Learning Objective:
To become familiar with newly identified demographic trends and new drug associations in pediatric IIH, and a new set of diagnostic criteria for the disorder.

CME Questions:
1. This relatively new medication has been associated with IIH in pediatric patients:
   A. Phenytoin
   B. Gabapentin
   C. Synthetic growth hormone.
   D. Lamotrigine
   E. Topiramate

2. This relatively new vitamin A-related chemotherapeutic agent has been associated with IIH in pediatric patients:
   A. All-trans retinoic acid (ATRA)
   B. Accutane
   C. Cis-trans retinoic acid
   D. Beta-carotene
   E. Retinyl palmitate

Key Words: Pediatric Pseudotumor Cerebri – Pediatric Idiopathic Intracranial Hypertension – Cerebrospinal Fluid Pressure – Headache – Brain Tumors – Growth Hormone – Acetazolamide – MR venography – Lumboperitoneal Shunting – Optic nerve sheath fenestration

Abstract
Our understanding of pediatric IIH has been refined since Dr. Lessell’s review in 1992. Recent studies’ use of rigorous methodologies and standard definitions has elucidated distinct demographic trends. Specifically, the incidence of IIH seems to be increasing among adolescent children, and within older children its clinical picture is similar to that of adult IIH. Within younger age groups there are more boys and nonobese children who may develop IIH. Although the pathogenesis of the disease still remains unclear, IIH among young children has been associated with several new etiologies including recombinant growth hormone and all-trans-retinoic acid. More modern neuroimaging techniques such as MRI and MRI-venograms are being used to exclude intracranial processes. While most cases of pediatric IIH improve with medical treatment, those who have had visual progression despite medical treatment have undergone optic nerve sheath fenestration and lumboperitoneal shunting. Because IIH in young children appears to be a different disorder than in adolescents and adults, separate diagnostic criteria for younger children are warranted. We propose new criteria for pediatric IIH in which children should be prepubertal, have normal sensorium, can have reversible cranial nerve palsies, and have an opening CSF pressure greater than 100 mm H2O if less than age 8.

I. INTRODUCTION
Idiopathic intracranial hypertension (IIH) is a condition defined by elevated intracranial pressure but no clinical, lab, or radiographic evidence of infection, vascular abnormality, space occupying lesion, or hydrocephalus. Simmons Lessell’s review of IIH in children, published in this journal in 1992, provided a general overview, protocol for diagnosis, and review of conditions associated with this disorder in the pediatric age group. Since then, however, further delineation of the demographics of children with IIH, additional cases with reversible cranial nerve palsies, new associated etiologies, and updated management strategies have been described in the literature. In light of these developments, we consider it important to provide an updated review. We plan to focus specifically on advances since 1992, with the goal of supplementing ophthalmologists’ current fund of knowledge regarding pediatric IIH and its diagnosis and management. Finally, our review has prompted us to propose criteria for the diagnosis of pediatric IIH.

A. Nosology
Because IIH is the preferred term, a brief nosological discussion is warranted. A multitude of terms including “serious meningitis,” “pseudotumor cerebri,” and “benign intracranial hypertension” have been used to describe the syndrome. Initially, “pseudotumor cerebri” was preferred because the patient’s presenting symptoms were consistent with those of a cerebral
mass, but researchers soon criticized the name. Subsequently, the adjective “benign” also was deemed unsuitable since permanent vision loss, a known complication, could hardly be associated with a benign disease process. For these reasons, “idiopathic intracranial hypertension (IIH)” is currently the most favored term.126,137 We should point out, however, that we do not believe that the disease is truly “idiopathic.” Although the exact mechanism is still elusive, there are several hypotheses regarding the possible etiologies. As a result, we shall use prudently the name “idiopathic intracranial hypertension,” recognizing that in years to come, this term too may also become outdated.

B. Diagnostic Criteria
Idiopathic intracranial hypertension’s definition has evolved, and currently the modified Dandy criteria must be met as a prerequisite for adult diagnosis.147,166
With advances in neuroimaging and recognition of secondary causes, the criteria have been updated to include: 1) general signs and symptoms of generalized ICP or papilledema, 2) elevated cerebrospinal fluid pressure (greater than 250 cm H20), measured in a lateral decubitus position, with normal composition, 3) no evidence of hydrocephalus, mass, structural, or vascular lesion on MRI or contrast-enhanced CT for typical patients, and MRI and MR venography for all others, and 4) no other identified cause of intracranial hypertension.48 However, no specific diagnostic criteria for pediatric IIH currently exist. We believe that as our understanding of pediatric IIH and its demographics and clinical manifestations have evolved, the current criteria warrant revision as they may be exclusive in some cases and overly inclusive in others.

C. Pathogenesis
The pathogenesis of IIH is still not completely understood. Although brain edema, increased cerebral blood volume, and increased cerebrospinal fluid secretion have been postulated to be associated with the condition,70,149 most attention has been focused on increased venous sinus pressure and decreased cerebrospinal fluid absorption. Decreased absorption at the level of the arachnoid villi has been elucidated by radioisotype cisternography, although it is unclear whether it is secondary to compression of the arachnoid villi or by elevated intracranial pressure itself.49 Karahalios et al have suggested that elevated intracranial venous pressure is a universal mechanism of all IIH, both adult and pediatric.74 Elevated venous pressure may increase resistance to CSF absorption, subsequently causing the cerebrospinal pressure to increase as well. Others have refuted this theory suggesting that because venous sinus stenoses reverse with correction of elevated pressure, elevated venous pressure could be an effect, rather than a cause, of intracranial pressure.10,62,108 In another study, the authors argued that reduced venous sinus pulsatility may be a marker for IIH secondarily to raised venous pressure.11 Most of the studies regarding pathogenesis of IIH have studied adults; similar studies in children have not been done.

D. Hereditary Basis
A hereditary basis has been suggested for IIH by several reports.51,52,75,139 The cases include homozygous female twins,51 heterozygous female twins,52 siblings,75 mother-daughter pairs,75 mother-son pairs,139 and cousins.75 Genetic linkage analyses are lacking, and there is poor knowledge about the means of transmission of the disease.

II. DEMOGRAPHICS AND EPIDEMIOLOGY
The incidence of idiopathic intracranial hypertension in the overall population is 1 out of 100,000.55 However, recent studies have elucidated demographic trends in pediatric IIH.

