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Idiopathic Intracranial Hypertension

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Idiopathic intracranial hypertension (IIH) is a disorder of elevated cerebrospinal fluid pressure of unknown cause. Quincke in 1897 reported the first cases of IIH shortly after he introduced the lumbar puncture into medicine. I was named pseudotumor cerebri in 1904 but was not well delineated clinically until the 1940's when cerebral angiography was added to pneumoencephalography to identify cases of cerebral mass lesions. Foley coined the term benign intracranial hypertension in 1955 but reports from the 1980's demonstrated a high incidence of visual loss[1, 2] and the term “benign” is no longer appropriate.

Idiopathic intracranial hypertension (IIH) is a syndrome characterized by elevated intracranial pressure that usually occurs in obese women in the childbearing years. The signs and symptoms of intracranial hypertension are that the patient maintains an alert and oriented mental state, but has no localizing neurologic findings. There is no evidence of deformity or obstruction of the ventricular system and neurodiagnostic studies are otherwise normal except for increased cerebrospinal fluid pressure (greater than 200 mm of water, in the non-obese and probably greater than 250 mm of water in the obese patient).[3] Neuroimaging signs of increased intracranial pressure include empty sella syndrome, lateral sinus collapse (smooth-walled venous stenoses, Figure 1), flattened globes and fully unfolded optic nerve sheaths. In addition, no secondary cause of intracranial hypertension can be found. This definition comprises the modified Dandy criteria for IIH.[4]

The symptoms of increased intracranial pressure are headache, pulse synchronous tinnitus (pulsatile tinnitus), transient visual obscurations and visual loss. Signs are diplopia due to sixth cranial nerve paresis and papilledema with its associated loss of sensory visual function. The only major morbidity with IIH is visual loss.

Epidemiology

The annual incidence of IIH is 0.9/100,000 persons and 3.5/100,000 in females 15 to 44 years of age. It is increasing in incidence in parallel with the current epidemic of obesity.[5, 6] In obese women aged 20 to 44 years who were 20% or more over ideal weight, the incidence of IIH is 19 per 100,000.[5] More than 90% of IIH patients are obese and over 90% are women of childbearing age. Although symptoms and signs may be recurrent in at least

10%, asymptomatic elevated intracranial pressure may persist for years.[7] The mean age at the time of diagnosis is about 30 years.[8]

Studies of conditions associated with IIH are mostly uncontrolled and retrospective. This has led to erroneous conclusions because investigators have tried to implicate IIH using chance and spurious associations with common medical conditions and medications. Also, there are a host of case reports of associations with IIH where the cases do not meet the modified Dandy criteria of IIH.

Table 1 lists the etiologies of intracranial hypertension that meet the modified Dandy criteria for IIH except that a cause is associated. The highly likely category is a list of cases with many reports of the association with multiple lines of evidence. Probable causes have reports with some convincing evidence. Possible causes have suggestive evidence or are common conditions or medications with intracranial hypertension as a rare association. Also listed are some frequently cited but poorly documented or unlikely causes; three case-control studies suggest these associations are not valid.[9-11]

Any disorder that causes decreased flow through the arachnoid granulations or obstructs the venous pathway from the granulations to the right heart is accepted as a cause of intracranial hypertension because of its biologic plausibility. Arteriovenous malformations or dural fistulae with high flow may overload venous return and result in elevation of intracranial pressure.

Although steroid withdrawal and Addison's disease are clearly associated with IIH,[12-14] as is hypoparathyroidism, links to other endocrine abnormalities remain unproven. For example, corticosteroid use has been associated with many suspected cases of IH; however, none of the cases fulfill the modified Dandy criteria.

Several other purported associations with IIH have been refuted by controlled studies. Pregnancy, irregular menses and oral contraceptive use have been shown to be simply chance associations.[5, 11, 15] In case-control studies, no association is found between IIH and multivitamin, oral contraceptive, corticosteroid or antibiotic use.[10, 11] However, case reports associating some drugs appear convincing: nalidixic acid,[16] nitrofurantoin,[17] indomethacin[18] or ketoprofen in Bartter's syndrome, [19] vitamin A intoxication,[20] isotretinoin,[21] thyroid replacement therapy in hypothyroid children,[22] lithium[23] and anabolic steroids.[24] While corticosteroid use is not associated with intracranial hypertension, steroid withdrawal clearly is linked.[12, 13]

Arterial hypertension has been associated with IIH.[7, 11] However, spuriously elevated blood pressure is commonly reported in obese people due to the use of standard size rather than oversize sphygmomanometer cuffs and obesity is associated with arterial hypertension. It is unlikely that there is a direct association of arterial hypertension and IIH.

A case-control study has found strong associations between IIH and obesity and with weight gain during the 12 months before IIH diagnosis. In this study, there was no evidence that IIH was associated with any other medical conditions or pregnancy.[11] In summary, other than obesity and recent weight gain, many conditions thought to be associated with IIH are just common disorders of women in childbearing years and are likely chance associations.

Pathogenesis

Any hypothesis of pathogenesis of IIH should explain the following observations of patients with the disorder:

1. high rate of occurrence in obese women during the childbearing years.

2. reduced conductance to CSF outflow.[25]
3. normal ventricular size; no hydrocephalus[26]
4. no histologic evidence of cerebral edema[27]

Changes in cerebral hemodynamics, that is, increased cerebral blood volume and decreased cerebral blood flow, have been reported.[28] However, others have found no significant changes in these factors.[29] The most popular hypothesis is that IIH is a syndrome of reduced CSF absorption. Decreased conductance to CSF outflow may be due to dysfunction of the absorptive mechanism of the arachnoid granulations or possibly through the extracranial lymphatics.[30] This latter mechanism of an alternative route of drainage along extracranial and spinal nerve roots to the extracranial lymphatics, proposed by Miles Johnston and coworkers,[30] may be an important factor in the mechanism of IIH as this route may account for a substantial percentage of CSF absorption.

So, regardless of the outflow mechanism, if outflow resistance is increased then intracranial pressure must increase for CSF to be absorbed. Although interstitial and intracellular edema have been reported in brain biopsy specimens,[31] a study with current methods of analysis has concluded that the histological features of the brain parenchyma are normal and the findings from the initial report are artifactual.[27]

Clinical Features

The symptoms of IIH patients are headache (94%), transient visual obscurations (68%), pulse synchronous tinnitus (58%), photopsia (54%), and retrobulbar pain (44%). Diplopia (38%) and visual loss (30%) are less common accompaniments of IIH; however, some of these symptoms are common in controls (Figure 2).

Headache

The presence of headache is common in patients with IIH and is the usual presenting symptom. The headache profile of the IIH patient[32] is that of severe daily pulsatile headaches. They are different from previous headaches, may awaken the patient and usually last hours. The headache is often reported as the worst head pain experienced. Associated nausea is common and vomiting is uncommon. In addition, other headache syndromes frequently coexist such as rebound headache from analgesic or caffeine overuse and require their own therapy.[33]

Transient visual obscurations

Visual obscurations are episodes of transient blurred vision that usually last less than 30 seconds and are followed by visual recovery to baseline. Visual obscurations occur in about 2/3 of IIH patients.[8] The symptom may be monocular or binocular. The cause of these episodes is thought to be transient ischemia of the optic nerve head related to increased tissue pressure.[34] While transient visual obscurations are anxiety provoking for the patient, they do not appear to be associated with poor visual outcome.[8]

Pulse-synchronous tinnitus

Pulsatile intracranial noises or pulse synchronous tinnitus is common in IIH.[11] The sound is often unilateral with neither side predominating. In patients with intracranial hypertension, jugular compression or head turning ipsilateral to the sound abolishes it.[35] The sound is thought to be due to transmission of intensified vascular pulsations by means of CSF under high pressure and turbulence through smooth walled venous stenoses related to transverse sinus collapse from high CSF pressure (Figure 1).[36]

The major signs of IIH are papilledema and sixth nerve paresis.

Ophthalmoscopic examination

Papilledema, optic disc edema due to increased intracranial pressure, is the cardinal sign of IIH. Optic disc edema either directly or indirectly is the cause of visual loss of IIH. The higher the grade of the papilledema, the worse the visual loss.[37] But, in the individual patient, the severity of visual loss cannot accurately be predicted from the severity of the papilledema. A partial explanation for this is that with axonal death from compression of the optic nerve, the amount of papilledema decreases.

Frisén has proposed a useful staging scheme for papilledema with good sensitivity and specificity based on the ophthalmoscopic signs of disturbed axoplasmic transport.[38] It has been modified recently[39] with a key finding added for each stage or grade. Grade 0 represents a normal optic disc. Grade 1 is characterized by the presence of a C-shaped or reverse C-shaped halo of peripapillary edema obscuring the retina adjacent to the optic disc. The temporal border of the optic disc is spared presumably due to the fine caliber of these axons (Figure 3). The C-shaped halo becomes circumferential with grade 2 papilledema (Figure 4). In grade 3 papilledema, there is complete obscuration of at least one major vessel as it leaves the optic disc (Figure 5). With the increased optic disc edema of grade 4 there is complete obscuration of at least one major vessel on the optic disc (Figure 6). Grade 5 is characterized by total obscuration of at least one vessel on the disc and leaving the disc and at least partial obscuration of all major vessels leaving or on the disc (Figure 7).

Ocular motility disturbances

Horizontal diplopia is reported by about 1/3 of IIH patients and sixth nerve palsies are found in 10-20%.[8] Motility disturbances other than sixth nerve palsies have been reported. Some of these reflect erroneous conclusions from the small vertical ocular motor imbalance that is known to accompany sixth nerve palsies. Bell's type palsies of CN VII rarely occur and are usually transient. The common thread here is that the cranial nerves that make nearly a 90° bend (CN II, VI, VII) appear to be susceptible to damage at the site of the bend.[40] The diagnosis of IIH should be viewed with suspicion in patients with ocular motility disturbances other than sixth nerve palsies.

Sensory visual function

Visual acuity usually remains normal in patients with papilledema except when the condition is long-standing and severe or if there is a serous retinal detachment present and optic disc edema extends to the macula. Snellen acuity testing is insensitive to the amount visual loss present when compared to perimetry. It is also insensitive to worsening of papilledema grade.[8]

Perimetry

Visual field loss occurs in almost all cases of IIH. In a prospective study of IIH, visual loss in at least one eye (other than enlargement of the physiological blind spot) was found in 96% of patients with Goldmann perimetry using a disease-specific strategy and in 92% with automated perimetry.[8, 41] About 1/3 of this visual loss is mild and unlikely to be noticed by the patient but serves as a marker with which to guide therapy.[8]

The visual field defects found in IIH are the same types as those reported to occur in papilledema due to other causes. The most common defects are enlargement of the physiologic blind spot and loss of inferonasal portions of the visual field along with constriction of isopters (Figure 8). Central defects are distinctly uncommon and warrant a search for another diagnosis unless there is a large serous retinal detachment from high

grade optic disc edema spreading toward the macula. The loss of visual field may be progressive and severe, leading to blindness in about 5% of cases. The time course of visual loss is usually gradual; however acute severe visual loss can occur.

