“Pseudotumor cerebri” is the most encompassing term, accounting for both idiopathic and secondary causes of this syndrome. “Idiopathic Intracranial Hypertension” (IIH) specifically refers to patients who meet the diagnostic criteria delineated in Table 1 where no secondary cause is identified (obese women of childbearing age generally fall into this group). Older terms that are no longer acceptable but are often found in the literature include “Benign Intracranial Hypertension” (while not cancerous, the frequency of permanent visual loss, that may be severe, is anything but benign), and “otitic hydrocephalus” (referring to PTC associated with venous sinus thrombosis following a middle ear infection). For the purposes of integrity and research funding, the term “pseudotumor cerebri” is used less commonly in publication now, as it suggests that the disorder is not real (a “pseudo” disease). This monograph, and in my talk, I will refer to the condition as PTC, unless specifically referring to items that are specific to the idiopathic form of the syndrome (IIH).

EPIDEMIOLOGY AND DEMOGRAPHICS

Studies in the 1980s calculated the annual incidence of pseudotumor cerebri (PTC) as 0.9/100,000 in the general population, rising to 3.5/100,000 in women 15--44 years and 19.3/100,000 in women ages 20-44 years who are 20% or more above their ideal body weight. With the epidemic of obesity in America, recent studies show that the incidence of PTC has essentially doubled over the past 20 years, with an alarming increase among obese young men.[Garrett, Jacobs] This relatively high frequency ensures that neurologists and ophthalmologists will encounter such patients in their practice and should be familiar with the presentation, diagnosis and management of PTC.

The “typical” patient with PTC is a young, obese, woman of childbearing age. PTC occurs in childhood, but rarely develops in patients over 45 years of age. It is uncommon in men and slim adults – an “atypical” profile raises suspicion that a secondary cause or another disease is present.

See Table 1 for the diagnostic criteria of IIH. The criteria were modified in 2002 to include asymptomatic patients with papilledema (encountered most often by ophthalmologists), as well as those with intracranial hypertension but no papilledema (encountered most frequently by neurologists and headache specialists). Both of these situations are uncommon.

SYMPTOMS
Headache

Almost all patients (90-95%) with PTC have headache, although occasionally they come to medical attention when papilledema is detected on a routine eye examination. The headache is often daily, retro-ocular and worsened with eye movement.[Giuseffi] Some patients will describe increased severity upon awakening. The headache may also be unilateral, throbbing with nausea, vomiting and photophobia, resembling migraine. Neck and back pain are often prominent features, especially in children. It is not unusual for patients with PTC to have co-existing migraine headaches, making the diagnosis difficult unless other symptoms and signs are present. While headaches are common in PTC, their character is non-specific, and not strongly predictive of the intracranial pressure. Additionally, patients with PTC often have other co-existing headaches, such as migraine or episodic tension-type headache.[Fiedman & Rausch] Chronic daily headaches also raise the possibility of analgesic overuse, which is common in PTC patients, and may worsen their headaches.

The mechanism whereby pain is generated in PTC is uncertain but the pain likely arises from either direct compression and distention of the dura, or from changes in the caliber or pressure in the cerebral veins. The underlying mechanism of the disease is also uncertain. As we produce and absorb CSF constantly, PTC results from an imbalance in the system. There is no convincing evidence that there is increased CSF production. Most investigators endorse the concept of reduced CSF absorption. Although classical teaching holds the arachnoid granulations/villi responsible for CSF resorption and diffusion into the cerebral veins, there is little evidence that this is truly the case. Newer studies suggest that lymphatics in the olfactory area are much more important for CSF egress from the cranial cavity.[Johnston]

Transient Visual Obscurations

While not specific for PTC, transient visual obscurations are most commonly experienced in this disorder. They likely are a result of transient ischemia of the optic nerve head caused by local effects. However, they occur in PTC much more frequently than with other conditions producing papilledema.

Patients describe brief episodes of monocular or binocular visual loss that may be partial or complete. The obscurations are present in about 75% of PTC patients, typically last seconds and do not correlate with the degree of disc edema or visual loss.

Intracranial Noises

Pulsatile tinnitus occurs in roughly 60% of patients.[Giuseffi] Patients should be queried about this symptom, as it is often not volunteered. The noises may be unilateral or bilateral, often described as a heartbeat or whooshing sound. They are abolished with a lumbar puncture or jugular venous compression. The return of this symptom after a period of stable disease is useful in predicting recurrent increased intracranial pressure.

Intracranial noises have been attributed to transmission of intensified vascular pulsations via CSF under high pressure to the walls of the venous sinuses, converting laminar to turbulent flow. Others postulate that the endolymphatic duct may transmit pressure sensations from the CSF to the endolymph of the membranous labyrinth. Other otologic manifestations are hearing loss or a “high altitude” sensation.[Sismanis]

Visual Loss

Some patients experience subjective visual loss with PTC. They may report blurred vision, a dark spot temporally that correlates with enlargement of the physiologic blind spot, or tunnel vision. In severe cases, profound visual loss or complete blindness
occurs. Like glaucoma, PTC generally spares macular function in the early stages (i.e., visual acuity, central visual field, and color vision). When central visual loss occurs, coexistent ischemic optic neuropathy, central or branch retinal vein occlusion, subretinal hemorrhage, macular edema or macular exudates may be present. (Early loss of central vision is a red flag!) Note that functional (non-organic) visual loss may also occur, particularly in patients who have IIH without papilledema.