A. Pubertal vs. Prepubertal
Previously, IIH was thought to occur with equal incidence in all age groups.7,92 It now appears that there is an increasing incidence of IIH among adolescents (12-15 yrs) as compared to young children (2-12 years).55 This might reflect the growing trend of obesity in adolescence. One study reports that as many as 60% of children who develop the disorder are over 10 years of age.7

B. Obese vs. Nonobese
In adults, there is a well established association between obesity and IIH.134 According to one meta-analysis of children with IIH and one retrospective review, only 30% of children with IIH were overweight, and both sets of authors suggested at best a weak association between pediatric IIH and obesity.7,143 However, these studies did not incorporate standard definitions of pediatric obesity, age subgroups were not examined, and complete ascertainment of data pertaining to obesity was not always achieved.
More useful information has been provided by the study by Balcer et al., which used rigorous methodolo-
gies and standard definitions of obesity in children with IIH, and trends with age were examined. The
records of forty patients were studied; all met the clini-
cal criteria for IIH and had height and weight recorded
disease presentation. Obesity was defined as weigh-
ing more than 120% of ideal body weight. The
authors found that 43% of patients aged 3 to 11 years
were obese, whereas 81% of those in the 12- to 14-year
age group and 91% of those in the 15- to 17- year age
met criteria for obesity (p=.01). With the use of
statistical methods, this study established that older
children with IIH were more likely to be obese.4

C. Male vs. Female
In adulthood, patients are typically women of child-
bearing age.8,126 Previously, it was thought that there
was no sex predilection in IIH among children.92
Recent studies, however, have shown that in prepuber-
tal children there is a predominance of males, and in
the pubertal age group, more girls are affected with the
disease.7 In the study by Balcer et al., 50% of patients
aged 3 to 11 years were female, whereas 88% of those
in the 12- to 14-year age group and 100% of those in the
15- to 17- year age group were female.

These recent findings which associate obesity and
female gender with IIH in older children suggest that
among the pubertal and postpubertal age groups, risk
factors for developing IIH might be similar to those in
adults. Younger children with IIH are less likely to be
obese or female, and it is possible that IIH in this
younger age group has a different mechanism. Much
has yet to be learned about their differing risk factor
profile. Larger collaborative studies need to examine
the potential role of neuroendocrine factors in deter-
mining the relation between age and obesity in the
pediatric IIH population.

III. CLINICAL CONSIDERATIONS
A. Presenting Symptoms
The course of pediatric idiopathic intracranial hyper-
tension varies, and a child may present hours to several
years after symptoms begin. While headache, nausea,
and vomiting are known classic symptoms, patients
may complain of blurry vision, diplopia, and stiff neck
as well.7,122 Other reported symptoms include increas-
ing head size, photophobia, anorexia, retro-orbital

pain, lightheadedness, myalgia, head tilt,7,122 as well as
preferring a knee-chest position.153 Level of conscious-
ness and functioning are both intact in IIH, in contrast
to some children with intracranial mass lesions.149
Until recently, cranial nerve VI palsies were the only
accepted neurological abnormalities permitted in diag-
nosing IIH. Documented in only 12% of adults,147
sixth nerve palsies continue to be more common
among children with IIH, occurring in 9 to 48% of
this population.7,79,122 Additionally, palsies of cranial
nerves III,79,177 IV,79,122,150 VII,126,122 IX,177 XII177 have
also been noted in children. In the series of Phillips et
al.,122 children younger than 11 years old were more
likely to have cranial nerve deficits (59%) compared
with older children (39%). The reason for indirect
relationship with age is uncertain. There may be con-
tant esotropia that is worse at distance but without
obvious abduction defects. Reversal of the cranial
nerve palsy with lowering of the intracranial pressure
is required to associate the palsy with IIH. Additionally,
other abnormal neurological symptoms including
hyperreflexia and nystagmus177 may occur extremely
ininfrequently; most often IIH is considered as a source
of these abnormalities only after all other related diag-
noses are ruled out. While the mechanism causing
these abnormalities is still poorly understood, likely
there is some element of nerve traction. For instance,
it is possible that in cranial nerve VI palsies, increased
intracranial pressure causes inferior displacement of the
pons, with traction on the abducens nerve.1,86
Asymptomatic idiopathic intracranial hypertension,
which is diagnosed when papilledema is incidentally
noticed during a routine physical exam, has become a
more well-recognized entity in children.70,79,171,174,177
These children have no headache or visual complaints.
It is unclear why this occurs; one plausible explanation
is that preschool and young school age children often
undergo routine eye exams. Except for headache man-
gagement, these children often receive the same treat-
ment as those with symptoms. Furthermore, the inci-
dence of asymptomatic IIH raises multiple questions
regarding the incidence of undetected cases.

B. Headache
Headache is the single most common complaint
among children with idiopathic intracranial hyperten-
sion, and has been documented in 62-91% of
cases.7,79,177 Unfortunately, “headaches” are a frequent,
vague complaint amongst most children, including
those that are healthy. The distinction is complicated
by the fact that children are not able to articulate their symptoms effectively, and also by the similar quality of migraine and IIH headaches. Although IIH headaches have been described as being characteristically frontal, severe, pulsatile, and worse on lying down, most suggest that they are similar to migrainous headaches except that IIH headaches tend to be continuous, while migrainous headaches are generally more severe and intermittent. Furthermore, studies show that in many cases, differentiating between IIH and migraine headaches may be difficult because of the fact that IIH may be superimposed upon a primary migraine headache disorder.

Of note, there are also reports of IIH in the absence of headache, either because the child is too young to articulate symptoms or because headaches are completely absent. The reason for lack of headache development in a setting of increased cerebrospinal pressure is not known, but recently, it has been suggested that those children with IIH but no headaches have more neurological signs and vision loss at presentation, and tend to have poorer long-term outcomes. Thus, it is possible that headaches may serve as a warning sign to protect against vision loss, and aggressive reduction of opening pressure and treatment of papilledema is critical.

C. Papilledema

Papilledema, ranging from mild blurring of the disc margins to gross disc swelling with hemorrhages and peripapillary exudates, has generally been regarded as a hallmark physical finding of IIH. Most often the disc edema is bilateral, although it can be asymmetric or unilateral as well. Children's papilledema often resolves after three to six months of medical treatment, although in some it can last for several more months and lead to optic atrophy. In our experience the severity of papilledema, particularly if pallor and cotton wool spots are present, is positively correlated with the risk of visual loss. Clinicians should be careful to differentiate papilledema from pseudopapilledema, defined as an abnormal disc which appears swollen but burying of the vessels by the nerve fiber layer, peripapillary hemorrhages, cotton wool spots, and exudates are absent. Most of the cases of pseudopapilledema are due to optic nerve head drusen.

As there are children who lack headaches, some patients with IIH, especially infants with open sutures, may not have papilledema. Accounting for lack of papilledema may include acquired or congenital optic nerve sheath abnormalities and resolution of papilledema in chronic IIH. In patients without papilledema, there should be no threat of vision loss, and treatment is usually geared towards symptomatic headache management.

D. Visual Abnormalities

The incidence, type, and temporal resolution of visual deficits in children are similar to those in adults. For instance, vision loss in children with IIH is usually mild to moderate and reversible, but in rare instances can be serious, devastating, and permanent. At presentation, visual acuity loss is reported in 6 to 20% of pediatric cases, while visual field loss occurs in 85 to 91% of cases. Children can describe various afferent symptoms including transient visual loss, photophobia, and “shimmering lights with colored centers.” The most common visual field changes include enlarged blind spots, inferior nasal field loss, and constricted fields, all of which usually improve with resolution of disc swelling. As in adults, most children with mild to moderate visual field defects in IIH experience complete recovery after treatment. Caution should be applied in children with IIH, moderately to severely constricted visual fields, and only mild disc swelling as a contribution of functional visual loss should be considered.

