depressed skull fracture and stenosis of the superior sagittal sinus [92]. Venous hypertension and secondary increase in intracranial hypertension can also be caused by cerebral arteriovenous malformations, dural arteriovenous malformations, and arteriovenous fistulas, as well as by increased right heart pressure and superior vena cava syndrome [31,36,93-102]. Some patients thought to have IIH have later been discovered to have one of these conditions [36,53,83,103].

**Optic disc abnormalities** — There are many causes of an elevated optic nerve head. While the term papilledema is sometimes used to describe the findings in these conditions, it should be reserved for patients who have elevated optic disc heads as a consequence of increased intracranial pressure. The Table lists the causes of optic disc swelling (table 2). These are discussed in detail separately. (See *Overview and differential diagnosis of papilledema*.) Funduscopic examination by an ophthalmologist is recommended to confirm the presence of true
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- Basics topics (see "Patient information: Idiopathic intracranial hypertension (pseudotumor cerebri) (The Basics)"

SUMMARY AND RECOMMENDATIONS

- A typical presentation of idiopathic intracranial hypertension IIH is that of an obese woman of childbearing age who presents with headaches and is found to have papilledema on funduscopic examination.
  - Headache characteristics in IIH are variable and nonspecific, but usually include daily occurrence, unusual severity, and a throbbing quality. (See 'Headache' above.)
  - Papilledema is usually bilateral and symmetric; the severity of papilledema is associated with the risk of permanent visual loss. (See 'Papilledema' above.)
  - Other common features of IIH that are unusual in other primary headache disorders are transient visual obscurations, pulsatile tinnitus, and diplopia. (See 'Symptoms' above.)
  - Other common examination features include restricted visual field examinations and uni- or bilateral abducens palsy. (See 'Examination' above.)

- A neuroimaging study is required in patients suspected as having increased intracranial pressure to exclude other causes of elevated intracranial pressure. Magnetic resonance imaging (MRI) with and without contrast and including postcontrast MR venography is the imaging study of choice. (See 'Magnetic resonance imaging' above.)

  MRI findings which suggest, but are not diagnostic for IIH include empty sella, flattening of the posterior aspect of the globe, distension of the perioptic subarachnoid space (with or without a tortuous optic nerve), and transverse venous sinus stenosis. (See 'Magnetic resonance imaging' above.)

- Lumbar puncture should follow MRI unless a source of elevated intracranial pressure is clearly delineated. An opening pressure greater than 250 mmH₂O taken with the patient lying on his side with legs extended confirms elevated intracranial pressure. Pressures between 200 and 250 mmH₂O are considered equivocal and require presence of associated clinical findings like stenosis of the transverse venous sinuses. Higher upper limits of normal may be considered in the obese or sedated child. Cerebrospinal fluid composition is normal in IIH. (See 'Lumbar puncture' above.)

- Visual field testing is an essential part of the evaluation of patients with IIH and provides a means for following the patient and directing treatment (see 'Ophthalmologic evaluation' above).

- Diagnostic criteria of IIH (pseudotumor cerebri) require the presence of each of the following: (See 'Diagnosis' above.)
  - Papilledema OR sixth (abducens) nerve palsy (unilateral or bilateral)
• Normal neurologic examination, except for papilledema and cranial nerve abnormalities
• Neuroimaging (MRI with and without gadolinium and MR venography is preferred) shows normal brain parenchyma without evidence of hydrocephalus, mass, structural lesion, or meningeal enhancement
• Normal cerebrospinal fluid (CSF) composition
• Elevated lumbar puncture opening pressure

IIH must be distinguished from other causes of increased intracranial pressure and other etiologies of optic nerve head swelling. Cerebral venous thrombosis in particular may have a very similar clinical presentation to IIH. (See ‘Differential diagnosis’ above.)

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REFERENCES


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