The earliest visual field defect in IIH is often an inferior nasal step defect (Figure 8) followed by peripheral nasal loss. Arcuate defects may appear next followed by a gradual depression of the entire field, most pronounced peripherally (Figure 9).

Blind spot enlargement is ubiquitous in IIH. Since refraction often eliminates this defect,[42] blind spot enlargement should not be considered significant visual loss unless it encroaches on fixation. Also, since blind spot size is so dependent on refraction, it should not be used to follow the course of therapy.

With treatment there is significant perimetric improvement about 50% of patients.[8] A study that evaluated a subgroup of patients with worsening of their vision showed recent weight gain was the only factor significantly associated with decline in vision.[8] Other groups at risk for severe visual loss are black men, those with glaucoma and patients being rapidly tapered off corticosteroids. The course of IIH is often chronic with recurrences especially during periods of weight gain.[43]

Mechanisms of Visual Loss

The visual field defects found in IIH patients are optic disc-related. In other words, they are the type found when nerve fiber bundles are damaged at the level of the optic disk. These types of defects also occur with glaucoma and anterior ischemic optic neuropathy. This suggests a common mechanism for the visual loss in these disorders.

Degree of Papilledema and Visual Loss

"Is visual loss related to degree of papilledema or is the amount of optic disc edema an independent factor?" A study of patients with highly asymmetric papilledema was aimed at answering this question.[37] The patients were tested with automated perimetry and a variety of sensory visual function tests. Interestingly and unexpectedly, a generalized depression of the visual field in eyes with high-grade papilledema was found. The visual loss increased in magnitude with increasing visual field eccentricity and while nerve fiber bundle-like defects were frequently observed, visual loss occurred across the visual field. However, this finding was only appreciated when a comparison was made with the low-grade papilledema eye. This is because the values of the tests of foveal visual function in the high-grade papilledema eye, remain in the normal range but are significantly depressed compared to controls or the low grade eye.

This study and another[44] showed that the amount of visual loss correlates with the severity of disc edema — eyes with more disc edema had more visual loss (Figure 10). However, there was considerable interindividual variation. That is, some patients with marked optic disc edema appeared to have mild or no visual loss unless a comparison was made to a fellow eye with less disc edema. This relationship of degree of papilledema with visual loss implies that visual loss in IIH occurs due to papilledema (at the optic disc) and not from visual damage occurring posterior to the optic disc.

Factors Interacting with Optic Disc Edema that Lead to Visual Loss

The occurrence of papilledema is primarily dependent on the relationship of three factors: cerebrospinal fluid pressure, intraocular pressure, and systemic blood pressure.[45] Either elevated cerebrospinal fluid pressure, low intraocular pressure or low perfusion pressure can cause axoplasmic flow stasis, optic disc edema and resultant intraneuronal ischemia.

Hayreh showed the nerve sheath is composed of fibrous tissue and after it unfolds, it cannot expand any further.[46] Optic nerve width is greatest just behind the globe and narrowest within the optic canal. Thick fibrous bands within the canalicular nerve sheath interrupt the subarachnoid space (Figure 11). Hayreh found the number of these bands varied from animal to animal sometimes being scanty.[46] He observed in monkeys and man that when dye is injected into the optic nerve sheath, fluid usually passes easily into the cranial cavity. The force needed depended on the quality of the fibrous bands within the subarachnoid space. Although the dye usually flowed freely, it concentrated in the subarachnoid space adjacent to the optic canals. There may be differences within individuals in this trabecular meshwork of the optic nerve sheath subarachnoid space contiguous with the optic canal.

Relationship of Papilledema to Visual Loss

As stated earlier, the site of histologic damage in visual loss due to increased intracranial pressure is at the optic disc. Brain parenchyma tolerates *generalized* raised intracranial pressure well. Patients do not develop hemianopias. It is unlikely that the intracranial or intraorbital optic nerve is the location of the damage since the visual field defects are not typical and there is no histologic evidence to support this location. There is much evidence that the optic nerve head is an important site of damage in this disorder. This is based not only on histologic evidence, but also, the types of visual field defects seen in patients with IIH are similar to those found in disorders known to affect the optic nerve head -- glaucoma and anterior ischemic optic neuropathy. The last site of damage is the retina. Here, there may be either a neurosensory detachment or visual loss from choroidal folds. However, the main location for visual loss in IIH is at the optic disc.

There are two leading mechanisms for damage to the optic disc from intracranial hypertension:1) disruption of axonal transport and 2) intraneuronal optic nerve ischemia. There is considerable evidence that the primary insult to the optic nerve is a slowing of axonal transport.[45, 47, 48] It is likely that raised intracranial pressure in the subarachnoid space is reflected along the optic nerve sheath. As noted above, the health of the optic nerve is dependent upon the harmonious interaction of cerebrospinal fluid pressure, intraocular pressure, and systemic blood pressure. Raising intracranial pressure, a drop in intraocular pressure or a marked rise or fall of systemic blood pressure can all result in optic disc edema. It is likely that high cerebrospinal fluid pressure disturbs the normal gradient between intraocular and retrolaminar pressure and results in increased tissue pressure within the optic nerve. This likely interferes with axoplasmic flow with resultant stasis involving both slow and fast axoplasmic transport resulting in intra-axonal edema.[49]

Another potential mechanism is ischemia of the optic nerve head. Support for this mechanism comes from 1) Hayreh's work showing delays in prelaminar arterial filling with fluorescein angiography and 2) the visual field defects that occur are similar to those found in other optic neuropathies with ischemic final common pathways as their mechanism of visual loss (glaucoma and anterior ischemic optic neuropathy). It is most likely though that the mechanism of visual loss in IIH is through a combination of these two mechanisms… High cerebrospinal fluid pressure is reflected along and through trabeculations in the subarachnoid space of the optic nerve sheath. This results in a disturbance of the pressure gradient across the optic nerve head. There is resultant axoplasmic flow stasis, intra-axonal swelling and compression of small arterioles resulting in intraneuronal ischemic damage to the optic nerve.

Diagnostic criteria

The accepted criteria initially proposed by Walter Dandy have been modified.[4] Patients that fulfill these criteria are diagnosed as having idiopathic intracranial hypertension. These criteria are found in Table 1.

Patients with findings on examination other than papilledema, sixth nerve and rarely seventh nerve paresis should be suspected of having a diagnosis other than IIH. Laboratory evaluation in IIH patients is normal except for increased intracranial pressure.

There are several issues surrounding the criteria of the measurement and limits of the opening pressure. Whether the patient is supine, prone or sitting, one must be sure that the reference level for CSF pressure measurement is the level of the left atrium. Next, spuriously high values can occur with Valsalva,[50] and the hypoventilation associated with sedation. The latter is particularly a recurring issue in the pediatric population. Artifactually low values can occur with hyperventilation in the anxious patient from reduction in carbon dioxide levels and, of course, the patient undergoing multiple needle punctures may have falsely low results. The final issue here is that CSF pressure fluctuates throughout the day and at times is normal so a single normal CSF measurement does not exclude IIH as the diagnosis.

The normal limits for CSF opening pressure remain controversial. Normal limits are less than 200 mm water in non-obese subjects but in obese patients there are conflicting studies. Whiteley and coworkers[51] prospectively recorded CSF opening pressure in 242 adults and measured patients' weights and heights. The 95% reference interval for the CSF opening pressure was 10 to 25 cm CSF. However, neither neck nor hip flexion was altered in their protocol suggesting some of their subjects may have been prone to valsalva and falsely elevated pressures. In addition, the inclusion and exclusion criteria of the study may not have been appropriate.[52] Corbett and colleagues [3] found a cutoff of 250 but their numbers were somewhat small. Bono and coworkers[53] measured CSF pressure in obese and non-obese subjects with neck and legs extended and no patients had pressures over 200 mm water. In summary, the cutoff value for increased intracranial pressure remains unclear. Values between 200 and 250 may be considered borderline with values over 250 mm water definitely elevated.

Diagnostic confusion can result from anomalous optic discs in patients with borderline increased intracranial pressure. The main culprit here is buried optic nerve drusen – which can cause optic disc edema indistinguishable from low grade papilledema. Orbital ultrasound (echography) is an excellent test to reveal calcified buried optic disc drusen; the non-calcified variety can be problematic to prove. We recommend ultrasound of the optic disc in all cases of IIH with borderline elevated CSF pressures and low grade optic disc edema. Tilted discs, “little red discs,” and optic discs with anomalous branching and tortuosity can also mimic optic disc edema.

Recommendations for evaluation

A history tailored to search for the secondary causes of intracranial hypertension is imperative. A series of evaluations can then be selected based on the likelihood of secondary causes (Table 1).

Corbett and Thompson have correctly pointed out that many physicians follow IIH patients with the wrong tests.[54] Snellen acuity and the visual evoked potential are insensitive methods to detect visual loss in IIH. Repeated measurements of cerebrospinal fluid pressure can be misleading as it fluctuates throughout the day and does not correlate well with the

clinical state. Patients with IIH should be followed with perimetry with a known sensitive strategy and either serial stereo fundus photos, drawing-documented indirect ophthalmoscopy or optic disc grading using the Frisén scheme.[38] Automated perimetry is used for attentive and motivated subjects; in others manual perimetry gives more reproducible results.

Treatment

Once intracranial hypertension is discovered one should first eliminate presumed causal factors such as excessive vitamin A or tetracyclines and begin a low sodium weight reduction diet. Therapy aimed at reversing and preventing visual loss should then be instituted. Then symptomatic headache treatment can be introduced if this symptom persists in the face of intracranial pressure lowering agents and procedures. Many treatments both medical and surgical have been used for idiopathic intracranial hypertension with varying success. All reports to date are anecdotal. Visual loss is the only serious complication and it may occur anywhere from the time of first appearance to many years later. We therefore recommend tailoring the treatment primarily to the presence and progression of visual loss.

Medical Therapy

Medical treatment is aimed at lowering of intracranial pressure and treating symptoms directly such as headache. Unfortunately, there is no evidence-based data from controlled clinical treatment trials for idiopathic intracranial hypertension but such a trial is currently in progress.

Weight Loss

Weight loss has been used to treat IIH for many years. Newborg in 1974 reported remission of papilledema in all nine patients placed on a low calorie adaptation of Kempner's rice diet. The patients' intake was 400-1000 calories per day by fruits, rice, vegetables and occasionally 1-2 oz of meat. Fluids were limited to 750-1250 ml/day and sodium to less than 100 mg/day. All patients had reversal of their papilledema. Unfortunately, there was no mention of the patients' visual testing.[55] Others have also documented successful outcomes associated with weight loss [56-58] and it appears only modest degrees of weight loss in the range of 5-10% total body weight are needed for reversal of symptoms and signs.[56]

Gastric weight reduction surgery has been used with some success in 24 morbidly obese women with IIH.[59] Symptoms resolved in all but one patient within 4 months of the procedure. Two patients regained weight associated with return of their symptoms. There were many significant but treatable complications of this surgery. We reserve this treatment for IIH patients with morbid obesity.

Since marked recent weight gain is a predictor of visual deterioration[8] and papilledema can resolve with modest weight loss as the only treatment, we strongly encourage our patients to pursue a supervised weight loss program. Institution of a low salt diet and mild fluid restriction appear to be beneficial for many IIH patients. This may be especially true in patients that lose only a 5-10 percent of their total body mass, yet have resolution of their papilledema. It is not yet clear whether improvement occurs because of weight loss *per se* or other changes in diet such as fluid or sodium restriction or decrease in the intake of a molecule such as vitamin A.