E. Differentiation from Brain Tumors

The diagnosis of IIH in children is one of exclusion, as central nervous system neoplasms may similarly present with headaches, nausea, vomiting, and papilledema. One study reported that in childhood, brain tumors required on average up to three visits to a medical professional before the diagnosis was made. Unlike children with IIH, those with tumors tend to have headaches that are non-throbbing, deep-aching, and intermittent in nature. Also, behavior changes, seizures, and focal neurologic deficits are more likely in children with brain neoplasms, as compared to those with IIH. A contrast enhanced CT or MRI scan of the brain is usually sufficient to rule out a central nervous system neoplasm when IIH is suspected. Exceptions include subtle infiltrating neoplastic processes such as gliomatosis cerebri, which may escape initial detection by neuroimaging. Leptomeningeal spread of lymphoma, leukemia, and germ cell tumors may also lead to signs and symptoms of elevated intracranial pressure.
in children with only subtle abnormalities on neuroimaging. The diagnosis may be evident by meningeal enhancement on MRI or cerebrospinal fluid elevation in protein, pleocytosis, hypoglycorrhachia or abnormal CSF cytology. In addition, spinal cord tumors may block CSF protein, cause elevated intracranial pressure, and mimic IIH. However, usually there is some clue to the spinal cord process such as back pain, upper motor neuron signs, or sensory level.

IV. ETIOLOGIES/ASSOCIATED CONDITIONS

Although secondary causes for IIH are less commonly identified in adults – most of whom are obese, 53.2-77.7% of pediatric cases have been associated with identifiable conditions, the most common of which include infectious diseases, endocrine abnormalities, and drugs. Previously recorded associated causes of idiopathic intracranial hypertension in children include viral infection, hypoparathyroidism, menarche, corticosteroid withdrawal, thyroid treatment, nalidixic acid, tetracyclines, vitamin A toxicity, vitamin A and D deficiencies, head trauma, lupus, acute lymphocytic leukemia, Turner syndrome, galactosemia, galactokinese deficiency, and nitrofurantoin. Although there are no case control studies to date which have identified definitive causes in children, there have been several papers as well as case reports citing conditions that seem to be strongly associated with pediatric IIH. We will elaborate on advances made in understanding previously established etiologies, and will reference new associated conditions (Table 1).

A. Endocrine Conditions

1. Thyroid replacement

New cases of pediatric idiopathic intracranial hypertension following thyroid replacement therapy in juvenile hypothyroidism have been described. In all the cases, IIH occurred after increasing the dose of thyroid hormone levels. Thus, it has been hypothesized that rapid correction of hypothyroidism with thyroxine, a major regulator of sodium transport, may result in altered CSF dynamics. Except in one case, the IIH occurred in peripubertal children. Therefore, it is possible that pubertal children may have some endocrine or hormonal factors that predispose them to developing IIH in this setting. Additionally a child with hypothyroidism who developed IIH prior to thyroxine treatment has been reported, but given that the child was female, obese, and pubertal, it cannot be confirmed that hypothyroidism and IIH are associated.

2. Adrenal Corticosteroids

Steroid withdrawal in children with inflammatory bowel disease (IBD) leading to IIH was the subject of two reports. In one study, an adolescent with IBD developed IIH during corticosteroid withdrawal after chronic steroid treatment of his gastrointestinal condition. In another, three cases of IIH subsequent to budesonide, a new-generation potent steroid, treatment for Crohn disease in children were published. All three patients in this paper had previously been treated with prednisone, experienced symptom resolution with withdrawal of budesonide, and were successfully treated with prednisone later. However, it is difficult to establish a definite causal relationship between budesonide, a drug with low systemic bioavailability, and IIH in these patients, as confounding risk factors such as hypervitaminosis and iron deficiency anemia were also present in at least one case in this report.

3. Growth Hormone

First reported in 1993, there have been multiple cases of IIH in children treated with recombinant (biosynthetic) human growth hormone (GH). In a large database analysis, the prevalence of IIH in the GH-treated population was approximately one hundred times greater than in the normal population. An increase in the occurrence of IIH after insulin growth-factor I (IGF-1) therapy has also been reported. It appears that risk factors such as obesity, Turner syndrome, chronic renal failure, Prader-Willi syndrome, empty sella syndrome and delayed puberty can increase the risk of developing IIH in this setting. One study cites 15 patients with renal insufficiency who developed IIH subsequent to treatment with growth hormone. All of these patients were concurrently being treated with other medications that have been associated with IIH, but IIH developed shortly after beginning growth hormone therapy. It has been proposed that growth hormone passes the blood-brain barrier and acts locally to increase levels of IGF-1 which, in turn, increases CSF production from the choroid plexus. Furthermore, it seems as though aggressive GH dosing places a child at a higher risk of developing IIH; thus, starting hormone therapy at the lowest recommended dose, with prudent gradual titration to higher doses if needed has been advised.
Caution must be applied when diagnosing papilledema in a patient with GH deficiency as congenital disk anomalies (hypoplasia or small crowded discs) may be seen in children with hypopituitarism.\textsuperscript{29} When IIH is due to GH treatment, stopping replacement hormone therapy is often sufficient to resolve headaches, papilledema, and elevated CSF pressure. Other causes of intracranial hypertension should still be excluded with neuroimaging and CSF examination. We have used acetazolamide when headaches and vision loss are present. Restarting the growth hormone later at a lower dose typically prevents symptom recurrence.

4. Addison Disease
While earlier reports suggested a possible association between papilledema and Addison disease (adrenal insufficiency in spite of elevated ACTH levels), definite associations have been made between the two only in the last decade.\textsuperscript{3,30} Lumbar punctures had not been performed in previous cases, and patients had multiple other medical conditions and risk factors that may have contributed to development of IIH. The more recently published cases have met diagnostic criteria for both Addison disease and IIH, and glucocorticoid and mineralocorticoid replacement resulted in resolution of symptoms.\textsuperscript{3,30} Future studies need to further investigate the pathophysiological mechanism leading to IIH; it is possible elevated levels of serum vasopressin may mediate an increase in brain volume and elevated pressures.

5. Other
Levonorgestrel implants\textsuperscript{2} and desmospressin nasal spray\textsuperscript{118} have been associated in children with IIH, but the mechanism in each case was unclear.

B. Infections
1. Acute Sinusitis
While infections such as mastoiditis and chronic sinusitis are known to cause secondary intracranial hypertension via venous sinus thrombosis, there has been a recent report of acute frontal sinusitis resulting in true pediatric IIH that is worth mentioning.\textsuperscript{78} As compared to chronic sinusitis, this case was not associated with sinus thrombosis. The reason for the development of IIH is unclear.

