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Pediatric Idiopathic Intracranial Hypertension: A Review

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Author Disclosure
Drs Mercille and Ospina did not disclose any financial relationships relevant to this article.

Objectives After completing this article, readers should be able to:

1. List the diagnostic criteria for idiopathic intracranial hypertension (IIH).
2. Discuss the epidemiology, risk factors, and clinical manifestations of IIH in a pediatric population.
3. Describe the differential diagnoses and conditions associated with IIH.
4. Suggest appropriate therapeutic options for IIH.
5. Identify the principal complication of IIH and how it may be prevented.

Definition
Idiopathic intracranial hypertension (IIH), previously referred to as pseudotumor cerebri or benign intracranial hypertension, was recognized initially in adults by Quincke in 1893 as “meningitis serosa.” (1) The syndrome is characterized by elevated intracranial pressure (ICP) without any evident underlying neurologic disease. The modified Dandy criteria, which were developed based on an adult population, can assist in establishing the diagnosis of IIH (Table 1) (2).

Interestingly, children who have IIH may display a greater spectrum of clinical presentations than adults, and the disorder may have special epidemiologic characteristics in children.

Epidemiology
IIH occurs most commonly in young adults and rarely is seen in those older than age 45 years. The overall annual incidence is 0.9 per 100,000 individuals, (4) and there is a strong female predilection among affected adults. The incidence of IIH increases to 3.5 per 100,000 in women ages 20 to 44 years. The association between IIH and obesity is very strong in adults. The incidence of IIH rises to 19.3 per 100,000 in women who are 20% or more above their ideal body weight. (5)

IIH has different characteristics in the pediatric age group, where it is considered to be relatively rare, (6) especially in the prepubertal child. (7)(8) In one case series, more than 60% of children who had IIH were older than 10 years of age. (9) Interestingly, the unequal sex distribution of the disease appears to begin only after puberty. (9)(10)

In contrast to the adult population, in which 66% of men and 90% of women presenting with IIH are obese, studies often show obesity not associated with the condition in younger children. (8)(11)(12)(13) As with the predilection for women, the association with obesity increases only after puberty, (8)(12) likely as a result of hormonal changes. There is no racial predisposition for IIH, (3) and even though familial cases have been reported, no genetic locus has been described. (14)

Pathophysiology
The pathogenesis of IIH remains elusive, despite many theories emerging from neuroradiologic research and studies of cerebrospinal fluid (CSF) hydrodynamics (Table 2). (15) The absence of an increase in ventricular size despite the raised ICP in this disease also is puzzling.

Vision loss in IIH is believed to be caused by transmission of high ICP to the optic nerve head (ONH). Damage may result from axoplasmic stasis and microvascular compromise.
Early vision loss may be caused by macular edema, subretinal or perimacular hemorrhages, and anterior ischemic optic neuropathy. (17)(18)

**Differential Diagnosis**

IIH is a diagnosis of exclusion. Following the Dandy criteria, by definition there should be no other identifiable neurologic disease. Numerous associations with IIH have been described (Table 3), and any of these related variables and potential causes of increased ICP must be excluded. Nomenclature dictates that identifiable causative factors be excluded from the diagnosis of IIH and be referred to, instead, as secondary causes of intracranial hypertension. However, many different “associations” with IIH are cited in the literature, and although many are well documented, others are based on anecdotal case reports or small case series. Pediatric ICP very often is found in association with an underlying causative factor, (40) such as ear infection, dural sinus thrombosis, steroid withdrawal, malnutrition associated with refeeding, hypervitaminosis A, minocycline, and others. (3)(9)(10)(12)(40)(41)(42)(43) It is very important to exclude any of these associated conditions or causative factors prior to commencing therapy. (44)

Optic nerve drusen can be confused with papilledema. Drusen are the most common causes of disc elevation, and confirming their presence may be challenging, more so in children because drusen tend to locate deeply in the ONH at a young age, only becoming more visible later in life. (11)(45)(46) Lorentzen (47) reported the prevalence of optic nerve drusen at 0.34%, increasing by a factor of 10 in relatives of affected individuals. Although most patients who have drusen never develop visual symptoms, some have visual field abnormalities as a result of axonal compression. Fortunately, other complications, such as ischemic optic neuropathy and peripapillary neovascular membranes, are rare.