Lumbar Puncture

Use of repeated lumbar punctures is controversial. Lumbar puncture has only a short-lived effect on CSF pressure[60] with a return of pressure to pre-tap level after only 82 minutes.[60]

Lumbar puncture measures CSF pressure at only one point in time. Since CSF pressure fluctuates, this information has only limited clinical use for modifying treatment plans. However, since transverse sinus collapse (smooth walled venous stenoses) can resolve immediately with lowering pressure,[61] CSF circulatory dynamics may be restored with this procedure and may give temporary relief until the sinus recollapses, usually within weeks.

Corticosteroids

Steroids are still occasionally used to treat IIH but their mechanism of action remains unclear. The side effects of weight gain, striae, and acne are especially unfortunate for these already obese patients. Although patients treated with steroids often respond well, there usually is recurrence of papilledema with rapid tapering of the dose. This may be accompanied by marked deterioration of visual function. A prolonged tapering may prevent return of symptoms and signs in some patients. Use of long-term steroids to treat IIH has largely been abandoned. Short-term use may have a role in the pre-operative period before a CSF shunting procedure.

Acetazolamide

McCarthy and Reed[62] showed acetazolamide (Diamox®) decreases CSF flow but not until over 99.5% of choroid plexus carbonic anhydrase was inhibited. Gücer and Viernstein [63] used intracranial pressure monitoring before and after treatment in four IIH patients. They monitored acetazolamide treatment in two of the patients and showed gradual CSF pressure reduction in both. They only reported the dose in one of the patients (four grams of acetazolamide was needed per day). Apparent efficacy of acetazolamide has also been shown by others[64, 65] but we await data from an ongoing multicenter, double-blind, randomized, placebo-controlled study of weight-reduction and/or low sodium diet plus acetazolamide vs diet plus placebo in subjects with mild visual loss.

We start with ½ to 1 gram a day of acetazolamide in divided doses and gradually increase the dose until either symptoms and signs regress, side effects become intolerable or a dose of 3-4 grams per day is reached. Most patients appear to respond in the 1-2 gram per day range.

The mechanism of action of acetazolamide is likely multifactorial. It has been found to reduce CSF production; also, it changes the taste of foods and sometimes causes anorexia aiding in weight loss. Patients nearly always experience tingling in the fingers, toes, and perioral region, and less commonly have malaise. Renal stones occur in a few percent of patients. Metabolic acidosis, evidenced by lowered serum bicarbonate, is a good measure of compliance. A rare but serious side effect is aplastic anemia. It occurs in one in 15,000 patient years of treatment with acetazolamide and usually occurs in the first six months of therapy. Aplastic anemia from acetazolamide has been reported most often in the elderly and is probably less common in younger idiopathic intracranial hypertension patients. Since this side effect is so rare and finding the case and stopping the medication does not necessarily cure the patient, repeated blood testing is not usually performed.[66]

While there are some structural similarities between acetazolamide and sulfa, there is little clinical or pharmacological evidence to suggest that a self-reported sulfa allergy is likely to produce a life-threatening cross-reaction with acetazolamide or furosemide.[67]

Topiramate (Topomax®) has also been used to treat IIH since it has carbonic anhydrase inhibitor activity and weight loss commonly occurs. In studies to date, it appears comparable to acetazolamide.[65, 68]

Furosemide

Furosemide has also been used to treat IIH.[7] It has been well documented that furosemide (Lasix®) can lower intracranial pressure.[69] It appears to work by both diuresis and reducing sodium transport into the brain. We initiate furosemide at a dose of 20 mg p.o. b.i.d. and gradually increase the dose, if necessary, to a maximum of 40 mg p.o. t.i.d. Potassium supplementation is given as needed.

Surgical Therapy

The surgical forms of therapy now used are various shunting and decompression procedures including stereotactic ventriculoperitoneal shunts and optic nerve sheath fenestration.

Subtemporal or suboccipital decompression

Subtemporal or suboccipital decompression was used from the 1940s to the 1960s for patients with visual loss from IIH. These procedures are now infrequently used because of complications, which although rare include seizures, otorrhea, and subdural hematoma. However, long-term success has been reported[70] and this procedure may be underutilized.

Optic nerve sheath fenestration

Optic nerve sheath fenestration consists of either creating a window or making a series of slits in the optic nerve sheath just behind the globe. This treatment is preferred for the patient with progressive visual loss with mild or easily controlled headaches, although over 50% of patients with the procedure gain adequate headache control (especially if the headache is frontal). Since improvement in papilledema may occur in the unoperated eye and fistula formation has been demonstrated the mechanism of action may be local decompression of the subarachnoid space (Figure 11). Occasional failure of the fellow eye to improve and the asymmetry of papilledema may be explained by the resistance to CSF flow produced by the trabeculations of the subarachnoid space. The mechanism of action may also be closure of the subarachnoid space in the retrolaminar optic nerve by scarring. It is likely that both mechanisms contribute to protection of the optic nerve head.

Many large case series attest to the efficacy of this technique.[71-77] In these series, postoperative visual acuity or perimetry results were as good as or better than preoperative studies in about 90%.[74] However, occasional patients lose vision in the perioperative period (Table 2).

CSF Shunting Procedures

Various shunting procedures have been employed for the treatment of idiopathic intracranial hypertension such as lumbar subarachnoid-peritoneal shunts, ventriculoatrial, ventriculojugular and ventriculoperitoneal shunts. In general, the indication for a CSF diversion procedure is failed medical therapy or intractable headache. Its use appears to be increasing.[78]

Eggenberger and coworkers[79] studied lumboperitoneal shunt retrospectively in 27 IIH patients. While initially successful, 56% required a shunt revision. Rosenberg and colleagues[80] reported on 37 IIH patients that underwent 73 lumboperitoneal shunts and nine ventricular shunts with modest success (38% of patients successfully treated after one shunting procedure). Shunt failure occurring in 55% and low-pressure headaches in 21% were the most common causes for reoperation. The vision of most patients improved or stabilized from the procedure, but three who had initially improved later lost vision and six had a decrease in vision postoperatively. Serious complications occurred in 3.6%. Other series are similar[81, 82] with the conclusion that there is initial success but at least half need

reoperations. Also, when the procedure is done primarily for headache relief, long-term success is only about 50%.[83] Inhospital mortality for new shunts is a surprising 0.5% with 0.9% for ventricular shunts and 0.2% for lumbar shunts.[84]

In summary, shunting procedures are successful in selected patients. Shunt occlusion that occurs in about half of those shunted, can be accompanied by severe visual loss, limiting the effectiveness of this procedure. Table 3 summarizes the results of shunting procedures that reported visual outcomes.

Gastric exclusion surgery

As discussed above, for the morbidly obese patient, successful treatment has been reported using gastric exclusion procedures.[59] This procedure may be especially useful in treating other conditions co-morbid with obesity such as arterial hypertension, diabetes mellitus, and sleep apnea. Complications include major wound infection and stenosis at the gastrojejunal anastomosis.

Venous sinus stenting

It has been suggested that the cause of IIH is collapse of the proximal transverse sinus. However, King and colleagues have shown lowering of CSF pressure from a cervical puncture abolishes the pressure gradient.[85] Since this collapse of the transverse sinus, which is ubiquitous in IIH[36] (and occurs in about 7% of normals), may obstruct venous return and hence CSF outflow, stents have been placed to keep this portion of the transverse sinus open. This procedure has been reviewed by Friedman with the conclusion that it can have major morbidity (subdural hematoma), remains unproven and needs further study.[86]

Treatment Overview

Medical and surgical treatment of patients with idiopathic intracranial hypertension is often challenging, requiring integration of the history, examination and clinical course. Many factors are involved and each is weighted in creating individualized therapy. The most important factor is usually the amount and progression of visual loss. Next in importance is the severity of the patient's symptoms with regard to how much they are disrupting the patient's activities of daily living. Headache is the most problematic symptom but pulse synchronous tinnitus, and diplopia, can be difficult to treat. Also factored in is the degree and change in papilledema grade. Figure 12 summarizes the options.

Patients with mild or no visual loss are treated with modest weight loss and sodium restriction often with the addition of acetazolamide (Diamox®). In cases with no visual loss, the decision on whether to add acetazolamide is based on the severity of headache or other symptoms and the degree of papilledema; the greater the grade of papilledema, the greater the risk for visual loss. Patients with mild or no visual loss are usually followed first at 4 month intervals. If there vision improves or papilledema lessens to Grade I or 0, we use 6 month or one year intervals. All patients are encouraged to enter a weight management program with a goal of 5-10% weight loss along with a low salt diet and modest fluid restriction (drinking only when thirsty rather than forcing fluids as is sometimes done to lose weight).

If the patient presents with moderate to severe visual loss (mean deviation on automated perimetry greater than −5 dB), the optimal management has yet to be determined. Some advocate early surgery while others give a medical trial. We have seen both approaches work. For maximal medical therapy we start with a gram of Diamox a day in divided doses and over weeks gradually increase the dose to the maximal tolerated dose. We define this the highest dose that does not interfere significantly with activities of daily living. There is

some evidence that furosemide (Lasix) can be added in increasing doses to 40 mg p.o. tid to further reduce CSF pressure. We use optic nerve sheath fenestration if there is worsening on maximal medical therapy; headache improves in about half of patients, especially if the pain is frontal and worsens with eye movements. This pain is likely due to distended optic nerve sheaths and pain sensitive structures are stretched with eye movements. If headache is severe and unresponsive to medical treatments we first make sure the patient does not have rebound headaches from daily analgesics or caffeine. If we believe the headaches are due to increased intracranial pressure, we proceed with a CSF shunting procedure although the surgery is successful for headache relief in only about half. We believe stereotactic ventriculoatrial or ventriculoperitoneal shunts are most successful.

Patients that fail to respond to therapy should have repeat neuroimaging looking for occult meningiomas or other tumors invading the venous sinuses and a sleep study looking for obstructive sleep apnea which should have treatment optimized. Patients with unrelenting visual loss should also have 24 hour blood pressure monitoring to look for periods of hypotension. Hypotension is a strong risk factor for visual loss, especially during surgery. Treatment decisions may be complicated and are further discussed elsewhere.[87]

Headache Treatment

Headache in IIH patients may improve after a lumbar puncture, but may remain as a management problem even after medications have been given to reduce edema. We have had success treating these patients with standard prophylactic vascular headache remedies. However, we try to avoid medications that cause hypotension, such as beta blockers or calcium channel blockers, because they may cause reduced perfusion of the optic nerve head. Tricyclic antidepressants can be problematic because of their side effect of weight gain. We use tricyclics in very low doses such as amitriptyline 10 - 25 mg at bedtime. Nonsteroidal anti-inflammatory agents are used as an adjunct but their use is limited to two days per week to prevent the development of rebound headaches. Topiramate may be useful both for its migraine prophylaxis, side effect of weight loss and for carbonic anhydrase inhibition.