2. Varicella
Varicella has previously been implicated as a cause of a variety of neurological conditions in childhood, and recent reports suggest that there might be an association between varicella and idiopathic intracranial hypertension.\textsuperscript{84,87} In the first case, a girl presented with headache, nausea, vomiting, and papilledema one week after chickenpox diagnosis. In the next, an 8-year-old girl presented with IIH and ileofemoral vein thrombosis 3 weeks after chickenpox, but was found to have a transient elevation of anti-protein S auto-antibodies. There were no definitive intracranial thromboses identified on neuroimaging studies. Neither case was associated with meningitis or encephalitis to suggest viral infection of the nervous system, and both children had normal mental status, making Reye syndrome unlikely. Although the second case may have been confounded by a missed venous thrombosis, the first case is convincing enough to believe that varicella itself may predispose a child to IIH.

C. Drugs
1. Tetracyclines
Tetracyclines, including related medications such as minocycline, have been linked to IIH.\textsuperscript{7,24,52,82,125,168} They are commonly prescribed drugs, especially for acne treatment. Previously, there was limited knowledge about risk factors that may predispose children treated with tetracyclines to the development of IIH, but in a recent retrospective study, it was shown that female gender and obesity may predispose some to developing IIH when these medications are used.\textsuperscript{125} Additionally, there have been several cases of IIH occurring in twins treated with tetracyclines, and thus, it is possible that genetic susceptibility may also predispose certain individuals to IIH.\textsuperscript{52} With cessation of antibiotics, and possibly additional treatment with acetazolamide, symptoms usually resolve.

2. Vitamin A
Vitamin A intoxication may produce signs and symptoms consistent with IIH. In a prospective study on adults, hypervitaminosis, either secondary to increased levels, altered metabolism, or hypersensitivity to vitamin A, was associated with IIH.\textsuperscript{47,65} Additionally, in a double-blind, randomized, placebo-controlled trial, infants given vitamin A supplementation were more likely to develop bulging fontanelles than those that did not.\textsuperscript{9} There have been several reports of infrequent cases of IIH after acne treatment with both tetracyclines (discussed above) and isotretinoin, a vitamin A
Combination therapy seems to increase the risk. While the mechanism of toxicity is still not well understood, recent studies have shown that both serum retinol binding protein (RBP) and levels of vitamin A in the cerebrospinal fluid are elevated in those with IIH, as compared to normal controls. It has been proposed that excess retinol and RBP in the serum are transported to the cerebrospinal fluid where retinol acts as a toxin on the arachnoid granulation resorption mechanism.

3. Other chemotherapy agents

Although neurotoxicities are common with chemotherapeutic agents, the incidence of IIH due to these medications is rare. Treatment with intermediate-dose cytarabine was associated with IIH in an 11-year-old male with acute myelocytic leukemia. The only other recent report of cytarabine-associated IIH has been in a child with high-dose treatment in an adult woman with APL. Cytarabine may disturb the ATPase-dependent choroidal secretion of CSF by depleting phosphorus stores. There has also been a recent case of IIH thought to be secondary to cyclosporine treatment after a bone marrow transplant in a child.

D. Anemia

IIH in children has been associated with several forms of acquired anemia including iron deficiency, acquired aplastic anemia, and sickle cell disease. The occurrence of IIH with aplastic anemia is rare, with only two reported cases in the last ten years. Although both patients were transfused, they showed improvement only with serial lumbar punctures and acetazolamide. The mechanism by which anemia causes IIH is unclear, but has been theorized to be a result of tissue hypoxia leading to increased capillary permeability or abnormalities in hemodynamics leading to increased cerebral blood flow (high-flow state).

E. Malnutrition and Renutrition

IIH has previously been associated with “catch up” growth following malnutrition. A case report describes the syndrome in a young boy with non-organic failure who subsequently gained 4.6 kg and 1.6 cm in height over 4 weeks. During that time, the boy developed papilledema and headaches. Both rapid escalations in growth hormone levels as well as rapid brain growth have been suggested to cause an increase in brain edema/intracranial hypertension. This may be the first case of IIH occurring with rapid catch up growth and recovery of endogenous growth hormone.

F. Miller Fisher Syndrome

Idiopathic intracranial hypertension has been reported as a complication of Miller Fisher syndrome. Miller Fisher syndrome, highlighted by ophthalmoplegia, ataxia, and areflexia, is a variant of Guillain-Barre syndrome. In the cited study, both young children presented initially with symptoms of raised intracranial pressure and were later diagnosed with Miller Fisher syndrome. Both children had anti-GQ1b antiganglioside antibodies in the serum, and the other had antimyelin antibodies. Both were treated with acetazolamide and intravenous immunoglobulin therapy with improvement of symptoms. Thus, we believe there may be an association between the acute demyelinating condition of the peripheral (and central?) nervous system and pediatric IIH.

G. Questionable and Mistaken Associations

The recent literature is unfortunately still replete with reports of other conditions purported to be causes of IIH. In many of these cases, standard criteria for the diagnosis of IIH have not been satisfied. In others, hypercoagulable states leading to undetected intracranial venous thromboses may have been present, and in some reports, the diagnosis of IIH was likely to be purely coincidental as no plausible explanation for the association could be provided. We review these supposed associations here to emphasize that these conditions have not been convincingly shown to cause IIH.
1. Lyme Disease

One report suggested that children with Lyme disease, infection caused by the spirochete borrelia burgdorferi, may later develop IIH.73 We present the argument that there is no association between the two syndromes because the standard criteria for the diagnosis of IIH requires the CSF profile to be normal without evidence of meningitis. For instance, in the case of purported IIH in a child with Lyme, the MRI showed enhancement of the dura consistent with inflammation, and cerebrospinal fluid was significant for 115 cells/mm3, glucose 53 mg/dL, and protein 56 mg/dL, consistent with infection.73 Although the child was “diagnosed” with IIH and aseptic meningoencephalopathy, we believe that her headaches, vomiting and diplopia were a result of increased intracranial pressure secondary to Lyme infection, rather than IIH. In another case reported of a boy with neuroborreliosis claimed to have IIH, the CSF pleocytosis rendered this diagnosis of IIH to be incorrect.37

2. Renal Transplantation and Impaired Renal Function

Children with impaired renal function may be at higher risk of developing idiopathic intracranial hypertension.115 Recently, it has also been suggested that those that undergo renal transplant, may also be at greater risk post-transplantation.44,53,76,121,145 The development of IIH does not appear to be temporally related to the time of surgery. In one retrospective case note analysis of children undergoing renal transplant in the United Kingdom over an eleven year period, it was claimed that 4.4% developed IIH post-transplantation.44 However, it must be noted that all of the reported patients were treated with immunosuppressive medication, including corticosteroids, and many had other risk factors, including obesity, that could have also increased their risk of developing IIH. Additionally, there have been multiple cases of renally compromised children, treated at some point with growth hormone, who developed IIH.82 There has also been a case of severe IIH in a boy with chronic renal failure on hemodialysis, who required a kidney transplant, with subsequent resolution of his symptoms.115 As a result of limited understanding, it is still unclear whether some aspect of care after transplantation or impaired renal function post-transplantation place children at higher risks of developing IIH. For example, one author presents a case of pediatric IIH following cyclosporine A treatment in a boy with tubulointerstitial nephritis, who had steroids withdrawn before the CSA was started.37