**Clinical Evaluation**

**History**

Headache is the most common symptom of IIH in both children and adults. (9)(12)(41)(42) As with most headaches induced by elevated ICP, they may be worse in the morning, awaken the patient from sleep, or increase with a Valsalva maneuver. The headaches can be accompanied by nausea and vomiting. Ophthalmic symptoms, such as decreased and blurred vision, diplopia, and transient visual obscurations, also are reported frequently. (12) Transient visual obscurations are, in our experience, relatively frequent in older children but rarely reported on routine questioning. The obscurations probably result from transient ischemia of the ONH and are elicited most often by changes in posture. The obscurations can be uni- or bilateral and last only a few seconds. The clinical picture in younger children and infants deserves special attention because the most notable findings may be irritability, (48) apathy, and somnolence. (10)(44) Other nonspecific neurologic manifestations can be encountered, including ataxia, dizziness, neck/shoulder/
back pain, stiff neck, seizures, facial or limb paresthesias, facial nerve palsy, and pulsatile tinnitus. (45)(49)(50) Finally, children may be entirely asymptomatic and present only with papilledema during a routine eye examination. (11)(51)

### Physical Examination

**OPHTHALMOLOGIC EXAMINATION.** The hallmark of IIH is papilledema (Fig. 1), which can be asymmetric and, very rarely, unilateral. IIH without papilledema has been described, but such a diagnosis should be made cautiously. (52) Papilledema may be present but not recognized, truly absent, or not yet developed when the raised ICP is discovered. Infants who have open fontanelles or suture diastasis also can develop papilledema,

<table>
<thead>
<tr>
<th>Table 3. Conditions Associated with Idiopathic Intracranial Hypertension</th>
</tr>
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<tbody>
<tr>
<td><strong>Medications</strong> (19)</td>
</tr>
<tr>
<td>• Vitamin A and analogs (19)</td>
</tr>
<tr>
<td>• Minocycline and tetracycline (20)(21)</td>
</tr>
<tr>
<td>• Human growth hormone (22)</td>
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<tr>
<td>• Steroids or steroid withdrawal</td>
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<tr>
<td>• Danazol</td>
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<td>• Nalidixic acid (23)</td>
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<tr>
<td>• Nitrofurantoin</td>
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<td>• Lithium</td>
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<tr>
<td>• Amiodarone</td>
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<tr>
<td>• Mesalamine (24)</td>
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<tr>
<td>• Thyroid replacement therapy (25)</td>
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<tr>
<td>• Oral contraceptive</td>
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<tr>
<td><strong>Endocrine Disorders</strong></td>
</tr>
<tr>
<td>• Ovarian dysfunction (26)</td>
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<tr>
<td>• Addison (27)/Cushing disease</td>
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<tr>
<td>• Hypocalcemia</td>
</tr>
<tr>
<td>• Hypo/hyperthyroidism</td>
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<tr>
<td>• Vitamin D-dependent rickets</td>
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<tr>
<td><strong>Infectious Disease</strong></td>
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<tr>
<td>• Viral disease (28)</td>
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<tr>
<td>• Otitis media</td>
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<tr>
<td>• Sinusitis (29)</td>
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<tr>
<td>• Tonsillitis</td>
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<tr>
<td>• Streptococcal B pharyngitis</td>
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<tr>
<td>• Febrile illness</td>
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<tr>
<td>• Upper respiratory tract infection</td>
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<tr>
<td>• Lyme disease (30)</td>
</tr>
<tr>
<td>• Varicella (31)</td>
</tr>
<tr>
<td>• Roseola</td>
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<tr>
<td><strong>Miscellaneous</strong></td>
</tr>
<tr>
<td>• Renal failure, renal transplant (32)</td>
</tr>
<tr>
<td>• Malnutrition/refeeding</td>
</tr>
<tr>
<td>• Vitamin A excess or deficiency</td>
</tr>
<tr>
<td>• Cystic fibrosis</td>
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<td>• Appendectomy</td>
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<td>• Tonsillectomy and adenoidectomy</td>
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<td>• Crohn disease</td>
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<td>• Asthma</td>
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<tr>
<td>• Chronic lung disease</td>
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<tr>
<td>• Heart murmur, mitral valve prolapse</td>
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<tr>
<td>• Postvaccination</td>
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<tr>
<td>• Galactosemia</td>
</tr>
<tr>
<td>• Guillain-Barré/Miller-Fisher variant (33)</td>
</tr>
<tr>
<td><strong>Collagenoses</strong></td>
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<tr>
<td>• Systemic lupus erythematosus (34)</td>
</tr>
<tr>
<td>• Polyangiitis overlap syndrome</td>
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<tr>
<td>• Behçet disease (35)</td>
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<tr>
<td>• Panuveitis (36)</td>
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<tr>
<td><strong>Hematologic Disease</strong></td>
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<tr>
<td>• Severe anemia (iron deficiency, aplastic, pernicious, paroxysmal nocturnal hemoglobinuria, sickle cell) (37)</td>
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<tr>
<td>• Hypercoagulable states (26)(31)(38)(39)</td>
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<tr>
<td>• Polycythemia vera</td>
</tr>
<tr>
<td>• Wiskott-Aldrich syndrome</td>
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Adapted from Kesler and Bassan (16).