Uncommonly, a CSF shunting procedure is needed for persistent headache; but it can produce the “hindbrain herniation” headache in return. Patients with IIH also have other headache syndromes. Especially in patients with a migraine history, analgesic rebound or caffeine rebound headaches may coexist. These patients may require IV dihydroergotamine to treat this troublesome headache syndrome.

IIH in children

The effect of papilledema on vision is the same in children as in adults. Fortunately some form of quantitative perimetry can be performed in most children over the age of 6. Excellent reviews of IIH in children can be found.[88-90] These authors point out interesting differences between adult and childhood forms of IIH. In IIH of childhood through puberty, the incidence in girls and boys is the same.[91] In addition, obesity does not appear to be an important factor in the pathogenesis or treatment of IIH in prepubertal children. The etiologies reported only with children are nutritional restoration after malnutrition and thyroid replacement therapy in hypothyroid children.[22]

IIH in Men

Digre and Corbett studied 29 men with IIH using a case control design and found IIH occurs in men in a similar age distribution to women. They noted that men may require surgical treatment for impending visual loss more often and suggest African American men to be at

greater risk to lose of vision. Bruce and colleagues also found men with IIH were two times as likely as women to have visual loss.[92]

The issue of IIH in men is complicated by the not infrequent co-occurrence of obstructive sleep apnea.[93] Two studies have documented increased intracranial pressure during apneic periods in these patients.[94, 95] Jennum and Borgesen documented the occurrence of increased intracranial pressure during waking hours in the absence of apnea in half their subjects.[95] Since there is a biologically plausible mechanism to explain increased intracranial pressure in sleep apnea and the co-occurrence in men is frequent, we recommend sleep studies in all men and in women with symptoms suggestive of obstructive sleep apnea.

IIH in Pregnancy

Digre and colleagues using a case control design found no increase in obstetric complications in IIH.[15] Visual loss occurred with the same frequency in pregnant and non-pregnant IIH patients. They concluded that treatment of IIH patients in pregnancy should be the same as for non-pregnant IIH patients, except that caloric restriction must be tempered.

The issue of acetazolamide use in the first trimester of pregnancy is complex. Due to potential teratogenic effects in animals and a single case of a sacrococcygeal teratoma in humans, the basis for withholding acetazolamide is not strong. Acetazolamide is an FDA category C agent and in our experience can be used after appropriate informed consent, discussion with the patient and the obstetrician, and for patients in whom the benefit outweighs the potential risk for treatment.[96]

Conclusion

Idiopathic intracranial hypertension is characterized by elevated CSF pressure of unknown cause. It is predominantly a disease of women in the childbearing years. Although the cause of IIH remains obscure, it has become clear that loss of visual function is common and patients may progress to blindness if untreated. Diagnosis should adhere to the modified Dandy criteria and other causes if intracranial hypertension sought. IIH patient management should include serial perimetry and optic disc grading or photography. Then, the proper therapy can be selected and visual loss prevented or reversed. Although there is no evidence based data to guide therapy, there is an ongoing randomized double blind controlled treatment trial of IIH investigating diet and medical therapy.

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References

1. Corbett JJ, Savino PJ, Thompson HS, et al. Visual loss in pseudotumor cerebri. Follow-up of 57 patients from five to 41 years and a profile of 14 patients with permanent severe visual loss. Arch Neurol 1982;39:461–474. [PubMed: 7103794]
2. Wall M, Hart WM Jr. Burde RM. Visual field defects in idiopathic intracranial hypertension (pseudotumor cerebri). Am J Ophthalmol 1983;96:654–669. [PubMed: 6638133]
3. Corbett JJ, Mehta MP. Cerebrospinal fluid pressure in normal obese subjects and patients with pseudotumor cerebri. Neurology 1983;33:1386–1388. [PubMed: 6684240]
4. Smith JL. Whence pseudotumor cerebri? J Clin Neuro-ophthalmol 1985;5:55–56.

5. Durcan FJ, Corbett JJ, Wall M. The incidence of pseudotumor cerebri. Population studies in Iowa and Louisiana. Arch Neurol 1988;45:875–877. [PubMed: 3395261]
6. Radhakrishnan K, Ahlskog JE, Cross SA, Kurland LT, O'Fallon WM. Idiopathic intracranial hypertension (pseudotumor cerebri). Descriptive epidemiology in Rochester, Minn, 1976 to 1990. Arch Neurol 1993;50:78–80. [PubMed: 8418804]
7. Corbett JJ. The 1982 Silversides lecture. Problems in the diagnosis and treatment of pseudotumor cerebri. Can J Neurol Sci 1983;10:221–229. [PubMed: 6652584]
8. Wall M, George D. Idiopathic intracranial hypertension. A prospective study of 50 patients. Brain 1991;114:155–180. [PubMed: 1998880]
9. Digre KB, Corbett JJ. Pseudotumor cerebri in men. Arch Neurol 1988;45:866–872. [PubMed: 3395260]
10. Ireland B, Corbett JJ, Wallace RB. The search for causes of idiopathic intracranial hypertension. A preliminary case-control study. Arch Neurol 1990;47:315–320. [PubMed: 2310315]
11. Giuseffi V, Wall M, Siegel PZ, Rojas PB. Symptoms and disease associations in idiopathic intracranial hypertension (pseudotumor cerebri): a case-control study. Neurology 1991;41:239–244. [PubMed: 1992368]
12. Greer M. Benign Intracranial Hypertension. II. Following corticosteroid therapy. Neurology 1963;13:439–441. [PubMed: 13950226]
13. Neville BG, Wilson J. Benign intracranial hypertension following corticosteroid withdrawal in childhood. Br Med J 1970;3:554–556. [PubMed: 4318283]
14. Walsh FB. Papilledema associated with increased intracranial pressure in Addison's disease. Arch Ophthalmol 1952;47:86.
15. Digre KB, Varner MW, Corbett JJ. Pseudotumor cerebri and pregnancy. Neurology 1984;34:721–729. [PubMed: 6539432]
16. Deonna T, Guignard JP. Acute intracranial hypertension after nalidixic acid administration. Arch Dis Child 1974;49:743. [PubMed: 4419059]
17. Mushet GR. Pseudotumor and nitrofurantoin therapy [letter]. Arch Neurol 1977;34:257. [PubMed: 843266]
18. Konomi H, Imai M, Nihei K, Kamoshita S, Tada H. Indomethacin causing pseudotumor cerebri in Bartter's syndrome [letter]. N Engl J Med 1978;298:855. [PubMed: 634325]
19. Larizza D, Colombo A, Lorini R, Severi F. Ketoprofen causing pseudotumor cerebri in Bartter's syndrome [letter]. N Engl J Med 1979;300:796. [PubMed: 423914]
20. Feldman MH, Schlezinger NS. Benign intracranial hypertension associated with hypervitaminosis A. Arch Neurol 1970;22:1–7. [PubMed: 5409596]
21. Spector RH, Carlisle J. Pseudotumor cerebri caused by a synthetic vitamin A preparation. Neurology 1984;34:1509–1511. [PubMed: 6238241]
22. Van Dop C, Conte FA, Koch TK, Clark SJ, Wilson-Davis SL, Grumbach MM. Pseudotumor cerebri associated with initiation of levothyroxine therapy for juvenile hypothyroidism. N Engl J Med 1983;308:1076–1080. [PubMed: 6835321]
23. Saul RF, Hamburger HA, Selhorst JB. Pseudotumor cerebri secondary to lithium carbonate. JAMA 1985;253:2869–2870. [PubMed: 3921728]
24. Shah A, Roberts T, McQueen IN, Graham JG, Walker K. Danazol and benign intracranial hypertension. Br Med J [Clin Res] 1987;294:1323.
25. Bercaw BL, Greer M. Transport of intrathecal 131-I risa in benign intracranial hypertension. Neurology 1970;20:787–790. [PubMed: 5468773]
26. Jacobson DM, Karanjia PN, Olson KA, Warner JJ. Computed tomography ventricular size has no predictive value in diagnosing pseudotumor cerebri. Neurology 1990;40:1454–1455. [PubMed: 2392235]
27. Wall M, Dollar JD, Sadun AA, Kardon R. Idiopathic intracranial hypertension: Lack of histologic evidence for cerebral edema. Arch Neurol 1995;52:141–145. [PubMed: 7848121]
28. Mathew NT, Meyer JS, Ott EO. Increased cerebral blood volume in benign intracranial hypertension. Neurology 1975;25:646–649. [PubMed: 1171396]

29. Brooks DJ, Beaney RP, Leenders KL, Marshall J, Thomas DJ, Jones T. Regional cerebral oxygen utilization, blood flow, and blood volume in benign intracranial hypertension studied by positron emission tomography. Neurology 1985;35:1030–1034. [PubMed: 3874372]
30. Boulton M, Armstrong D, Flessner M, Hay J, Szalai JP, Johnston M. Raised intracranial pressure increases CSF drainage through arachnoid villi and extracranial lymphatics. Am J Physiol 1998;275(3 Pt 2):889–896.
31. Sahs AL, Joynt RJ. Brain swelling of unknown cause. Neurology 1956;6:791–803.
32. Wall M. The headache profile of idiopathic intracranial hypertension. Cephalalgia 1990;10:331–335. [PubMed: 2289234]
33. Friedman DI, Rausch EA. Headache diagnoses in patients with treated idiopathic intracranial hypertension. Neurology 2002;58:1551–1553. [PubMed: 12034799]
34. Sadun A, Currie J, Lessell S. Transient visual obscurations with elevated optic discs. Ann Neurol 1984;16:489–494. [PubMed: 6497356]
35. Meador KJ, Swift TR. Tinnitus from intracranial hypertension. Neurology 1984;34:1258–1261. [PubMed: 6540416]
36. Farb RI, Vanek I, Scott JN, et al. Idiopathic intracranial hypertension: the prevalence and morphology of sinovenous stenosis. Neurology 2003;60:1418–1424. [PubMed: 12743224]
37. Wall M, White WN. Asymmetric papilledema in idiopathic intracranial hypertension: prospective interocular comparison of sensory visual function. Invest Ophthalmol Vis Sci 1998;39:134–142. [PubMed: 9430554]
38. Frisén L. Swelling of the optic nerve head: a staging scheme. J Neurol Neurosurg Psychiatr 1982;45:13–18. [PubMed: 7062066]
39. Scott CJ, Kardon RH, Lee AG, Frisen L, Wall M. Diagnosis and Grading of Papilledema in Patients with Raised Intracranial Pressure Using Optical Coherence Tomography (OCT) Compared to Clinical Expert Assessment using a Clinical Staging Scale. Arch Ophthalmol. 2010
40. Cushing H. Strangulation of the nervi abducentes by lateral branches of the basilar artery in cases of brain tumor. Brain 1910;33:204–235.
41. Wall M, George D. Visual loss in pseudotumor cerebri. Incidence and defects related to visual field strategy. Arch Neurol 1987;44:170–175. [PubMed: 3813933]
42. Corbett JJ, Jacobson DM, Mauer RC, Thompson HS. Enlargement of the blind spot caused by papilledema. Am J Ophthalmol 1988;105:261–265. [PubMed: 3344783]
43. Shah VA, Kardon RH, Lee AG, Corbett JJ, Wall M. Long-term follow-up of idiopathic intracranial hypertension: the Iowa experience. Neurology 2008;70:634–640. [PubMed: 18285538]
44. Wall, M. The morphology of visual field damage in idiopathic intracranial hypertension: an anatomic region analysis. In: Mills, RP.; Heijl, A., editors. Perimetry Update 1990/1991. Kugler Publications; Amsterdam: 1991. p. 20-27.
45. Hayreh SS. Pathogenesis of optic disc oedema in raised intracranial pressure. Trans Ophthalmol Soc UK 1976;96:404–407. [PubMed: 829180]
46. Hayreh SS. The sheath of the optic nerve. Ophthalmologica (Basel) 1984;189:54–63. [PubMed: 6472807]
47. Hayreh SS. Optic disc edema in raised intracranial pressure. V. Pathogenesis. Arch Ophthalmol 1977;95:1553–1565. [PubMed: 71138]
48. Hayreh SS, March W, Anderson DR. Pathogenesis of block of rapid orthograde axonal transport by elevated intraocular pressure. Experimental Eye Research 1979;28:515–523. [PubMed: 87337]
49. Tso MO, Hayreh SS. Optic disc edema in raised intracranial pressure. IV. Axoplasmic transport in experimental papilledema. Arch Ophthalmol 1977;95:1458–1462. [PubMed: 70201]
50. Neville L, Egan RA. Frequency and amplitude of elevation of cerebrospinal fluid resting pressure by the Valsalva maneuver. Can J Ophthalmol 2005;40:775–777. [PubMed: 16391647]
51. Whiteley W, Al Shahi R, Warlow CP, Zeidler M, Lueck CJ. CSF opening pressure: reference interval and the effect of body mass index. Neurology 2006;67:1690–1691. [PubMed: 17101909]
52. Bono F, Quattrone A. CSF opening pressure: reference interval and the effect of body mass index. Neurology 2007;68:1439–1440. [PubMed: 17452597]