Orthostatic Edema

Most women with PTC also have symptoms of systemic fluid retention.[Friedman & Streeten] Orthostatic edema is a benign condition characterized by abnormal sodium or water retention in the upright posture. The most common manifestations are swelling in the feet and ankles after prolonged standing, increased abdominal girth during the course of a day, weight gain of >1 kg during the day, swelling of the fingers or eyelids, and nocturia. Physical examination often reveals pedal edema.

Other Symptoms

Minor symptoms of PTC include diplopia, paresthesias, neck stiffness, arthralgias of the shoulders, wrists and knees, ataxia, dizziness, facial palsy, and radicular pain.[Round] The diplopia is generally horizontal, caused by unilateral or bilateral sixth nerve palsy, a nonlocalizing sign of increased intracranial pressure. Depression and anxiety are more common in patients with PTC than in obese or normal weight, control subjects.[Kleinschmidt] Complaints of impaired concentration and memory are common, but unsubstantiated on neuropsychological testing; apparent cognitive decline may be related to headache, visual impairment, fear of blindness, depression, anger and anxiety, but does not represent true dementia.

SIGNS

Papilledema

The hallmark of PTC is papilledema. There are reports of patients with chronic daily headache without papilledema who have increased CSF pressure, but this unusual scenario may represent analgesic overuse headache.[Marcelis, Wang] It is estimated that 5% of PTC patients in a neuro-ophthalmic practice, at most, do not have papilledema, and most of these patients had symptoms for years at the time of diagnosis. However, in the acute phase, the symptoms of increased ICP may precede the development of disc edema by several days (or longer) in some cases; this is neither well understood nor well studied. Although there is an association between high-grade papilledema and visual loss, the appearance of the optic nerves does not predict visual outcome in an individual patient.[Wall & White] Since early papilledema may be difficult to detect with the direct ophthalmoscope, stereoscopic viewing of the optic discs with indirect ophthalmoscopy is recommended. Stereoscopic fundus photography may be helpful to determine the presence of subtle papilledema, but treatment should not be based on the appearance of the optic nerves alone.

Early papilledema is characterized by disruption of the normal radial nerve fiber layer arrangement with grayish opacity accentuating the nerve fiber bundles. A subtle gray peripapillary halo is apparent with the indirect ophthalmoscope. There may be concentric or retinochoroidal folds. As the degree of papilledema grade, the borders of the optic disc become obscure, with progressive elevation of the disc margins. The nerve head diameter increases and one or more segments of major blood vessels leaving the disc are obscured. With severe papilledema, the optic nerve protrudes, the peripapillary halo becomes more demarcated and the optic cup is obliterated.
Hyperemia, vessel tortuosity, hemorrhages, exudates, nerve fiber layer infarcts (cotton wool spots) and optic nerve pallor are often observed but are too variable to use for staging purposes. [Frisén]

It is important to differentiate true papilledema from pseudopapilledema caused by optic disc drusen or tilted optic discs. Stereoscopic viewing of the fundus can usually distinguish these entities. Optic disc drusen may also cause transient visual obscurations and can easily be confused with PTC. Rarely, optic nerve drusen and PTC coexist. This diagnostic dilemma is resolved with ultrasonography or CT scan of the optic nerves. The drusen appear calcified on the CT scan or are visualized by ultrasonography as highly reflective areas on the optic nerve head. Loss of spontaneous venous pulsations is often used to gage intracranial pressure. Spontaneous venous pulsations typically disappear with CSF pressures above 250 mm CSF, although they can sometimes be present with much higher pressures. However, since many normal individuals lack spontaneous venous pulsations, it is not a reliable sign.

Visual Acuity and Optic Nerve Function Tests

Early papilledema is typically associated with normal Snellen visual acuity. In severe cases of PTC, the acuity may deteriorate rapidly. One study showed that 13% of eyes had visual acuities worse than 20/20 at the initial visit. [Wall & George 1991] Since Snellen visual acuity is not sensitive to visual loss found on perimetry, it should not be used as the sole indicator of visual function.

Contrast sensitivity is a sensitive and early indicator of optic nerve dysfunction in PTC but has not proved to be as useful as perimetry in the assessment patients with PTC. [Verplank, Wall & George 1991] Color vision testing is insensitive for detecting visual loss. There is no role for visual evoked potentials in this disorder; they are unreliable and remain normal until substantial vision is lost (the optic neuropathy is not demyelinating). [Verplank] The presence of a relative afferent pupillary defect indicates asymmetric visual loss. The optic neuropathy of PTC is often symmetric, so an afferent pupillary defect may be absent. The development of an afferent pupillary defect indicates deteriorating optic nerve function in that eye.

Perimetry

The most useful test in evaluating visual function in patients with PTC is perimetry. The visual field defects are similar to those in other causes of papilledema and are characteristic of optic nerve dysfunction. Goldmann or automated threshold perimetry is required for adequate assessment. Screening techniques, such as confrontation and tangent screen visual field testing, are insensitive for detecting early visual loss and following the patient. One study showed enlargement of the blind spot, representing papilledema, in 96% of patients by Goldmann perimetry and 92% of patients with automated perimetry. [Wall & George 1991] Patients may notice blind spot enlargement but it is usually asymptomatic.