3. Head Trauma

Minor closed head trauma was previously reported in association with pediatric IIH, but the etiology may have been cerebral venous sinus thrombosis.83 Over the last decade, there has been an additional reported case of head trauma in a child causing IIH,119 but neuroimaging demonstrated a thrombosis of the right lateral dural venous sinus. Increased intracranial pressure in head trauma may also be the result of cerebral edema.55,165

4. Prothrombotic States

Hypercoagulable states and dural sinus thromboses have been reported in association with some cases the mechanism for IIH.119,144,154 For instance, it has been proposed that patients with IIH may have genetic thrombotic risk factors that predispose them to microvascular occlusion in the arachnoid villi.34 In one recent large population study, those with IIH had 31% incidence of antiphospholipid antibodies, 27% had hyperfibrinogenemia, and 27% with other conditions related to thrombosis.154 Additionally, there are anecdotal reports of the association of antiphospholipid antibodies and IIH,90,91 although in one study some of the patients had other risk factors.90 Lupus and other rheumatologic conditions associated with a hypercoagulable state have been described as causing IIH.56 There have two reported cases of children with lupus, one of whom had leukoencephalopathy,164 and the other who had lateral sinus thrombosis.164 Similarly, Behcet’s syndrome is associated with intracranial hypertension secondary to venous thrombosis along with dementia in 5-50% of cases; hypercoagulable states were present in both reports of children with Behcet’s and intracranial hypertension.83,170 According to the standard criteria for IIH, venous thromboses should be excluded. Even when venous thromboses can not be demonstrated with MR-venography or even conventional venography in a patient with elevated intracranial pressure, the presence of a hypercoagulable state suggests that microthromboses might still be a possible cause. Therefore, it is definitely incorrect to diagnose patients with venous thromboses as having IIH, and it is questionable whether patients with hypercoagulable states should be allowed to have that diagnosis as well.
5. Cystic Fibrosis

It has been suggested that cystic fibrosis may be linked with IIH. \(^{14,100}\) One author reports an incidence of 7.7% IIH in children with newly diagnosed cystic fibrosis. \(^{13}\) In the study, three cases of possible IIH secondary to cystic fibrosis are cited; in all cases there were other causes of IIH development including hypovitaminosis, hypervitaminosis, and refeeding syndrome. In another study, \(^{100}\) IIH is described in a slightly older asymptomatic child in whom IIH was diagnosed with cystic fibrosis diagnosis. While this child had no signs of malnutrition, she did have iron deficiency anemia.

6. Others

There are several other reports in which the association with IIH is unclear because of confounding factors. For instance, in a reported case of a child with IIH post-orthotopic heart transplantation, \(^{142}\) the child was taking minocycline for acne. In a case of IIH secondary to cystic fibrosis, \(^{13}\) the child was taking minocycline for acne. In a case of IIH attributed to hemangioma \(^{133}\) the child was taking minocycline for acne. In a case of IIH attributed to hemangioma, \(^{133}\) the child was taking minocycline for acne. In a case of IIH attributed to hemangioma, \(^{133}\) the child was taking minocycline for acne. Similarly, in a report of children with cystinosis who developed IIH, \(^{35}\) several were treated with either prednisone, growth hormone, cyclosporine, vitamin D, oral contraceptive pills, or thyroid replacement, or had received renal transplants previously. In some cases, the diagnoses of IIH have been made in children who do not satisfy the standard criteria. For example, in a case of pediatric IIH attributed to hemophilia A, \(^{67}\) the child had an abnormal neurologic exam and had problems concentrating, difficulty with language, and changes in personality.

Several conditions may have occurred coincidentally. For example, in a case of pediatric IIH reported to be associated with optic nerve drusen, \(^{153}\) Goldenhar’s and Duane’s syndromes, \(^{160}\) Tolosa-Hunt syndrome, \(^{120}\) and subacute sclerosis panencephalitis. \(^{154}\)

V. CLINICAL EVALUATION

Children with suspected IIH should have careful documentation of visual acuity, color vision, pupillary examination, ocular motility, dilated ophthalmoscopy, and a neurological examination. In children who can cooperate, computerized threshold visual field testing (preferably SITA fast, 30-2) should also be performed. \(^{36,152}\) Although some authors have claimed reliable and repeatable SITA (Swedish interactive thresholding algorithm) visual field testing in children as young as 4, in our experience this is rarely accomplished before age 8. Partially cooperative children may be tested with Goldmann (kinetic) perimetry. However, a short child may not be able to sit in a chair and be large enough to have the chin reach the chinrest in most automated and kinetic perimetry setups. Confocal scanning tomography is a new tool which can be used to quantify the degree of change in papilledema and measure changes over time in some children with IIH. \(^{58,161}\) It has been suggested that tomography measurements correlate with opening pressures in adolescents and adults. \(^{18}\) Assessing the diameter of the optic nerve in relation to CSF pressure via orbital ultrasonography may be another useful tool especially in follow up, \(^{146}\) and ophthalmodynamometry may assist in noninvasive estimation of cerebrospinal fluid pressure though measurement of the central vein pressure. \(^{72}\) However, the future role of these new technologies in the evaluation of children with IIH may be limited to those who are uncooperative with the usual clinical measures, as it has yet to be demonstrated that they are better or add anything to the clinical examination of visual function, visual field assessment, and funduscopic examination.

VI. NEUROIMAGING

“Normal” neuroimaging studies are mandatory before diagnosing pediatric IIH. Computed tomographic (CT) scanning was previously considered adequate to exclude ventriculomegaly or mass lesions, however because there are conditions such as gliomatosis cerebri and cerebral venous thrombosis that can mimic pediatric IIH and may be missed by CT, it now considered suboptimal and MRI/MRV are the studies of choice in this setting. \(^{136}\)

A. Advances in MRI Imaging

Magnetic resonance imaging is superior to CT scanning because it offers better visualization of intracranial structures including the venous system, and it avoids the potential risks of radiation exposure. A number of findings on MRI have been demonstrated in pediatric patients with IIH. None of these abnormalities are specific for IIH, but without any other clinical explanation, they often are suggestive of the diagnosis. For instance, in one large study, Brodsky et. al showed
changes in the distal optic nerves including flattening of the posterior sclera (80% incidence), intraocular enhancement of the prelaminar optic nerve (50% incidence), distension of the periorbital subarachnoid space (45% incidence), and tortuosity of the optic nerves (40% incidence).\textsuperscript{15} These findings are best seen with high-resolution, thin-slice MR imaging through the optic nerves.\textsuperscript{15} In another study,\textsuperscript{61} a child with headaches, nausea, vertigo, progressive visual loss, and optic atrophy due to IIH had an MRI which showed enlarged periorbital nerve subarachnoid spaces. Additionally, variations in the appearance of the pituitary gland (including empty sella) have been demonstrated in 85-100% of those with IIH.\textsuperscript{197,178} No consistent endocrine abnormalities are found in patients with empty sella, which is thought to result from arachnoid herniation through a defect in the sella diaphragm secondary to chronically elevated intracranial pressure.