Figure 1. Papilledema in a 10-year-old girl who has IIH.
but for obvious reasons, it is noted less frequently. The appearance of the ONH does not seem to correlate with final functional visual status. (53)(54)

ONH drusen (Figs. 2 and 3) can elevate the disc and blur its margins in a manner that may be difficult to distinguish from papilledema. It is unusual, but the two can coexist. (55) In true papilledema, however, the vessels are obscured at the disc margins, the elevation extends into the retina surrounding the disc, venous congestion is present, and exudates may be present. (11)(45)(56) The presence of spontaneous venous pulsations at the ONH usually indicates that the ICP is less than 200 mm H2O. (57) This sign is only useful if the pulsations are seen because they can be absent in the normal population. Optic disc hemorrhages suggest papilledema but also can be seen with optic nerve drusen. Funduscropy and examination for these findings should be sufficient to diagnose papilledema in most cases, but detection may prove difficult in children.

Loss of visual acuity more commonly is a late finding in IIH. Looking for other ways to assess optic nerve function, therefore, is critical. The presence of a relative afferent pupillary defect or a color vision deficit indicates optic neuropathy, but should not be the only parameters examined.

Uni- or bilateral sixth nerve palsy is frequent (40% to 48%) in children who have IIH, (9)(10)(12)(43) and the incidence seems to be higher in children than in adults. Third and fourth nerve paresis can be seen but is much less common. (6)(15)(58) The absence of diplopia as a symptom should not discourage the assessment of eye movements and ocular alignment because children may not complain of diplopia.

**NEUROLOGIC EXAMINATION.** Excluding ophthalmic findings, a patient who has IIH should have normal neurologic examination results. Some case series, however, have reported facial and hypoglossal nerve palsies, neck stiffness, hyperreflexia with Babinski signs present, choreiform movements, and nystagmus. (15)(17)(59)

**Investigations**

**Imaging Studies**

Magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) are, at present, the imaging studies of choice for detecting IIH. Neuroimaging is mandatory not only to exclude the possibility of herniation prior to a lumbar puncture but to identify potential secondary causes of elevated ICP. MRI is superior to computed tomography (CT) scan in detecting a sinus or venous thrombosis, certain malignancies, gliomatosis cerebri, and meningeal abnormalities. (13)(52)(60)(61) In atypical patients (slim patients, children, and men), MRV should be considered. (3)

Neuroimaging results should be normal in IIH except for signs of ICP. The ventricles should be of normal to small size, and the following signs of raised ICP may be found: flattening of the posterior sclera (Fig. 4), empty sella (Fig. 5), distention of the perioptic subarachnoidal space (Fig. 4), enhancement of the prelaminar optic nerve, vertical tortuosity of the orbital optic nerve, and intraocular protrusion of the prelaminar optic nerve. (62)(63)

**Ancillary Ophthalmologic Tests**

When trying to differentiate papilledema from buried ONH drusen, CT scan (Fig. 6) and ultrasonography are useful tools that can demonstrate calcification of the...
ultrasonography in cases of IIH in cooperative children by performing the “30-degree test.” Rotating the eyes 30 degrees stretches the optic nerve and redistributes fluid that may have accumulated around the optic nerve in cases of elevated ICP. A measured reduction in the diameter of the nerve indicates raised ICP. (67)

Fluorescein angiography seldom is necessary but may be performed with a cooperative child. Papilledema causes dye leakage; drusen are autofluorescent and cause no leakage. An increasingly prevalent technique in ophthalmology—confocal scanning laser tomography with the Heidelberg Retinal Tomograph (HRT)—appears to be useful in distinguishing pseudoedema from true papilledema. The procedure does so by quantifying disc elevation above the retinal surface, which is greater and extends beyond the disc margin in true papilledema. (68) The clinical value of HRT in children who have IIH as well as how it compares with other examination techniques remains unknown.