Other common visual field defects include inferonasal loss and generalized constriction. Occasionally it is difficult to distinguish genuine visual field constriction from functional (nonorganic) visual loss. Central, paracentral, arcuate, and altitudinal scotomas may occur. The visual field loss may be severe, leading to blindness. In 50 PTC patients prospectively evaluated with automated and Goldmann perimetry, the most frequently detected visual field abnormalities were blind spot enlargement, generalized field constriction and nasal defects. [Wall & George 1991]
**Ocular Motility Abnormalities**

Unilateral or bilateral lateral rectus palsy is a nonlocalizing sign of increased intracranial pressure. It typically produces binocular, horizontal diplopia that is worse at distance. An esotropia may be detected. Vertical diplopia from a skew deviation, third or fourth nerve palsy is uncommon, and suggests another diagnosis. Baker, Frohman

Global ophthalmoparesis is rare, and generally indicates the presence of an underlying disorder such as venous sinus occlusive disease or thrombophilia. Friedman

The ocular motor paresis resolves when the intracranial pressure is lowered.

**DIAGNOSTIC TESTS**

**Neuroimaging**

Neuroimaging is mandatory prior to the performance of a lumbar puncture. Although early studies with computed tomography (CT) found small “slit-like” ventricles, a subsequent study showed no difference in ventricular size between patients and controls. Jacobson

CT or MRI signs of intracranial hypertension include dilated optic nerve sheaths and an empty sella. Silbergleit

Magnetic resonance (MR) imaging demonstrates an empty sella in up to 64% of patients with PTC. The optic nerve can be clearly differentiated from the sheath on high-resolution orbital MRI that shows distention of the perineural subarachnoid space. Protrusion of the optic papilla into the posterior aspect of the globe and flattening of the posterior sclera may be seen. A small percentage of patients also have a Chiari I malformation, usually small and asymptomatic. Smooth walled venous sinus stenosis on MRV may be present, a result of increased ICP rather than a cause of it. Intraluminal obstructions have been reported, possible enlarged arachnoid granulations. Farb

The contribution of these defects to the disorder is uncertain.

In obese, young women with typical signs and symptoms of PTC, MR imaging is recommended. A normal plain CT scan can be misleading. If available, MR angiography is recommended as part of routine imaging. If the patient is taking oral contraceptives, is post-partum, or has a known coagulopathy, an MR venogram is warranted to reveal a cerebral venous thrombosis. Lam

However, MR venography and catheter angiography sometimes fail to detect subtle cerebral venous thrombosis. Cremer

Moreover, venous sinus thrombosis is occasionally present in an otherwise “typical” PTC patient.

The question often arises of the necessity of MRV – would we suspect a venous thrombosis in a patient at risk to be more selective? In 131 patients with suspected IIH from three tertiary referral centers, definite cerebral venous thrombosis was detected in 10 patients (6 females, 4 males) and two other patients had equivocal MRV studies. Lin

Six of the 10 patients with definite venous thrombosis were of normal weight or only mildly obese and nine had an identifiable secondary cause (infectious, oral contraceptives, leukemia, hypercoaguable state). The four severely obese patients all had a secondary cause (postsurgical, hypercoaguable state, Lupus anticoagulant, carcinoma). The superior sagittal sinus, transverse and sigmoid sinuses, and internal jugular veins were affected in this group. At this point, I recommend and MRV on all patients, and definitely in “atypical” patients. Slim women, men, children, and those not responding to treatment, should be thoroughly evaluated for an underlying cause, including contrast-enhanced MR imaging and MR venography, CSF cytology (and repeated CSF analysis, if needed), ANA, antiphospholipid antibodies, and a thorough history and physical examination with a complete medication history.
Cerebrospinal Fluid Examination

The spinal fluid examination is critical for diagnosing PTC. No patient should be diagnosed presumptively without a lumbar puncture. There are several confounding conditions that may simulate PTC: (1) Patients with optic disc drusen or other congenital optic disc anomalies with or without chronic daily headaches; (2) CNS infections or malignancy producing increased intracranial pressure; (3) infiltrative optic neuropathies. The lumbar puncture is crucial to document elevated CSF pressure and assure normal CSF contents.

The accepted value of CSF pressure for diagnosing PTC is greater than 250 mm CSF. Values between 201 - 249 mm CSF are non-diagnostic. Since spinal fluid pressure fluctuates, the lumbar puncture may need to be repeated if the clinical suspicion is high but the pressure is initially normal. The patient’s pressure must be measured in the lateral decubitus position with the legs relaxed. Many patients with PTC are obese, making the procedure technically challenging. The clinician should be aware that pressures recorded in the sitting position will be artificially elevated, and those recorded in the prone position (i.e., under fluoroscopy) are unreliable. If a patient is nervous or in pain during the procedure, which may require several attempts, the intracranial pressure will rise. Administration of a sedative, such as diazepam or zolpidem tartrate, prior to the lumbar puncture is often very helpful to relieve anxiety. The spinal fluid should be analyzed for glucose, protein, cell count, VDRL, bacterial, fungal and tuberculosis cultures, and cytology during the diagnostic evaluation. A therapeutic, “large volume” spinal tap (removal of over 20 cc of fluid) is sometimes employed, realizing that patients with PTC are not protected against post-spinal headaches.

ASSOCIATED CONDITIONS

There are many medical disorders and exogenous agents associated with the development of PTC (Table 2).

COMMON MISTAKES IN DIAGNOSIS AND EVALUATION

Making a diagnosis without fulfilling the diagnostic criteria

Sometimes patients are referred for neuro-ophthalmic consultation and management without having a definite diagnosis of pseudotumor cerebri! Typically, the patient is “diagnosed” without having a lumbar puncture. Treatment should never be initiated without an accurate diagnosis. The diagnosis should be suspect in a patient with headaches and a slightly elevated CSF pressure, but none of the other associated symptoms or signs that are typical of PTC.