53. Bono F, Lupo MR, Serra P, et al. Obesity does not induce abnormal CSF pressure in subjects with normal cerebral MR venography. Neurology 2002;59:1641–1643. [PubMed: 12451215]
54. Corbett JJ, Thompson HS. The rational management of idiopathic intracranial hypertension. Arch Neurol 1989;46:1049–1051. [PubMed: 2679506]
55. Newborg B. Pseudotumor cerebri treated by rice reduction diet. Arch Intern Med 1974;133:802–807. [PubMed: 4821775]
56. Johnson LN, Krohel GB, Madsen RW, March GA Jr. The role of weight loss and acetazolamide in the treatment of idiopathic intracranial hypertension (pseudotumor cerebri). Ophthalmology 1998;105:2313–2317. [PubMed: 9855165]
57. Kupersmith MJ, Gamell L, Turbin R, Peck V, Spiegel P, Wall M. Effects of weight loss on the course of idiopathic intracranial hypertension in women. Neurology 1998;50:1094–1098. [PubMed: 9566400]
58. Wong R, Madill SA, Pandey P, Riordan-Eva P. Idiopathic intracranial hypertension: the association between weight loss and the requirement for systemic treatment. BMC Ophthalmol 2007;7:15. [PubMed: 17888152]
59. Sugerman HJ, Felton WL III, Sismanis A, Kellum JM, DeMaria EJ, Sugerman EL. Gastric surgery for pseudotumor cerebri associated with severe obesity. Ann Surg 1999;229:634–640. [PubMed: 10235521]
60. Johnston I, Paterson A. Benign intracranial hypertension. II. CSF pressure and circulation. Brain 1974;97:301–312. [PubMed: 4434179]
61. Scoffings DJ, Pickard JD, Higgins JN. Resolution of transverse sinus stenoses immediately after CSF withdrawal in idiopathic intracranial hypertension. J Neurol Neurosurg Psychiatry 2007;78:911–912. [PubMed: 17635988]
62. McCarthy KD, Reed DJ. The effect of acetazolamide and furosemide on CSF production and choroid plexus carbonic anhydrase activity. J Pharmacol Exp Ther 1974;189:194–201. [PubMed: 4207244]
63. Gucer G, Vierenstein L. Long-term intracranial pressure recording in management of pseudotumor cerebri. J Neurosurg 1978;49:256–263. [PubMed: 671078]
64. Tomsak RL, Niffenegger AS, Remler BF. Treatment of pseudotumor cerebri with Diamox (acetazolamide). J Clin Neuro-ophthalmol 1988;8:93–98.
65. Celebisoy N, Gokcay F, Sirin H, Akyurekli O. Treatment of idiopathic intracranial hypertension: topiramate vs acetazolamide, an open-label study. Acta Neurol Scand 2007;116:322–327. [PubMed: 17922725]
66. Zimran A, Beutler E. Can the risk of acetazolamide-induced aplastic anemia be decreased by periodic monitoring of blood cell counts? Am J Ophthalmol 1987;104:654–658. [PubMed: 3688107]
67. Lee AG, Anderson R, Kardon RH, Wall M. Presumed “sulfa allergy” in patients with intracranial hypertension treated with acetazolamide or furosemide: cross-reactivity, myth or reality? Am J Ophthalmol 2004;138:114–118. [PubMed: 15234289]
68. Shah VA, Fung S, Shahbaz R, Taktakishvili O, Wall M, Lee AG. Idiopathic intracranial hypertension. Ophthalmology 2007;114:617. [PubMed: 17324704]
69. Pollay M, Fullenwider C, Roberts PA, Stevens FA. Effect of mannitol and furosemide on blood-brain osmotic gradient and intracranial pressure. J Neurosurg 1983;59:945–950. [PubMed: 6415245]
70. Kessler LA, Novelli PM, Reigel DH. Surgical treatment of benign intracranial hypertension--subtemporal decompression revisited. Surg Neurol 1998;50:73–76. [PubMed: 9657496]
71. Goh KY, Schatz NJ, Glaser JS. Optic nerve sheath fenestration for pseudotumor cerebri. J Neuro-Ophthalmol 1997;17:86–91.
72. Acheson JF, Green WT, Sanders MD. Optic nerve sheath decompression for the treatment of visual failure in chronic raised intracranial pressure. J Neurol Neurosurg Psychiatr 1994;57:1426–1429. [PubMed: 7964827]
73. Sergott RC, Savino PJ, Bosley TM. Modified optic nerve sheath decompression provides long-term visual improvement for pseudotumor cerebri. Arch Ophthalmol 1988;106:1391–1397. [PubMed: 3273487]

74. Corbett JJ, Nerad JA, Tse D, Anderson RL. Optic nerve sheath fenestration for pseudotumor cerebri: the lateral orbitotomy approach. Arch Ophthalmol 1988;106:1391–1397. [PubMed: 3273487]
75. Plotnik JL, Kosmorsky GS. Operative complications of optic nerve sheath decompression. Ophthalmology 1993;100:683–690. [PubMed: 8493011]
76. Brourman ND, Spoor TC, Ramocki JM. Optic nerve sheath decompression for pseudotumor cerebri. Arch Ophthalmol 1988;106:1378–1383. [PubMed: 3178548]
77. Chandrasekaran S, McCluskey P, Minassian D, Assaad N. Visual outcomes for optic nerve sheath fenestration in pseudotumour cerebri and related conditions. Clin Experiment Ophthalmol 2006;34:661–665. [PubMed: 16970759]
78. Curry WT Jr. Butler WE, Barker FG. Rapidly rising incidence of cerebrospinal fluid shunting procedures for idiopathic intracranial hypertension in the United States, 1988-2002. Neurosurgery 2005;57:97–108. [PubMed: 15987545]
79. Eggenberger ER, Miller NR, Vitale S. Lumboperitoneal shunt for the treatment of pseudotumor cerebri. Neurology 1996;46:1524–1530. [PubMed: 8649541]
80. Rosenberg M, Smith C, Beck R. The efficacy of shunting procedures in pseudotumor cerebri. Neurology 1989;39:209.
81. Burgett RA, Purvin VA, Kawasaki A. Lumboperitoneal shunting for pseudotumor cerebri. Neurology 1997;49:734–739. [PubMed: 9305333]
82. Johnston I, Besser M, Morgan MK. Cerebrospinal fluid diversion in the treatment of benign intracranial hypertension. J Neurosurg 1988;69:195–202. [PubMed: 3392566]
83. McGirt MJ, Woodworth G, Thomas G, Miller N, Williams M, Rigamonti D. Cerebrospinal fluid shunt placement for pseudotumor cerebri-associated intractable headache: predictors of treatment response and an analysis of long-term outcomes. Journal of Neurosurgery 2004;101(4):627–32. [PubMed: 15481717]
84. Curry WT Jr. Butler WE, Barker FG. Rapidly rising incidence of cerebrospinal fluid shunting procedures for idiopathic intracranial hypertension in the United States, 1988-2002. Neurosurgery 2005;57(1):97–108. discussion 97-108. [PubMed: 15987545]
85. King JO, Mitchell PJ, Thomson KR, Tress BM. Manometry combined with cervical puncture in idiopathic intracranial hypertension. Neurology 2002;58:26–30. [PubMed: 11781401]
86. Friedman DI. Cerebral venous pressure, intra-abdominal pressure, and dural venous sinus stenting in idiopathic intracranial hypertension. J Neuroophthalmol 2006;26:61–64. [PubMed: 16518170]
87. Wall, M. Papilledema and Idiopathic Intracranial Hypertension (Pseudotumor Cerebri). In: Noseworthy, JH., editor. Neurological Theraputics Principles and Practice. Second ed.. Informa Healthcare; Abingdon UK: 2006. p. 1955-1968.
88. Cinciripini GS, Donahue S, Borchert MS. Idiopathic intracranial hypertension in prepubertal pediatric patients: characteristics, treatment, and outcome. Am J Ophthalmol 1999;127:178–182. [PubMed: 10030560]
89. Lessell S. Pediatric pseudotumor cerebri (idiopathic intracranial hypertension). Surv Ophthalmol 1992;37:155–166. [PubMed: 1475750]
90. Babikian P, Corbett J, Bell W. Idiopathic intracranial hypertension in children: the Iowa experience. J Child Neurol 1994;9:144–149. [PubMed: 8006364]
91. Balcer LJ, Liu GT, Forman S, et al. Idiopathic intracranial hypertension: relation of age and obesity in children. Neurology 1999;52:870–872. [PubMed: 10078746]
92. Bruce BB, Kedar S, Van Stavern GP, et al. Idiopathic intracranial hypertension in men. Neurology 2009;72:304–309. [PubMed: 18923135]
93. Lee AG, Golnik K, Kardon R, Wall M, Eggenberger E, Yedavally S. Sleep apnea and intracranial hypertension in men. Ophthalmology 2002;109:482–485. [PubMed: 11874748]
94. Sugita Y, Iijima S, Teshima Y, et al. Marked episodic elevation of cerebrospinal fluid pressure during nocturnal sleep in patients with sleep apnea hypersomnia syndrome. Electroencephalogr Clin Neurophysiol 1985;60:214–219. [PubMed: 2578929]
95. Jennum P, Borgesen SE. Intracranial pressure and obstructive sleep apnea. Chest 1989;95:279–283. [PubMed: 2914475]