B. MR Venography
Before pediatric IIH can be diagnosed, venous sinus thrombosis must also be excluded. The use of MR venography as a noninvasive tool for diagnosing venous sinus thrombosis has become popular over the last decade. Prior to that, conventional MRI and catheter angiography were used to visualize the intracranial vasculature; unfortunately, MRI was limited in accurate visualization of vessels, and angiography was invasive. MRV has allowed for much better visualization of the sagittal and transverse sinuses. Although to date there is limited data in the literature on the use of MRV in younger children with IIH, adolescent and adult patients with the disorder often have distinctive patterns on MRV—narrowing of the transverse (lateral) sinuses, suggesting possible abnormalities in venous blood flow.\textsuperscript{61} It is still unclear whether these signal abnormalities are the cause or the consequences of IIH. Previously, it was thought that unrecognized thrombi may be the cause of tapered stenoses and filling defects in transverse sinuses in patients with IIH.\textsuperscript{74} However, the sinus narrowing often resolves with lowering of CSF pressure, implying that increased intracranial pressure caused the collapse of the walls of transverse sinuses.\textsuperscript{81} It should be noted that while there is excellent visualization of most venous structures, there are limitations in the use of MRV. Visualization of transverse sinuses, especially in the setting of chronic thromboses, may be challenging because of wide variations in normal anatomy. One study argued that transverse sinus flow gaps may be normal in up to 30% of people, especially in nondominant (smaller) sinuses.\textsuperscript{6} Other studies have shown evidence for pediatric age-related changes in the venous anatomy such as variations in the dominance of sinuses, involvment of the occipital sinuses, and increasing frequency of absent transverse sinus.\textsuperscript{131,173} Furthermore, MRV may not provide views of sinus continuity, especially in-plane vascular flow, and artifacts may hinder diagnosis.\textsuperscript{6} Thus, flow gaps should be judged with caution, and careful interpretation of MRV is essential to avoiding pitfalls and catching artifacts in diagnosis.\textsuperscript{6}

VII. TREATMENT
Despite limited understanding about the cause and pathophysiology of the disease, further advances in treatment options have been made in the last decade. Unfortunately, there are still no randomized, controlled, double blind prospective studies of treatment of IIH in children, and therefore, treatment is empirically dictated by the level of vision loss and severity of headache. Toxic, metabolic, and nutritional causes must be promptly addressed, and weight loss must be encouraged in children who are overweight. Repeat lumbar punctures, although previously thought to effectively control IIH, are now discouraged because they are painful, poorly tolerated in young children, who often require sedation, and have short lived effects as the spinal fluid is replenished in a day.\textsuperscript{149} In unusual cases, CSF hypovolemia can occur from an LP fluid leak in children.\textsuperscript{85} Most cases of pediatric IIH respond to medical management; thus, surgical management is typically reserved only for those who fail medication.

A. Medical Management
Medical management of pediatric IIH, for the most part, includes acetazolamide or furosemide. Acetazolamide, a carbonic anhydrase inhibitor, is thought to reduce the rate of cerebrospinal fluid production, and it is generally the first-line treatment choice in children with IIH. We usually use an oral dose of 15 mg/kg in two to three divided doses per day, until headache, disc swelling, and visual field abnormalities abate—typically 3-9 months. Common dose-related side effects include GI upset, paresthesias involving the lips, fingers, and toes, anorexia, and electrolyte imbalance (metabolic acidosis). Kidney stones are rare, and aplastic anemia is exceedingly uncommon.
We do not monitor electrolytes as children are usually asymptomatic from the acidity. When the side effects become intolerable, the dose is lowered, or acetazolamide is replaced with furosemide 0.3-0.6 mg/kg per day. There are reports of combining acetazolamide with furosemide to produce additive results and reduce pressure more effectively than just acetazolamide alone.\(^4\)

When children are obese, topiramate (1.5-3.0 mg/kg per day in two divided doses), an antiepileptic medication with secondary carbonic anhydrase activity, can be used instead of acetazolamide. The use of this medication in IIH is relatively new, and it is unclear whether it is superior to acetazolamide in reducing CSF pressure. However, topiramate has the added benefit of appetite suppression, it is excellent for treatment of chronic daily headache, and it has been used safely for years in children with epilepsy. The dosage should be built up slowly over weeks (25 mg/week) to reduce the risk of cognitive side effects. Zonisamide, another drug with secondary carbonic anhydrase activity and appetite suppression, may be used in similar doses if the side effects of topiramate are not tolerated.

In acute situations when visual loss is severe, the combination of oral acetazolamide and IV methylprednisolone 15 mg/kg can be used when surgery is not immediately available.\(^6\)

B. Headache Management

Headaches usually resolve with reduction in cerebrospinal opening pressure. If needed, additional pain management is usually accomplished with conventional headache prophylaxis and symptomatic headache medications.\(^5\) Daily medications which are often used in children with headaches include beta blockers such as propranolol and tricyclic antidepressants such as nortriptyline. Sodium valproate can be used, but in our experience is more useful for migraine than for causes of chronic daily headache. Caution should be applied if nortriptyline and sodium valproate are used because of their potential for weight gain, which should be avoided in patients with IIH.\(^6\) For this reason, topiramate and zonisamide, as mentioned above, may be more preferable for headache prophylaxis in IIH. Abortive medications for headache that can be used include acetaminophen or non-steroidal anti-inflammatory agents such as ibuprofen or naproxyn sodium. Migraine specific triptan drugs are not typically used in patients with IIH. Unfortunately, even with aggressive medical management, headaches continue in 43 to 67% of children.\(^137\) While a few of these headaches may be a result of analgesic overuse and rebound headaches, in most cases, the reasons for persistent headaches are not well understood. CSF shunting may be necessary in cases of refractory headache.