Diagnosing PTC in a patient with headaches and pseudopapilledema

It can be difficult to differentiate true papilledema from pseudopapilledema with a direct ophthalmoscope. Tilted optic nerves and optic disc drusen, both benign conditions, can simulate optic nerve head swelling. Infiltrative optic neuropathies can also produce elevation of the optic disc. Stereoscopic viewing of the optic nerve using indirect ophthalmoscopy can usually distinguish these entities. When in doubt, fluorescein angiography, stereoscopic fundus photography, ocular coherence tomography, or orbital ultrasound/CT scanning (to look for buried drusen) are employed.
**Using inadequate imaging techniques**

PTC is a diagnosis of exclusion. The most common reason for misdiagnosis is a real tumor, leptomeningeal inflammation, infection or neoplasia. Venous sinus thrombosis, antiphospholipid antibody syndrome and systemic lupus erythematosus are other considerations. Additional testing, including MR venography, should be obtained in all patients who do not fit the “typical profile” (obese, young women) or those who do not respond to treatment.

**Not measuring the opening pressure**

Recording the opening pressure is paramount when making this diagnosis. Merely noting the “fluid shot out of the needle like it was under pressure” is not adequate! If the patient is not relaxed during the procedure, or if the stylet is removed when the patient is in the sitting position (see below), the CSF will likely “shoot out”.

**Not recording the opening pressure correctly**

Since patients with PTC are frequently quite obese, they are often sent to the neuroradiology suite for a diagnostic lumbar puncture under fluoroscopy. This method yields an inaccurate opening pressure more often than not. The radiologist typically performs the procedure with the patient prone, attaches the manometer directly to the needle (which is oriented vertically) and reads the pressure. Since the base of the manometer is not aligned with the cisterna magna, the pressure reading will be inaccurate. In other cases, increased intra-abdominal pressure occurring in the prone position may be transmitted to the central venous system and elevate the CSF pressure. If it is necessary to have the LP performed under fluoroscopy, ask the radiologist to reposition the patient in the lateral decubitus position before measuring the pressure (better yet, go to the radiology suite yourself to assist).

It is often easier to perform the LP in an obese patient in the sitting position (leaning on a bedside table or Mayo stand) using a large (18g, 6 inch) spinal needle. After the subarachnoid space is entered, the patient must be moved to the lateral decubitus position to measure the pressure. CSF pressure measurements in the sitting position will be artificially high.

**Neglecting to send the CSF for a complete analysis**

One of the diagnostic criteria for PTC is normal CSF content, with the possible exception of CSF total protein that may be in the low normal range. The spinal fluid from the initial diagnostic LP should always be sent for analysis, including cytology. For subsequent therapeutic LPs, basic analysis (glucose, protein, cell count) is suggested at a minimum.

**Diagnosing PTC without papilledema**

There are reports of increased CSF pressure in patients with chronic daily headaches and no papilledema.[Wang] Many of these patients have analgesic rebound headaches or may have had an inexperienced examiner viewing the discs. A thorough medication history is essential in patients with suspected PTC, including over-the-counter medications. If the patient is in pain (crying, Valsalva) during the LP (including the trauma of a difficult spinal tap), their CSF pressure will rise, leading to a spurious diagnosis. A Valsalva maneuver alone can increase the CSF pressure by 200-300 mm CSF![Neville] In general, the headaches in these patients do not generally improve with intracranial pressure lowering treatments and require conventional headache management with prophylactic medications.
Failing to persevere when the CSF pressure is normal, but you’re suspicious of PTC

CSF pressure fluctuates constantly. If the patient has typical features of PTC with papilledema and the initial LP reveals a normal opening pressure, repeat the LP several days to a week later. Consider continuous intracranial pressure monitoring as an inpatient.

Missing medication-induced PTC

Many cases of PTC are medication induced, particularly in children. Don’t forget about antibiotics (not only tetracyclines), medications that contain vitamin A (many are used to treat acne), over-the-counter vitamins and “natural” or “herbal” medications. Any medications that are not absolutely necessary for the patient’s health should be discontinued.

TREATMENT

General Aspects of Management

Not all patients with PTC need to be treated. A patient with asymptomatic papilledema or minimally symptomatic headaches, but with normal visual function (per the ophthalmologist), may not require specific medical or surgical therapy but should be monitored closely. Patients with progressing or severe visual loss, severe papilledema are treated using medications and other measures designed to lower intracranial pressure. Patients whose primary problem is headache are best managed medically. Address a secondary cause if it exists, i.e., discontinue offending medications, treat underlying infections or venous thrombosis. However, don’t assume that treating the secondary cause is enough - patients with a secondary cause also need management of their intracranial pressure as discussed here.

Since the principal goal of treatment is to preserve vision and reduce the degree of papilledema, the best measures of success or failure are visual function and optic disc appearance. Although this key aspect of management was discussed in detail earlier, it is worth emphasizing here that formal assessment of the visual field (not visual acuity or confrontation techniques) is the generally accepted measure that most reliably reflects papilledema-associated visual damage.[Wall 1990] The skill of the technician performing the study is probably more important than whether the visual field is tested using manual kinetic (Goldmann) or automated static (e.g., Humphrey) perimetry.[Wall & George 1987]

The change in appearance of the optic discs is often used as a barometer of the overall long-term average intracranial pressure transmitted to the anterior optic nerve. However, the disc appearance is neither 100% accurate nor reliable. It may take weeks for the optic nerve appearance to change in response to overall alteration of intracranial pressure. Observing changes of the optic disc appearance over time helps to assess the effectiveness of therapy, although many patients who are otherwise asymptomatic and have stable vision have persistent mild papilledema. It is helpful to photographically document the appearance of the optic discs at the initial evaluation and whenever there is a change in their appearance so that this measure can be objectively compared with subsequent examinations.