96. Lee AG, Pless M, Falardeau J, Capozzoli T, Wall M, Kardon RH. The use of acetazolamide in idiopathic intracranial hypertension during pregnancy. American Journal of Ophthalmology 2005;139(5):855–9. [PubMed: 15860291]

97. Hupp SL, Glaser JS, Frazier-Byrne S. Optic nerve sheath decompression. Review of 17 cases. Arch Ophthalmol 1987;105:386–389. [PubMed: 3827717]

98. Kelman SE, Heaps R, Wolf A, Elman MJ. Optic nerve decompression surgery improves visual function in patients with pseudotumor cerebri. Neurosurgery 1992;30:391–395. [PubMed: 1620303]

99. Plotnik JL, Kosmorsky GS. Operative complications of optic nerve sheath decompression [see comments]. Ophthalmology 1993;100:683–690. [Review] [36 refs]. [PubMed: 8493011]

100. Corbett JJ, Nerad JA, Tse DT, Anderson RL. Results of optic nerve sheath fenestration for pseudotumor cerebri. The lateral orbitotomy approach. Arch Ophthalmol 1988;106:1391–1397. [PubMed: 3273487]

101. Banta JT, Farris BK. Pseudotumor cerebri and optic nerve sheath decompression. Ophthalmology 2000;107:1907–1912. [PubMed: 11013197]

102. Rosenberg ML, Corbett JJ, Smith C, et al. Cerebrospinal fluid diversion procedures in pseudotumor cerebri. Neurology 1993;43:1071–1072. [PubMed: 8170543]

103. Shapiro S, Yee R, Brown H. Surgical management of pseudotumor cerebri in pregnancy: case report. Neurosurgery 1995;37:829–831. [PubMed: 8559316]

104. Bynke G, Zemack G, Bynke H, Romner B. Ventriculoperitoneal shunting for idiopathic intracranial hypertension. Neurology 2004;63(7):1314–6. [PubMed: 15477563]

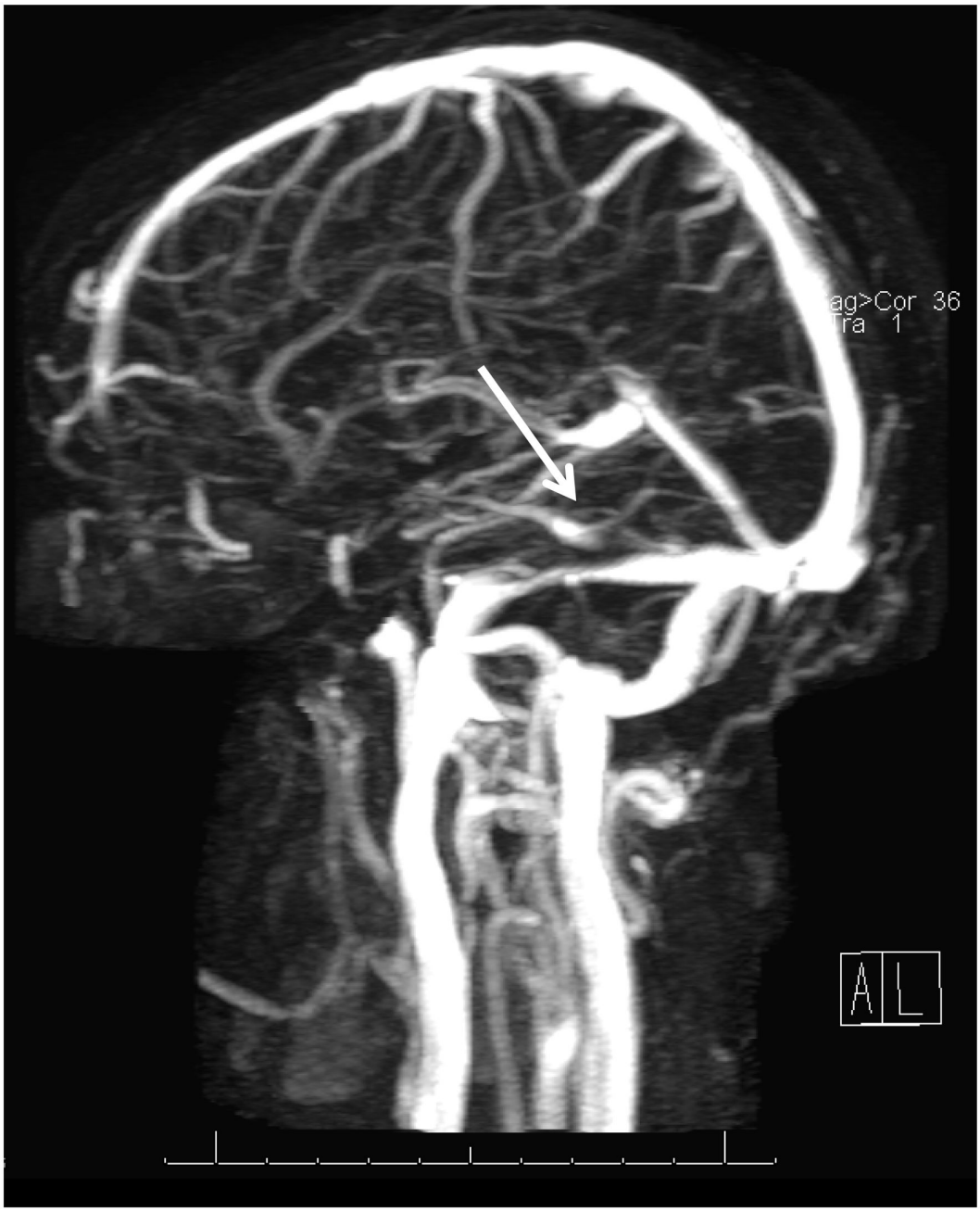

Figure 1.
Magnetic resonance venogram showing smooth-walled venous stenoses of the transverse sinus, characteristic of idiopathic intracranial hypertension.

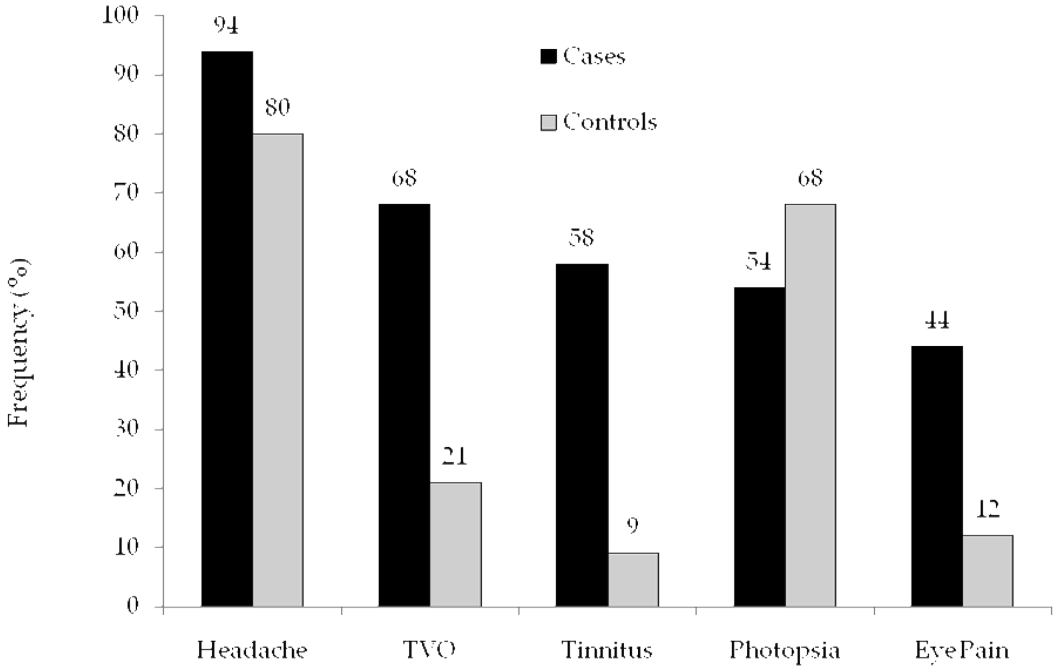

Figure 2.
Frequency in percent of symptoms in IIH and a control group. TVO - transient visual obscurations, ICN - intracranial noises. Reprinted with permision.[11]

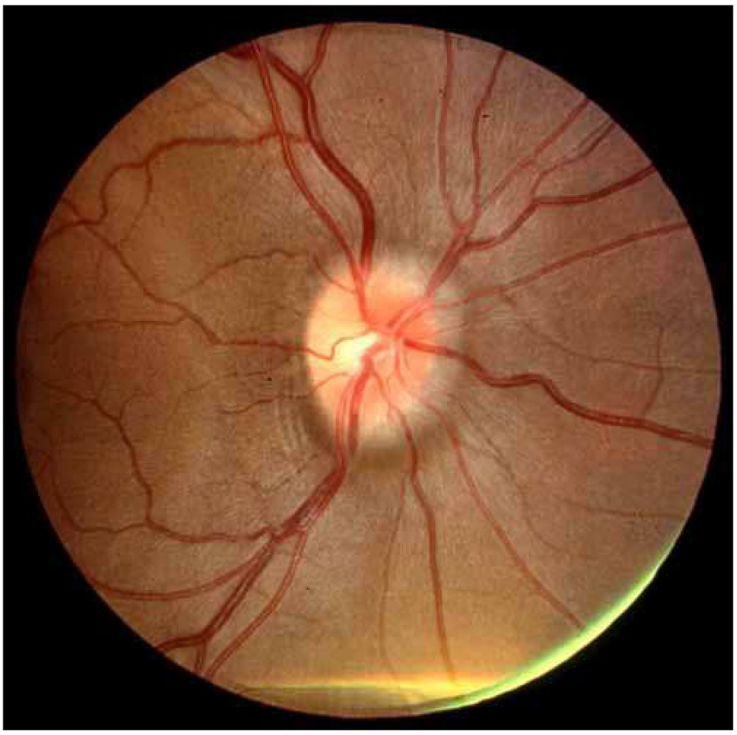

Figure 3.
characteristic “C-shaped halo” with a temporal gap surrounding the disc of early of (Frisén grade 1) papilledema.