Visual field testing is extremely important in the management of IIH. Visual field evaluations are statistically more sensitive than visual acuity and contrast sensitivity testing in the detection of worsening disease. (69) The most commonly reported visual field defect is an enlarged (often reversibly) blind spot due to papilledema. (70) Other reported visual field abnormalities include arcuate defects, inferonasal visual field loss, global constriction, generalized depression, and cecocentral scotomas, all of which can be permanent. (69) (70) (71) Recording the visual field (with either Humphrey or Goldmann perimetry) in a pediatric patient can be challenging and requires full cooperation. Such cooperation generally can be achieved by 7 years of age, but younger children sometimes do surprisingly well.

Fundus photography can be useful for monitoring optic nerve and fundus changes during follow-up. Visual evoked potentials are insensitive to visual loss in IIH. (72)

CSF Pressure

A lumbar puncture in a patient who has IIH should display an increased CSF opening pressure as well as a normal cell count, normal glucose concentration, normal or low protein content, and the absence of infection. (45) Performing a lumbar puncture on a child is not always easy. A Valsalva maneuver and crying may increase the measured opening pressure falsely. Sedation may be necessary.

The upper normal limit of CSF opening pressure in children is approximately 180 to 200 mm H2O, but precise cutoff values remain unknown. (3) Other studies
of ICP in children report an upper limit of 75 mm H₂O in those younger than 2 years of age and of 135 mm H₂O in those younger than 5 years. (73)(74) Obesity does not seem to affect the measured ICP directly. (75)(76) Moreover, ICP in the normal range does not exclude IIH because of diurnal fluctuations in CSF pressure. In these circumstances, repeating the lumbar puncture may be considered. Although prolonged pressure monitoring has been advocated, (15) it is invasive and does not mimic normal physiologic conditions. (74) Furthermore, Eide (77) recently showed that the quality of continuous ICP recordings in children is prone to error.

Management
Management of IIH is based almost entirely on clinical experience, due largely to the absence of randomized prospective trials that allow for evidence-based recommendations. (3)(15)(52) The goal of treatment is to relieve symptoms and to normalize ICP to preserve vision. (3)(52) Asymptomatic patients who have normal vision and minimal papiledema may be monitored closely without treatment. (3)(16) Follow-up should be particularly attentive in children, in whom ocular examination and visual field evaluation often are difficult or unreliable. When treatment is necessary, medications are sufficient in most patients. Surgery should be considered for progressive visual loss despite maximum medical therapy, if there is severe visual loss or rapid progression at presentation, and when severe papilledema causes exudation and macular edema. (9)(11)(16)(52)(78) The surgical options are optic nerve sheath decompression (ONSD) or CSF shunting procedures.

Any potential precipitating factors should be removed. Weight loss is a time-honored treatment and should be advised when appropriate. (3)

Medical
Acetazolamide, a sulfa-derived diuretic and carbonic anhydrase inhibitor that reduces CSF production, often is used as the first-line therapeutic agent for IIH. The starting dose recommended in children is 25 mg/kg per day, which may be increased to 100 mg/kg per day (maximum, 2 g/d). (11) Well-recognized adverse effects of acetazolamide include gastrointestinal upset, metallic taste, tingling of the lips and digits, loss of appetite, electrolyte imbalances, metabolic acidosis, and nephrocalcinosis. (19) Acetazolamide is contraindicated in the presence of sulfonamide allergy and significant renal or liver disease.

Furosemide, a loop diuretic, can be used in combination with or as an alternative to acetazolamide if there is an intolerance of or contraindication to this drug. The effect of furosemide on CSF production is weaker than that of acetazolamide. (79) The most common adverse effects are electrolyte imbalances, dehydration, and hypotension. The risk of hypokalemia increases when diuretics are combined. The suggested dose of furosemide is 1 mg/kg per day.

Corticosteroids can be useful in the management of IIH but should be administered with caution. Corticosteroid withdrawal is associated with an elevation of ICP. (80)(81) The adverse effects of corticosteroids are numerous and well documented and include weight gain, which could be deleterious for IIH. Steroids have been used in conjunction with diuretics to treat children whose response to diuretics is poor. (11)(79) More commonly, steroids are used to treat rapid visual deterioration while patients are awaiting surgery.

Some patients have been cured by the diagnostic lumbar puncture. (13)(44) Repeated lumbar punctures are not recommended for long-term management because they are technically difficult in children. There are well-recognized risks associated with lumbar punctures, and their pressure-lowering effect is only temporary. (19)

Surgical
No randomized controlled studies have compared CSF diversion procedures to ONSD. (82) The choice of procedures depends largely on personal experience and the availability of resources. (9)(52) Both types of surgery appear to be effective.