A team approach is the best way for a neurologist to manage a patient with pseudotumor cerebri. An ophthalmologist or neuro-ophthalmologist is best trained to measure and record the crucial variables of vision that allow the neurologist to manage
the patient. Ideally, the ophthalmologist should see the patient shortly before, perhaps even earlier in the same day, as the neurologist. Then, the two consultants should discuss the results of vision testing so that the neurologist has current visual information. If the goal of treatment is not fulfilled then a change in management must occur. The importance of good communication among treating physicians, and one physician (preferably a neurologist or neuro-ophthalmologist) coordinating care cannot be overemphasized.

Neurologists frequently assume that assessing opening pressure during lumbar puncture is a helpful variable to follow when managing a patient with PTC. As will be discussed below, this measurement correlates poorly with the patient’s degree of headache and papilledema. It is far more important to know the the status of vision and well being of the patient than the value itself.

Proper assessment of visual field and interpretation, along with comparison of optic disc appearance, are the principal measurements to follow when managing a patient with PTC.[Corbett & Thompson] Note that there are no randomized clinical trials to guide treatment recommendations for patients with PTC.

**MEDICAL MANAGEMENT**

**Diuretics**

Diuretics are usually used to lower intracranial pressure when pharmacological therapy is indicated. Surprisingly, there are no published treatment trials proving the efficacy of any of these agents. There are successes, as well as failures, with virtually all of the commonly prescribed diuretic agents. Acetazolamide (Diamox™) is the diuretic most commonly used by neuro-ophthalmologists, followed by furosemide (Lasix™). A single one-gram dose of IV Diamox transiently reduces CSF production by as much as 60% but it takes approximately 4 grams of oral acetazolamide to have a significant effect of suppressing CSF secretion in humans.[Rubin] Triamterene (Dyrenium™) and spironolactone (Aldactone™) can be used in patients who are allergic to acetazolamide and thiazide diuretics. Note that allergy to sulfa antibiotics does not correlate with allergy to the sulfonamide in carbonic anhydrase inhibitors or other diuretics. All medications used for PTC are considered “off label”. There is no evidence that severe fluid restriction is beneficial but patients with systemic fluid retention (orthostatic edema) should be counseled limit their sodium and water intake.

**Acetazolamide (Diamox) and Other Diuretics**

The usual dose of acetazolamide used to treat a patient with visual loss is 1.5 to 3.0 grams daily in three to four divided doses. If there is no visual loss, 1 gram daily is the usual dosage. The sustained release 500 mg “sequel” preparation is better tolerated than the standard 125 mg or 250 mg tablet but may be difficult to obtain. Methazolamide (Neptazane™) 150 to 300 mg daily in two to three divided doses may be better tolerated by patients who cannot tolerate the gastrointestinal side effects of acetazolamide. Furosemide (Lasix™), which also reduces cerebrospinal fluid production, is generally considered a second line agent. The usual dose of furosemide for patients with PTC and visual loss ranges from 40 to 160 mg per day in two divided doses. Careful period monitoring of serum potassium concentration, and replacement as appropriate, is required for a patient receiving furosemide.

It is important to warn patients about the commonly-experienced systemic effects of acetazolamide so that they will not assume they are having serious side effects and discontinue the medication. Patients will most likely experience a metallic taste, intolerance of carbonated beverages, tingling around their lips and fingertips, fatigue,
mild anorexia, and perhaps some gastrointestinal symptoms or diarrhea. These symptoms are so common that patient compliance is questioned when they do not report them! A patient tends to tolerate higher doses if the medication is introduced slowly. For example, a typical regimen would be to start with acetazolamide 500 mg at bedtime for three days, then twice a day for three days, then three times daily for three days, then four times daily (or increase gradually to the desired dose).

Expect that a patient treated with acetazolamide will develop mild and generally asymptomatic metabolic acidosis. It is not necessary to measure serum electrolytes in otherwise healthy patients. Only rarely does sustained and clinically important hypokalemia occur. Renal stones may develop while receiving acetazolamide presumably due to alkalization of urine and reduction of renal secretion of citrate; this is an infrequent complication. For that reason, be cautious about using this agent in a patient with a history of renal tract calculus and advise your patient to avoid dehydration. Rare instances of aplastic anemia and other blood dyscrasias have been reported as an idiosyncratic reaction. Acetazolamide is contains a sulfonamide moiety but it not a typical ‘sulfa drug’. Approximately 3% of the population has a ‘sulfa’ sulfonamide allergy. However, it is the arylamine group, present in antibiotics but not in acetazolamide, the generally precipitates the type I hypersensitivity reaction. Thus, a sulfa allergy is not an absolute contraindication to trying acetazolamide. People who are allergic to acetazolamide are often “allergic” people who react to penicillins, sulfa antibiotics, and other common antigenic stimulants.