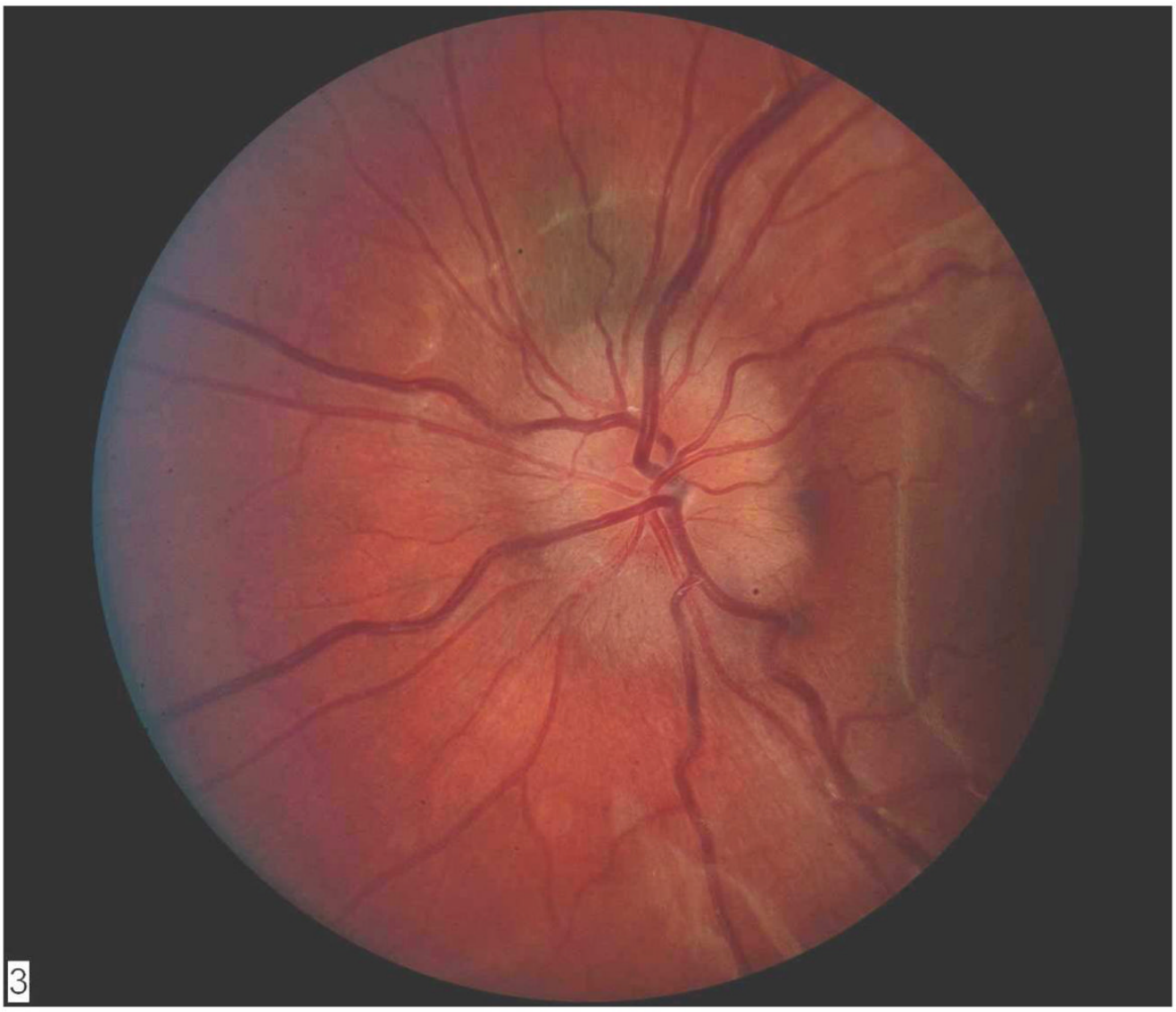

Figure 4.
With grade II papilledema the halo becomes circumferential.

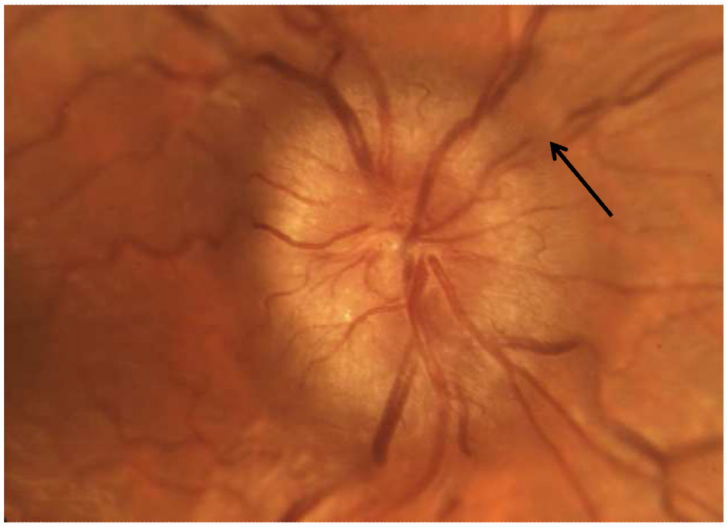

Figure 5.
Grade III papilledema is characterized by Loss of major vessels as they leave the disc (arrow).

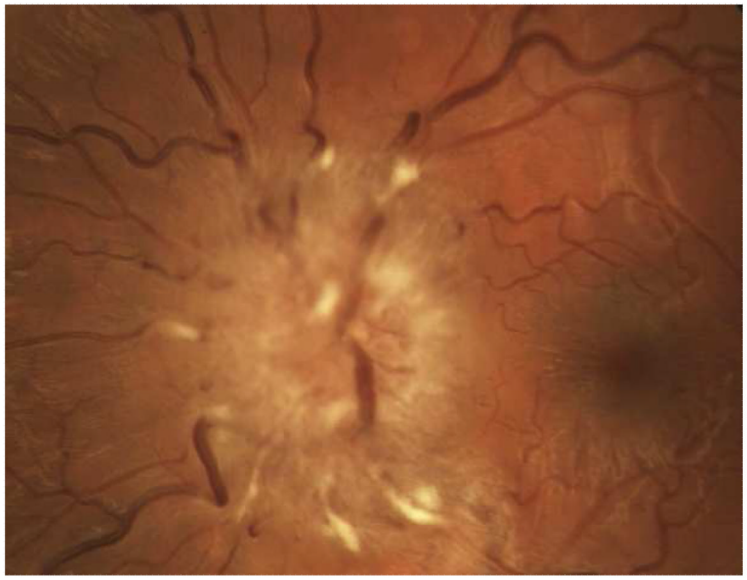

Figure 6.
Grade III papilledema is characterized by Loss of major vessels on the disc.

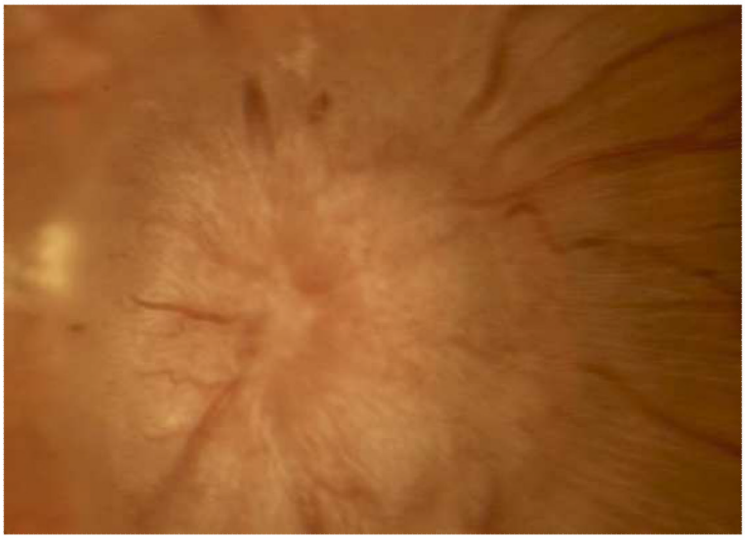

Figure 7.
Grade V has the criteria of Grade IV plus partial or total obscuration of all vessels on the disc.

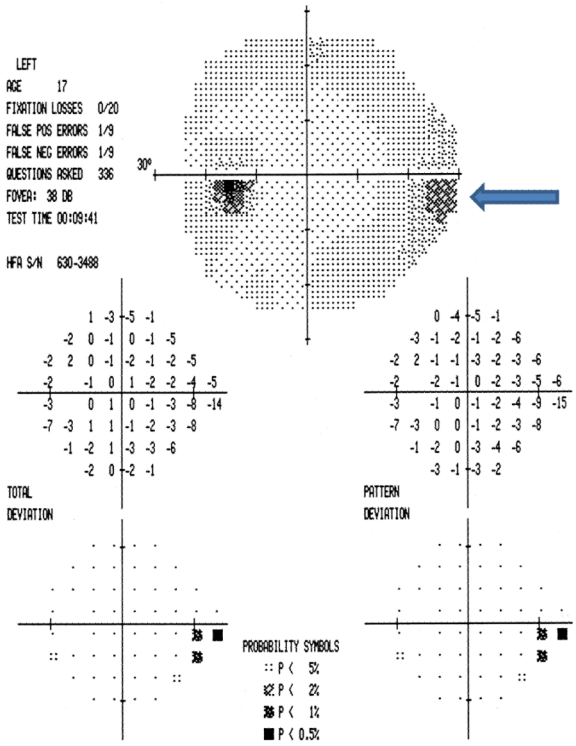

Figure 8.
A typical inferonasal step defect (arrow) of early optic disc edema in IIH.

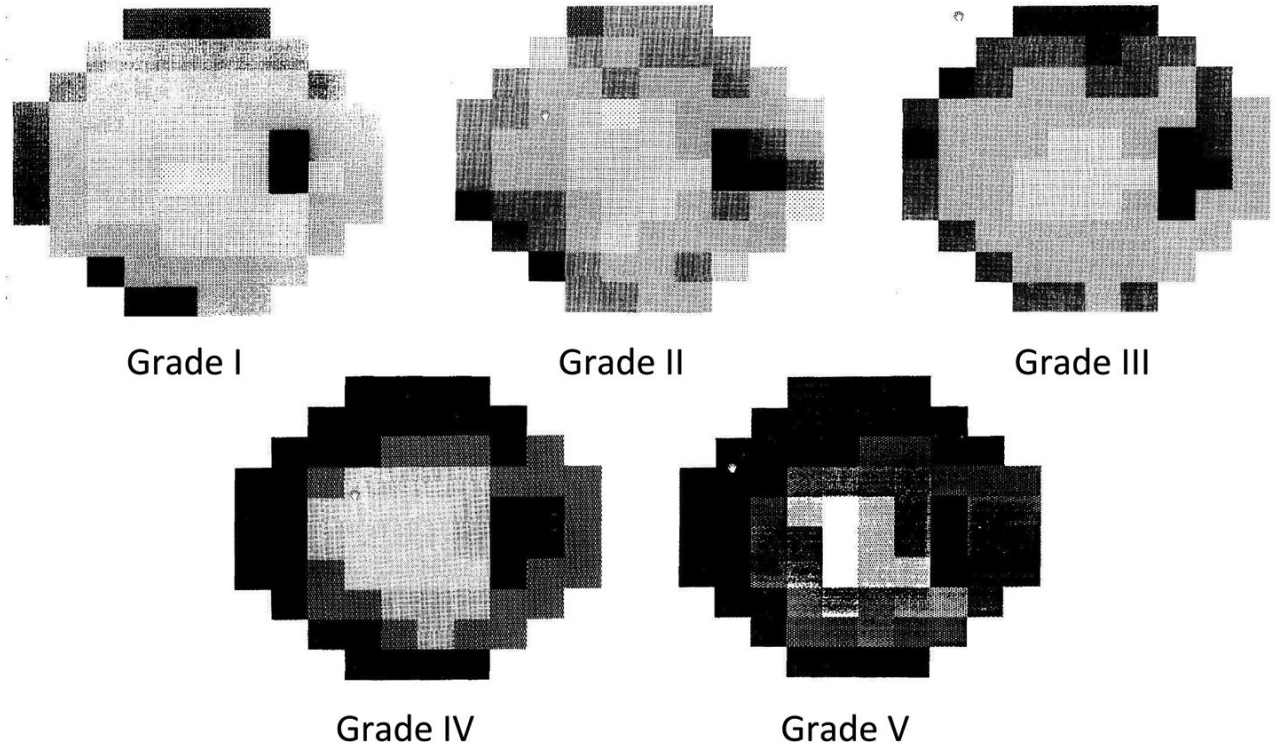

Figure 9.
Grades of visual loss in IIH found by grading the visual field examinations and then averaging the values from within each grade.