C. Surgical Management

The two major surgical options are optic nerve sheath fenestration and CSF shunting. Optic nerve sheath fenestration (ONSF) is most widely used when vision loss is severe or progresses despite medical management. Only one case of pediatric ONSF in an 11-year-old boy with lateral sinus thrombosis was reviewed by Lessell,\(^7\) but over the last decade, other reported cases of pediatric patients with IIH undergoing ONSF have been mentioned in the literature.\(^89,159\) Both lateral and medial approaches have been used. Three-quarters to all of children were noted to experience resolution of optic disc edema,\(^89,159\) and visual acuity and visual fields stabilized or improved in most patients.\(^54\) Furthermore, about 50% of those with unilateral surgery experienced bilateral improvement in visual acuity, but the mechanism for this is unclear.\(^71,89,159\) Unfortunately, initial success of surgery does not guarantee permanent visual correction. Of the 25 children cited in the literature who required ONSF, three had deterioration of vision postoperatively.\(^89,110,159\) CSF shunting is preferred for those children who have intractable headaches as well as visual loss and papilledema unresponsive to ONSF. While various shunting procedures have been experimentally used, including cisterna magna shunting,\(^71\) lumbo-peritoneal (LP) shunting seems to be the most successful in alleviating patients’ symptoms. The procedure, however, is associated with various complications including shunt obstruction,\(^26,40\) lumbar radiculopathy,\(^26,40\) and rarely, infection,\(^16\) as well as tonsillar herniation.\(^26\) Children, specifically, may be at higher risk for developing complications, possibly secondary to increased mechanical stress (growth) or the size of the shunt tubing in the thecal sac.\(^26,40\) In a recent study focusing on the pediatric population, 9 out of 10 patients experienced improvement in symptoms, but 7 required a total of 16 revisions as a result of shunt migration, obstruction, and tube fracture.\(^26\) Duration of shunt life is unclear. In one report, shunts lasted only 6 months, with an average time to failure of 9 months;\(^29\) in another, they lasted an average of 18 months.\(^16\) Additionally, LP
shunting has failed to halt progressive vision loss in some cases.\textsuperscript{26} Unfortunately, to date there are no reliable risk factors which predict poor shunt tolerance, and the long term outcome of visual function after LP shunting has yet to be studied systematically. Because of technological advances, ventroperitoneal (VP) shunting has been more widely used even in patients with relatively small ventricles.\textsuperscript{18} The authors of this study of VP shunting concluded that the revision rate was less compared with LP shunting. At this time, ONSF is the preferred surgical procedure when vision loss is the major issue. That being said, there are still many unanswered questions that prevent us from knowing how patients will do long-term. Since limited information is known about how ONSF relieves IIH symptoms,\textsuperscript{113} further research is needed to understand the underlying mechanisms. Also, it should be noted that there are different techniques as well as methods of orbital approach for each procedure which need to be studied.\textsuperscript{107} A study is needed to assess risk factors that may predict a poor surgical outcome. In spite of the lack of evidence based medicine research, ONSF is more effective, has fewer complications than LP shunting, and is generally the surgical procedure of choice. In the future, prospective randomized trials comparing LP shunting and ONSF in children will be crucial in order to better understand the clinical indications for each procedure. Such a study in adults is being planned.

\textbf{VIII. OUTCOME}

In the 1990s, reports suggested that visual field and acuity loss among children may have occurred in up to a 50\%,\textsuperscript{166} while recent reports cite an incidence of 25\%.\textsuperscript{7,137,149} Most children have complete resolution of disc swelling and visual abnormalities after treatment. The recurrence rate is low, and in our experience is related to weight gain. We typically follow patients for 6-9 months once medications are stopped, then on an as needed basis after that.

\textbf{IX. CONCLUSION/DIAGNOSTIC CRITERIA FOR PEDIATRIC IIH}

Our understanding of pediatric IIH has progressed since Dr. Lessell's review in 1992. Recent studies using of rigorous methodologies and standard definitions have elucidated distinct demographic trends. Specifically, the incidence of IIH seems to be increasing among adolescent children, and within older children its clinical picture is similar to that of adult IIH. Within younger age groups boys and nonobese children may develop IIH most frequently. Although the pathogenesis of the disease still remains unclear, IIH among young children has been associated with several new etiologies including recombinant growth hormone and all-trans-retinoic acid. More modern neuroimaging techniques such as MRI and MRI-venograms are being used to exclude intracranial processes. While most cases of pediatric IIH improve with medical treatment, those who have had visual progression despite medical treatment have undergone optic nerve sheath fenestration and lumbo-peritoneal shunting. Because IIH in young children appears to be a different disorder than in adolescents and adults, separate diagnostic criteria for younger children are warranted. This seems best accomplished by modifying the published standard criteria for IIH in adults.\textsuperscript{48,147,166}

Firstly, pediatric neuro-opthalmologists and IIH experts are seeking to restrict the term "pediatric" for younger children only. As it is generally used, the term "pediatric" can be confusing. Although eighteen years is the legal limit for childhood, from a biologic perspective, puberty is a more accurate marker for the completion of this phase of growth. The Tanner staging system is a well-known and acceptable method of determining a child's sexual maturity but there is a great variation in the progression of biological pubertal changes in both boys and girls.\textsuperscript{104,105} Furthermore, most ophthalmologists, neurologists, and neuro-opthalmologists would feel uncomfortable performing a genital and complete physical exam complete enough for complete Tanner staging (Table 2). Therefore, we believe it may be more practical for non-pediatricians and non-gynecologists to screen for any pubertal changes by history in determining whether puberty has commenced. For instance, one could simply ask a female patient or the parent whether pubic hair, breast enlargement, or menstrual cycle has appeared, without a genital examination or plotting of the growth curve. The term "pediatric" IIH would then be reserved for prepubertal children who have yet to develop any secondary sexual characteristics.

Secondly, reversible cranial nerve palsies have been convincingly documented in several children with IIH, so it would seem reasonable to include children with these signs. Also, to re-emphasize that cortical function should be intact in IIH, children should be required to have a normal sensorium.
Finally, the parameters for spinal fluid opening pressures in younger children are different than they are in adolescents and adults. Normal values for CSF opening pressure and cell composition are well established in adults, but determination of “normal” cerebrospinal fluid pressure and composition in children is challenging because of practical reasons and from lack of reliable published data. For example, accurate measurements are often complicated by agitation and crying in young unsedated patients, and this can transiently elevate pressure readings. Several studies in the literature have sought to identify normal levels for both neonates and young children, but studies are often cross referenced and methodologies are inconsistent (Table 3). After compiling results of previous studies, Fishman suggested that normal levels in a young child can vary between 10-100 mm H2O and will approach adult levels only after the age of eight. Therefore, using 250 mm H2O as an upper limit of normal may result in missed cases of IIH, and we suggest using 100 mm H2O as an upper limit of normal in children younger than eight in order to be more inclusive.

Additionally, for poorly understood reasons, cell and protein counts can be elevated in neonates. We performed a review of the literature to better identify the ranges of accepted values in a neonate. Mean levels of 8.3 WBC cells/mm3, with an upper limit of 32 cells/mm3 should be allowed, and do not preclude a diagnosis of pediatric IIH. CSF protein can also be relatively elevated in neonates (up to 150 mg/dl in the first 30 days of life), but will decline to normal levels (15-45 mg/dl) after the first six months of life. For these reasons, we suggest modifying the diagnostic criteria to allow for these normal variations in CSF content in neonates.

Therefore, in Table 4 we propose criteria for the diagnosis of pediatric IIH. We hope that these new criteria will allow more accurate diagnoses as well as more directed future research into the pathogenesis, diagnosis, and treatment of this disorder in children.