Other Medications

Corticosteroids (e.g., oral prednisone, intravenous methylprednisolone, oral or intravenous dexamethasone) will also reduce papilledema. Their routine use is not recommend for several reasons. These agents have numerous and potentially serious long-term side effects. Weight and fluid retention are important considerations in the management of affected patients. Individuals cannot lose weight, and typically gain weight and retain fluid, while receiving these agents. The other long-term side effects, such as glucose intolerance, osteoporosis, fracture, capillary fragility, striae and gastric ulcer also argue against prolonged usage. Finally, corticosteroid withdrawal has been associated with intracranial hypertension.[Liu]

Intravenous corticosteroids are sometimes employed in patients with severe or rapidly deteriorating visual loss, who may experience stabilization, or even improvement, when exposed to a brief course of high dose oral or intravenous corticosteroid.[Liu] This may buy some extra time to consider other options or arrange for a surgical solution in a patient who is rapidly losing vision and not responding to standard medical therapy. However, there are expert clinicians whose experience suggest that corticosteroids may actually be detrimental in this setting.

Medications for headache prevention are useful in the setting of disabling headache and may be used in combination with intracranial pressure lowering agents, if needed. The side effects of various agents should be considered for each patient. For example, valproate and tricyclic antidepressants commonly cause weight gain and calcium channel blockers may produce peripheral edema, all undersirable in IIH patients. Topiramate (Topamax™) has garnered attention because of its effectiveness in headache prevention, possible side effect of weight loss and carbonic anhydrase activity. The carbonic anhydrase activity of topiramate is minimal and its use as monotherapy in patients with visual loss is not justifiable at this time. However, it is a good choice for headache prevention if there are no other contraindications. One must
use caution when combining topiramate with acetazolamide as they have additive metabolic effects.

Serial Lumbar Punctures
Performing lumbar puncture to withdraw sufficient cerebrospinal fluid to lower intracranial pressure will typically (although not always) produce immediate improvement in headache for several hours or days. Most clinicians are aware of the rare patient whose symptoms are effectively treated for extended periods of time, and even “cured.” The volume of cerebrospinal fluid withdrawn will be reproduced within the day, so that this form of management does not seem rational unless lowering the pressure “resets” some aspect of the CSF production/absorption feedback process. Furthermore, repeated lumbar punctures are traumatic for the patient, as well as for the physician. There is no accepted volume of spinal fluid removal that is recommended for treatment; I typically remove enough CSF so that the closing pressure is about 150 mm CSF. Post-lumbar headache and transient worsening of neuro-ophthalmic symptoms/signs are possible with very large volume spinal taps.

The degree of intracranial hypertension measured by the opening pressure during lumbar puncture correlates poorly with the degree of the patient’s symptoms and papilledema. Patients with essentially no headache may have an opening pressure greater than 500 mm CSF, and others with chronic daily and debilitating headaches whose opening pressures may be consistently lower than 300 mm water.

Lumbar puncture as a first or second line treatment is not recommended for the majority of patients with PTC. They are useful for management during pregnancy.

Weight Loss
Weight loss is recommended but the evidence supporting therapeutic weight loss is surprisingly scant. Several retrospective reports indicate that loss of 6% of body weight is associated with a reduction in papilledema.[Sugarman, Kupersmith, Johnson] It is uncertain whether the weight loss prompted the improvement in papilledema, or whether the overall condition improved, including some weight loss (usually water weight accounts for initial weight loss in dieters). The majority of patients with PTC, men as well as women, are overweight. Recent weight gain was identified as an important risk factor for developing PTC.[Ireland] It is possible for PTC to go into remission once weight loss occurred, only to recur during periods of recent weight gain. However, long-term follow-up of such patients does not show a correlation between their weight and CSF pressure. Substantial weight loss has no benefit on their PTC in some patients, who may continue to have chronic headaches. A formal, supervised weight loss and exercise program is recommended (swimming is generally well tolerated). Monitoring their weight at each visit and providing them with support and feedback emphasizes the importance of this therapy. Newly diagnosed overweight patients may benefit from dietary consultation. Bariatric surgery is considered below.

In some obese patients, superimposed obstructive sleep apnea may contribute to severe nocturnal intracranial hypertension and headaches upon awakening. diagnosed patients and available bed partners should be queried about symptoms of obstructive sleep apnea. Those with suspicious responses are referred for polysomnography.

Interestingly, obesity has been identified as a risk factor for the progression from episodic headache to chronic daily headache. This may be relevant to the subpopulation with “IIH without papilledema.”
Low Tyramine Diet and Discontinuation of Sulfato-conjugated Medications

The pathophysiology of PTC is uncertain, but there is evidence implicating certain enzymes that regulate neurotransmitters (norepinephrine and serotonin) controlling the production of CSF. Monoamine oxidase and phenol sulfatransferse are the enzymes that are important in maintaining appropriate neurotransmitter levels. Placing patients on a low tyramine diet and discontinuing their sulfato-conjugated medications has been effective in some patients; this may be a non-specific dietary effect on headache control.

Surgical Management

Indications

In general, the major indication for employing a surgical option for a patient with PTC is progressive visual failure despite maximally tolerated medical therapy or severe visual loss at initial presentation. For most patients, “maximally tolerated medical therapy” refers to variable doses of acetazolamide as a single agent. Adding an additional oral agent generally does not benefit patients who are already losing vision while treated with a single agent. As a general rule, surgical treatment is not recommended for treating headache alone.

Surgical Procedures

There are two generally accepted surgical procedures for lowering intracranial pressure, shunting and optic nerve sheath fenestration. Subtemporal decompression (removing part of the temporal bone to give the brain more room) was done in the past but rarely used as a treatment now. Historically, ventriculoperitoneal (VP) or ventriculoatrial (VA) shunts were used less frequently, although they are regaining favor, particularly with the advent of stereotactic techniques for cathether placement. While initially effective in most patients, lumboperitoneal (LP) shunts are associated with a high failure rate and need for revision. In one representative series, 83 shunting procedures were performed in 37 patients with pseudotumor cerebri during a mean follow-up period of 31 months.[Rosenberg] The average number of shunts placed per patient was 2.2. The greatest reason for revision was shunt failure, occurring on average nine months from the original procedure. Other common complications that lead to shunt revision included low cerebrospinal fluid pressure headache, infection, and abdominal pain.