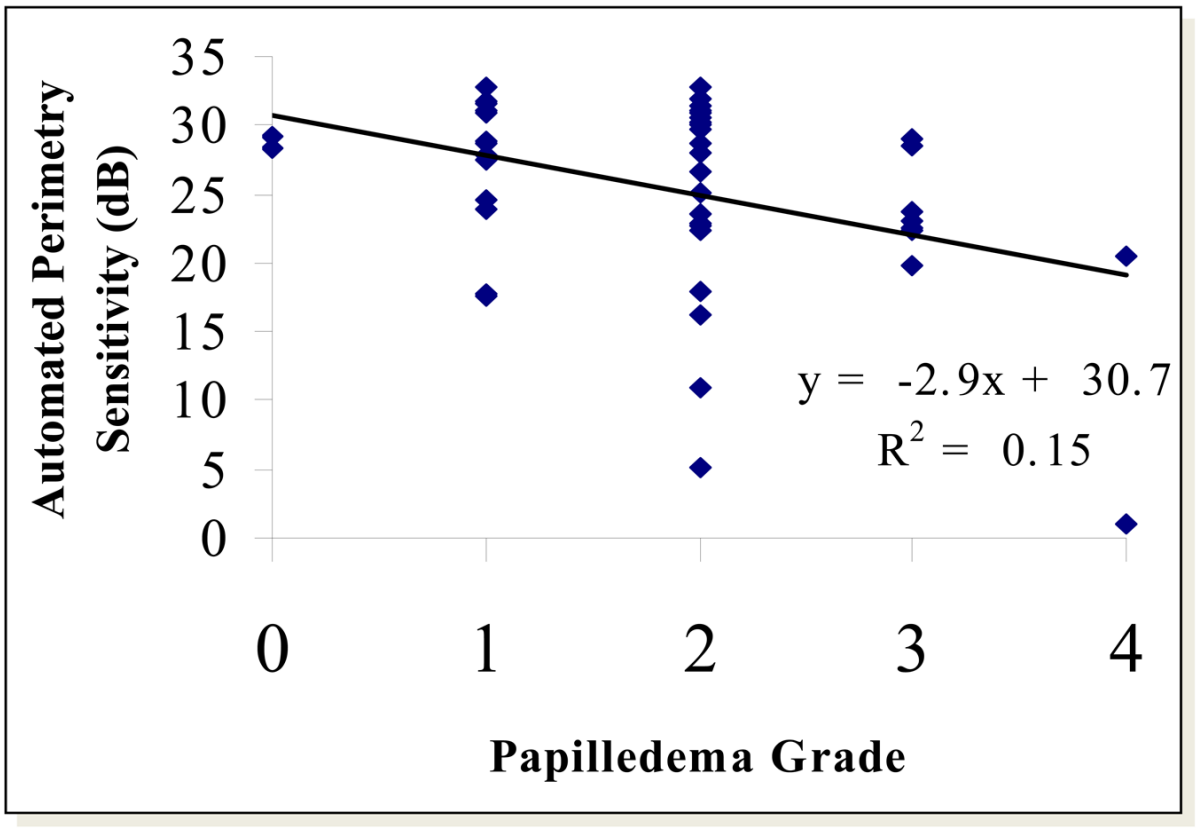

Figure 10.
Relationship of VF loss by mean threshold value and papilledema grade.

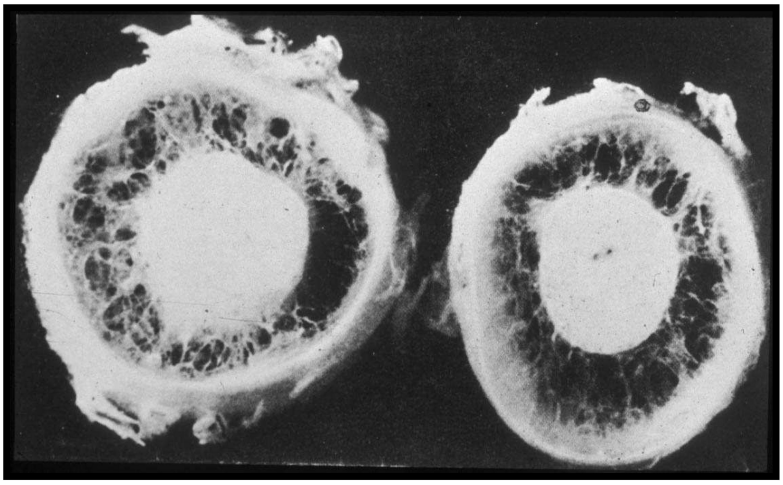

Figure 11.
Gross pathologic specimen of optic nerve (central core), optic nerve sheath and arachnoid trabeculations in between (from Sergott et. al.[73]) Note the well-developed series of arachnoid trabeculations and the fully unfolded optic nerve sheaths.

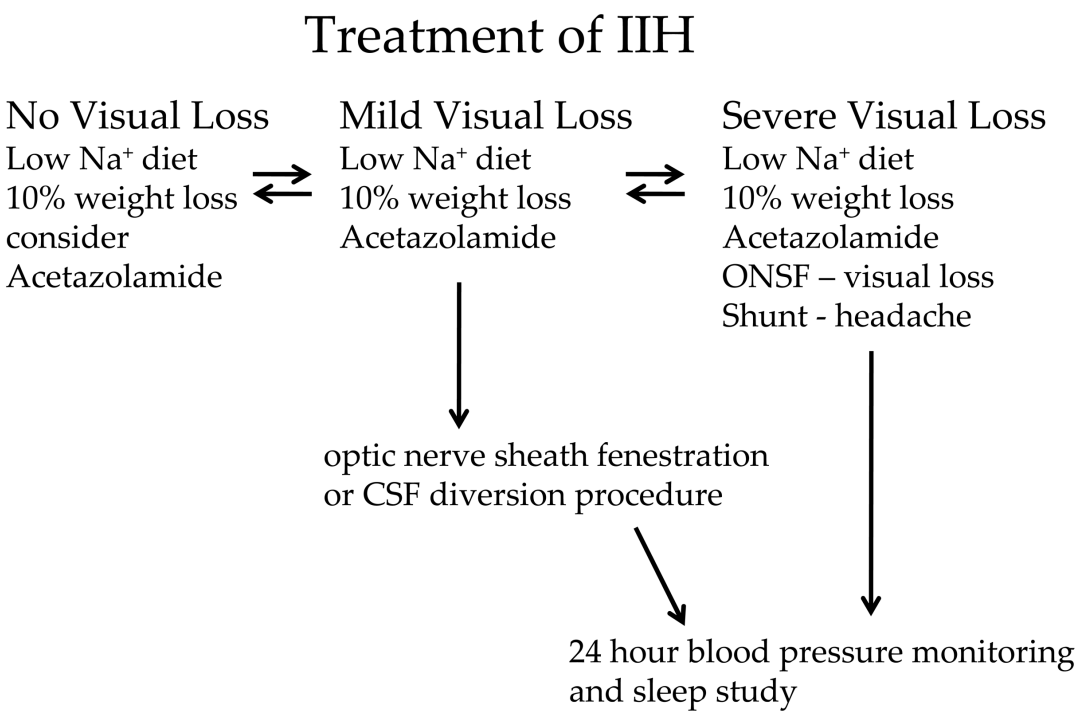

Figure 12.
Treatment algorithm for idiopathic intracranial hypertension. Visual loss does not include enlargement of the blind spot unless it is compromising vision. Optic nerve sheath fenestration is preferred over steroids.

Table 1

Differential diagnosis of IIH (cases must meet the modified Dandy criteria of IIH except that a cause is found)

Highly likely
decreased flow through arachnoid granulations
scarring from previous inflammation. e.g. meningitis, sequel to subarachnoid hemorrhage
obstruction to venous drainage
venous sinus thromboses
hypercoaguable states
contiguous infection (e.g. middle ear or mastoid - otitic hydrocephalus)
bilateral radical neck dissections
superior vena cava syndrome
glomus tumor
increased right heart pressure
endocrine disorders
Addison's disease
hypoparathyroidism
obesity
steroid withdrawal
growth horomone use in children
nutritional disorders
hypervitaminosis A (vitamin, liver or isotretinoin intake and all-trans retinoic acid for acute pro-myelocytic leukemia)
hyperalimentation in deprivation dwarfism
arteriovenous malformations and dural shunts
Probable causes
anabolic steroids (may cause venous sinus thrombosis)
chlordecone (kepone)
ketoprofen or indomethacin in Bartter's syndrome
systemic lupus erythematosus via venous sinus thrombosis
thyroid replacement therapy in hypothyroid children
tetracycline and its deriviative
uremia
Possible causes
amiodarone
hypovitaminosis A
iron deficiency anemia
lithium carbonate
nalidixic acid
sarcoidosis
sulfa antibiotics
Causes frequently cited that are unproven and unlikely
corticosteroid intake
hyperthyroidism

menarche

menstrual irregularities

multivitamin intake

oral contraceptive use

pregnancy

The table lists the etiologies of intracranial hypertension that meet the modified Dandy criteria except a cause is associated. The *highly likely* category is a list of cases with many reports of the association with multiple lines of evidence. *Probable causes* have reports with some convincing evidence. *Possible causes* have suggestive evidence or are common conditions or medications with intracranial hypertension as a rare association. Also listed are some frequently cited but poorly documented or unlikely causes; three case-control studies suggest this group of associations is not valid.

Table 2

Case series with visual results from operations for idiopathic intracranial hypertension done with optic nerve sheath fenestration.

Investigators	Year Published	Vision Worse	Vision not Worse	Total Patients
Hupp[97]	1987	6	11	17
Sergott[73]	1988	0	23	23
Brourman[76]	1988	0	10	10
Kelman[98]	1992	1	21	22
Goh[71]	1997	3	26	29
Plotnik[99]	1993	4	27	31
Acheson[72]	1994	3	17	20
Corbett[100]	1988	9	31	40
Banta[101]	2000	10	148	158
Total		**36**	**314**	**350**

Table 3

Reported cases with visual results from CSF shunting operations for idiopathic intracranial hypertension.

Investigators	Year Published	Shunt type	Shunt Failures	Vision Worse	Vision not Worse	Total
Rosenberg[102]	1993	LP/VP/V+	20/37	9	28	37
Shapiro[103]	1995	LP	0/4	1	3	4
Eggenberger[79]	1996	LP	15/27	0	14	14
Burgett[81]	1997	LP	19/30	1	29	30
Bynke[104]	2004	VP	7/17	0	17	17
Total			**61/115**	**11 (10.7%)**	**91**	**102***