OUTLINE
I. Introduction
   A. Nosology
   B. Diagnostic Criteria
   C. Pathogenesis
   D. Hereditary Basis
II. Demographics and Epidemiology
   A. Pubertal vs. Prepubertal
   B. Obese vs. Nonobese
   C. Male vs. Female
III. Clinical Considerations
   A. Presenting Symptoms
   B. Headache
   C. Papilledema
   D. Visual Abnormalities
   E. Differentiation from Brain Tumors
IV. Etiologies/Associated Conditions
   A. Endocrine Conditions
   B. Infections
   C. Drugs
   D. Anemia
   E. Malnutrition and Renutrition
   F. Miller Fisher Syndrome
   G. Questionable and Mistaken Associations
V. Clinical Evaluation
   A. Neuroimaging
      B. MRI Imaging
      C. MR Venography
VI. Treatment
   A. Medical Management
   B. Headache Management
   C. Surgical Management
VII. Outcome
VIII. Conclusion/Diagnostic Criteria for Pediatric

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Table 1. Recently associated conditions

Endocrine
Recombinant (Synthetic) Growth hormone\textsuperscript{28,35,45,82,99,102,103,124,128,130,135}
Addison’s disease\textsuperscript{3,30}
Levonorgestrel implants\textsuperscript{2}
Desmopressin nasal spray\textsuperscript{114}

Other Drugs
Cytarabine\textsuperscript{43}
All-trans retinoic acid (ATRA)\textsuperscript{46,101,138,165}

Infections
Acute sinusitis\textsuperscript{78}
Varicella\textsuperscript{84,87}

Other
Miller Fisher Syndrome\textsuperscript{111}

Table 2. Patterns of Pubertal Development in Boys & Girls\textsuperscript{104,105}

<table>
<thead>
<tr>
<th>Event</th>
<th>Female (median age in years\textsuperscript{*})</th>
<th>Male (median age in years\textsuperscript{*})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast development</td>
<td>11.2</td>
<td>--</td>
</tr>
<tr>
<td>Testicular development</td>
<td>--</td>
<td>11.6</td>
</tr>
<tr>
<td>Pubic hair development</td>
<td>11.7</td>
<td>13.4</td>
</tr>
<tr>
<td>Peak height velocity</td>
<td>12.1</td>
<td>14.1</td>
</tr>
<tr>
<td>Menarche</td>
<td>13.5</td>
<td>--</td>
</tr>
<tr>
<td>Adult pubic hair config</td>
<td>14.4</td>
<td>15.2</td>
</tr>
</tbody>
</table>

\textsuperscript{*Standard deviation of one year.}
Table 3. Published and cited normal CSF opening pressures (mm H\textsubscript{2}O) in infants and children.

<table>
<thead>
<tr>
<th>Paper (year)</th>
<th>Pressure in infants</th>
<th>Pressure in children</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lumbar puncture</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Munro, 1928</td>
<td>30-80</td>
<td>90-120</td>
<td>Determined from patients treated for cranial and intracranial injury, but symptom free at discharge</td>
</tr>
<tr>
<td>Sidbury, 1920</td>
<td>30-70</td>
<td>45-95</td>
<td>Cited by Fishman$^{42}$</td>
</tr>
<tr>
<td>Levinson 1923</td>
<td>20-70</td>
<td>40-80</td>
<td>Cited by Fishman$^{42}$</td>
</tr>
<tr>
<td>Levinson 1928</td>
<td>10-14</td>
<td>40-100</td>
<td>Cited by Fishman$^{42}$</td>
</tr>
<tr>
<td>Quincke 1891</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Gerlach et al 1967</td>
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<td></td>
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<tr>
<td>Lups and Haan, 1954</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fontanelle or other method</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Welch, 1980$^{172}$</td>
<td>20-70</td>
<td>14-122</td>
<td>Intracranial pressure determined by tilting the infant until the fontanelle is flat and then comparing to the atmospheric pressure at that level. Cited by Minns et al.$^{112}$</td>
</tr>
<tr>
<td>Gaab et al, 1980</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Hearsay</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipton, 1993$^{95}$</td>
<td>50</td>
<td>85</td>
<td>Incorrectly ascribed to Minns et al.$^{112}$</td>
</tr>
<tr>
<td><strong>Textbook or review</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fishman, 1992$^{42}$</td>
<td>100</td>
<td>10-100</td>
<td>Compiled from previous studies</td>
</tr>
<tr>
<td>Behrman, 2004$^{12}$</td>
<td>50</td>
<td>60-180</td>
<td></td>
</tr>
<tr>
<td>Menkes, 1995$^{110}$</td>
<td></td>
<td>110-150</td>
<td></td>
</tr>
<tr>
<td>Roberts, 2004$^{129}$</td>
<td></td>
<td>85</td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Proposed diagnostic criteria for pediatric IIH (modified from $^{49,147,166}$)

1. Prepubertal$^*$
2. If symptoms or signs present, they may only reflect those of generalized intracranial hypertension or papilledema. Normal mental status.
3. Documented elevated intracranial pressure (age appropriate) measured in the lateral decubitus position. Age less than 8 with papilledema: $>$100 mm H\textsubscript{2}O Age 8 or above or less than 8 without papilledema: $>$250 mm H\textsubscript{2}O
4. Normal CSF composition except in neonates who may have up to 32 WBC/mm\textsuperscript{3} and protein as high as 150 mg/dl.
5. No evidence of hydrocephalus, mass, structural, or vascular lesion on MRI, with and without contrast, and MR venography. Narrowing of the tranverse sinuses is allowed.
6. Cranial nerve palsies allowed if they are of no other identifiable etiology and improve with reduction in cerebrospinal fluid pressure or resolution of other signs and symptoms of intracranial hypertension.
7. No other identified cause of intracranial hypertension.

$^*$In boys, supported by no evidence of pubic hair. In girls, supported by lack of breast development, growth of pubic hair, or menarche.
REFERENCES


In addition to searching MEDLINE, all related articles cited in reference lists of other articles were included. Non-English articles have not been included, nor have abstracts. Given that the last review was published in 1992, only a few articles before 1992 have been included for historical purposes, but otherwise this review focuses mainly on articles published since 1992. Finally, only those articles available through the University of Pennsylvania Library and Children’s Hospital of Philadelphia systems (electronic or paper), without cost from journal websites, or by direct communication from the authors, were used.

Method of Literature Search

To draft this review, “Pediatric Idiopathic Intracranial Hypertension,” a thorough MEDLINE search of all English articles between 1992 and 2005 was conducted. Search terms include: pediatric pseudotumor cerebri, pediatric idiopathic intracranial hypertension (IIH), pediatric neoplasms, pediatric pseudotumor cerebri diagnosis, pseudotumor cerebri AND drug therapy, IHH AND drug therapy, pseudotumor cerebri AND headache, IHH AND headache, pseudotumor cerebri AND acetazolamide, IHH AND acetazolamide, pseudotumor cerebri AND corticosteroids, IHH AND corticosteroids, pseudotumor cerebri AND MRI, IHH AND MRI, pseudotumor cerebri AND MRI venogram, IHH AND MRI venogram, pseudotumor cerebri AND segmental sinus stenosis, IHH AND stenosis, pseudotumor cerebri AND lumbar peritoneal shunting, IHH AND lumbar peritoneal shunting, pseudotumor cerebri AND optic nerve sheath fenestration, IHH AND optic nerve sheath fenestration, pseudotumor cerebri AND visual outcome, and IHH AND visual outcome.


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1994


CME Answers
1. C
2. A