A retrospective series of 42 patients (115 shunt procedures; 79 LP and 36 VP or VA) shunted for intractable headache of PTC over a 30-year period showed significant improvement in 95% immediately after surgery.[McGirt] Severe headache returned despite a functioning shunt in 19% of patients at 12 months and 48% by 36 months. The risk of headache recurrence was increased 5-fold in patients without papilledema (n=17), and increased 2.5-fold in patients with symptoms for longer than two years (n=19). LP shunts were 2.5 times more likely to become obstructed than VP and VA shunts. The risk of catheter migration, overdrainage and shunt infection were similar across the three types of shunts.

Shunting may seem attractive for the rare patient with intractable headache and stable vision, but should be discouraged in most cases. These patients will generally benefit from medical headache (prophylaxis) management, reserving optic nerve sheath fenestration or shunting for preserving vision.

I warn all of my patients who are candidates for shunts that they frequently fail, and they should expect to have repeated shunt procedures in the future.
Optic Nerve Sheath Fenestration

Optic nerve sheath fenestration should be performed by an experienced, fellowship-trained orbital surgeon, or similarly experienced ophthalmic surgeon. The perioptic arachnoid can be accessed by either a medial or lateral orbital approach. Each approach is probably equally effective. The decision to perform one technique over the other depends upon a variety of factors, including training, anatomic considerations, and slight difference in complication profile. There is no strong bias that one approach is better than the other.

Once the surgeon has exposed the optic nerve, a surgical slit or window is made in the arachnoid. This causes a small volume of perioptic sheath cerebrospinal fluid to egress into the orbit until the arachnoid heals. Presumably, the local subarachnoid pressure at the level of the optic nerve head is relieved by the egress of cerebrospinal fluid. In later stages of healing, subsequent scarring of the subarachnoid tissue is thought to protect the optic nerve head from the direct effect of elevated cerebrospinal fluid pressure. Papilledema usually resolves within several weeks following a successful fenestration. The efficacy of this procedure for relieving papilledema and improving vision in the majority of operated eyes has been convincingly documented in large series of patients.[Keltner]

Two unexpected benefits of this procedure include improvement of papilledema in the non-operated eye in roughly 50% of patients and substantial improvement of headache in roughly 65% patients.[Corbett 1988, Sergott] Still, optic nerve sheath fenestration is not recommended as a primary procedure for treating headache, particularly in patients with normal vision, or those patients whose disc edema has resolved but their headaches persist. If time permits, it is rational to operate on one eye first and wait to see if the papilledema and vision in the other eye improve before proceeding with contralateral fenestration (bilateral, simultaneous procedure may be performed).

The procedure, while usually safe, is not without complications. In one representative series, a total complication rate of 40% was documented.[Plotnick] Fortunately, most of these complications are not visually threatening and are transient. Complications that fall into the latter category include transient double vision and tonic pupil. More serious complications causing visual loss occur in as many as 20% of operated eyes.[Corbett 1988] These complications tend to be vascular in nature, and include retrobulbar hemorrhage, hemorrhage into the optic nerve sheath, central and branch retinal artery occlusion, choroidal ischemia, and injury of the optic nerve.

Despite the excellent initial visual results in response to optic nerve sheath fenestration, long-term deterioration of visual function occurs in as many as one-third of operated eyes a mean of about 10 months following an initially successful procedure.[Spoor] However, failure of vision can occur at anytime, even a few years later. Thus, patients treated surgically still need to undergo careful serial follow-up to detect developing papilledema and visual loss, signs of optic nerve sheath decompression failure.

Bariatric surgery

Like dietary weight loss, surgically induced weight loss may be helpful for the long-term management in patients who are morbidly obese. [Sugarman] There is no guarantee that weight reduction will cure the PTC, but this procedure may be desirable in patients who have other medical co-morbidities associated with obesity.
Venous Sinus Stenting

Abnormalities in the cerebral venous sinuses may be seen in PTC patients, smooth-walled stenosis of the transverse sinus being the most frequent. Large pressure gradients across the transverse sinus have been measured by direct manometry in some of these patients. In most cases, the sinus stenosis resolves after the intracranial pressure is lowered, and the pressure gradient returns to normal, so the venous changes are probably a secondary occurrence.

Recent case series of approximately 40 patients suggest that transverse sinus stenting with or without thrombolytic therapy may be helpful in some patients.[Higgins, Owler, Donnet] The results are inconsistent and the procedure needs further study before recommending it for routine usage. Reported complications of stenting include severe headache during the procedure (which may persist for up to a week after the procedure), transient hearing loss, transient unsteadiness and one life-threatening acute subdural hematoma. The subdural hematoma developed during venography and stenting in a patient who also had an optic nerve sheath fenestration and external ventricular drainage. Venous re-stenosis has also occurred.

COMMON MISTAKES IN MANAGEMENT

Relying on visual evoked potential (VEP) to monitor status of vision

Pattern check VEP largely probes only the function of the retinal ganglion cell axons subserving the central 5-10 degrees of the visual field (i.e., the papillomacular optic nerve bundle). This portion of the visual field, like visual acuity, is insensitive to change as the papilledema and visual field worsen. A patient may have a normal VEP while silently losing substantial portions of their visual field.