Both lumboperitoneal and ventriculoperitoneal shunts have been recommended in the treatment of IIH. (83)(84) No strong evidence supports one procedure over the other. (82) Recently published data suggest that the choice of shunting procedure depends on the surgeon’s preference. (85) Lumboperitoneal shunts obstruct frequently; reintervention is needed in 50% to 75% of cases. (19)(86)(87) Other complications include overshunting, catheter migration, radiculopathy, infection, CSF leak, Chiari malformation, and shunt dependency. (3) Whether ventricular shunts require revision less frequently remains unclear. (85)

Information on ONSD to treat pediatric IIH is limited. Pediatric case series suggest that ONSD is a safe and effective method of stabilizing visual acuity and visual field loss in children. (78)(88)(89) It is unclear whether the therapeutic effect is due to a filtration bleb effect or to the proliferation of fibroblasts around the optic nerve causing obstruction and preventing further passage of CSF distal to the operative site. (90)(91)(92)(93)(94)(95) The optic nerve can be ap-
proached medially or laterally; recently, an endoscopic endonasal approach has been advocated. (90) Papilledema may improve bilaterally after unilateral ONSD, perhaps by way of CSF filtration through the posterior orbit and optic chiasm. Improvement in visual function can be expected in the first weeks following surgery, a trend that may continue for the first 3 months. (78) Vision may worsen subsequently, and reoperation may be necessary. (52)(78)(96) The risks of this surgery are low. The most feared complication is central retinal artery occlusion; transient oculomotor palsy is the most common complication. Acute angle-closure glaucoma, hyphema, corneal ulceration, and retinal ischemia all have been described following ONSD. (97)

Bariatric surgery (gastroplasty or gastric bypass) appears to be a safe and efficient method of losing weight and diminishing comorbidities related to obesity, such as IIH, hypertension, and diabetes. (85)(98)(99) Such surgery is indicated in severely obese adolescents but does not replace a program of diet and exercise. (100) There has been an increase in bariatric surgery to treat IIH over the last 20 years, probably reflecting the increasing epidemic of obesity in the United States. (85) Due to the delayed effect of bariatric surgery on lowering ICP, this procedure should not be used as emergent treatment of IIH.

**Prognosis and Follow-up**

Little is known about the natural history of IIH. Although earlier literature suggested a good visual prognosis in pediatric IIH, it now is clear that vision loss can be permanent. This condition should be recognized as a potential cause of visual impairment. Baker and associates (43) found moderate visual impairment or worse in 17% of 36 children who had experienced IIH, a finding confirmed by other case series. (9)(12)(101)

The course of IIH often is protracted. Close surveillance of affected children is vital because vision loss can occur at presentation, during treatment, or following recurrences. Due to the sometimes conflicting and entirely retrospective analyses of risk factors for this condition, interpretation of their role in the disease process remains difficult. (3)(9)(102) Although high-grade papilledema is associated with vision loss, the disc appearance cannot be used to predict final visual outcome. (53)(54) Recent weight gain, subretinal hemorrhage, significant visual field loss at presentation, and hypertension also have been identified as predictors of vision loss in IIH. (3)

Close follow-up includes evaluation of visual acuity, color vision, pupillary function, and visual fields. Fundus photographs are useful because they allow comparison over the course of the disease. In the absence of conclusive evidence, arbitrary guidelines as to the frequency of follow-up have been proposed. Shin and Balcer (19) suggest follow-up at 1-month intervals for 6 to 12 months and then less frequently once the disease has stabilized. Kesler and associates (103) suggest follow-up visits for a minimum of 5 years on the basis of disease recurrence in almost 40% of patients. Strong data regarding optimum follow-up in children who have IIH do not exist.

**Summary**

The demographics of IIH differ between children and adults. IIH appears to affect boys and girls equally until puberty, when it becomes more frequent in girls, as it is in adult women. The association of IIH with obesity is lesser in children, but this relationship increases with age. The clinical presentation of IIH in children differs significantly from that of adults, and its identification is crucial because it can cause permanent visual impairment. A high degree of suspicion is necessary to establish the diagnosis of IIH in infants and young children, who are more difficult to examine and whose signs and symptoms often are substantially different from those of adults. Data on medical and surgical treatment of this disease are scarce, with management based largely on clinical experience. Despite the apparent efficacy of current therapies, further prospective, randomized trials are necessary to define treatment guidelines and maximize follow-up. Close surveillance and interdisciplinary management of pediatric IIH is recommended to optimize the treatment of this potentially blinding disorder.

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