Treating on the basis of optic nerve appearance

The appearance of the optic nerve, particularly in a chronic course, is not indicative of the visual function or outcome. Many patients will have mild, persistent disc edema but remain asymptomatic. Treatment should be based predominantly on quantitative assessment of visual field.

Using visual acuity and confrontation fields to monitor status of vision

These office tests are easy for a neurologist to perform, but are inadequate to measure visual field loss and to assess changes in the visual function! Follow patients with an ophthalmologist or neuro-ophthalmologist who can measure and document changes in visual field and optic disc appearance using more quantitative and sensitive techniques.

Not following vision at all, or relying on patient’s perception of vision

Worse yet, not formally testing vision, or relying on the patient to tell you how they think their vision is doing, will certainly set you up to miss serious visual loss in some patients. Neurologists tend to concentrate on the opening pressure as a measure of effectiveness of treatment. This measure is insensitive to visual loss, and does not correlate with degree of symptoms or papilledema.

Not maximizing medical management

When using acetazolamide for visual loss, sufficient doses should be used before concluding that it not working. The minimal dose that we usually find effective is
1 grams daily. Often, 2-3 grams daily in three to four divided doses are needed if the patient can tolerate it.

**Mixing diuretics**
Combining diuretics is highly unlikely to provide any additional benefit for a patient who has not responded to maximally tolerated doses of a single agent. Furthermore, the added time to determine whether adding a second agent will preserve vision may actually cost the patient vision. Vigilant monitoring is required as patients may become seriously ill from severe hypokalemia resulting from combining acetazolamide with one or more diuretics, or topiramate.

**Discontinuing Diamox prematurely because of patient-reported “side effects”**
Despite the lack of evidence-based support of efficacy, acetazolamide remains most neuro-ophthalmologists’ “big gun” for patients with visual loss. Patients will often stop taking it if they fear that the common systemic effects (e.g., paresthesias) represent serious side effects. Educating patients what to expect, and building up the dose gradually, are the two most effective means to help your patient remain compliant.

**Treating chronic headaches with surgery**
In almost all cases, this just creates a bigger headache for the patient, the neurosurgeon and you. If the vision is good, treat headaches medically. PTC patients often evolve into “headache patients” after their ICP is controlled.[Friedman & Rausch]

**Too many cooks, no master chef**
Patients sometimes develop complications of PTC or its treatment because multiple physicians were contributing to their care but no one was directing it. It is extremely important that one physician be “in charge”. Neurologists and neuro-ophthalmologists are best prepared to assume this role.

**SPECIAL CIRCUMSTANCES**

**PTC in Pregnancy**
Although there is no increased incidence of PTC during pregnancy compared to age matched controls, PTC sometimes develops during pregnancy.[Digre & Varner] Most pregnant women with PTC can be managed with careful neuro-ophthalmic follow-up and intermittent lumbar punctures. Acetazolamide appears to be safe for treating PTC during pregnancy, particularly after the first trimester [Lee]. If the vision deteriorates, optic nerve sheath fenestration may be performed. Steroids may be used if necessary. There are no special considerations regarding delivery or anesthesia in these patients.

**PTC in Children and Adolescents**
Adolescents with PTC are treated similarly to adults. In pre-adolescent children, there is no difference in the incidence of PTC between boys and girls, and obesity is less common.[Lessell, Balcer] Guidelines for the diagnosis of PTC in pre-adolescent children were recently published; one of the difficulties in creating diagnostic criteria is that normal CSF pressures were not previously established in the literature (Table 3) [Rangwalla and Liu]. A secondary cause such as infection, venous sinus thrombosis, or medication is often found in pre-adolescents. Therapeutic modalities for children are
identical to those used in adults. Pubescent teens may be at higher risk for visual loss than younger children or adults [Stiebel-Kalish].

“Fulminant” PTC

Some patients present with a fulminant, rapidly deteriorating course that requires aggressive treatment. [Thambisetty]  This may include high doses of acetazolamide, rapidly sequential or simultaneous optic nerve sheath fenestration, and shunting (or ventriculostomy/CSF drainage in the intensive care unit). Unfortunately, some patients lose vision despite vigorous management. Systemic hypertension, anemia, venous sinus thrombosis and renal failure increase the risk of a poor outcome. Visual loss at presentation is an ominous sign that should prompt vigilant attention.

Table 1. CRITERIA FOR DIAGNOSING PTC [Friedman & Jacobson]

1. If symptoms are present, they may only reflect those of generalized intracranial hypertension or papilledema
2. If signs are present, they may only reflect those of generalized intracranial hypertension or papilledema.
3. Documented elevated cerebrospinal fluid pressure measured by lumbar puncture in the lateral decubitus position
4. Normal cerebrospinal fluid composition
5. No evidence of hydrocephalus, mass, structural, or vascular lesion on MRI or contrast-enhanced CT scan for typical patients, and MRI and MR venography for all others
6. If no other etiology is identified, the disorder is termed Idiopathic Intracranial Hypertension

Table 2. ASSOCIATED CONDITIONS

Obstruction to venous drainage
Cerebral venous sinus thrombosis
Aseptic (hypercoagulable state)
Septic (middle ear or mastoid infection)
Bilateral radical neck dissection with jugular vein ligation
Superior vena cava syndrome
Increased right heart pressure
Cerebral arterial-venous sinus shunts

Endocrine disorders
Addison’s disease
Hypoparathyroidism
Obesity, recent weight gain*
Orthostatic edema*
Polycystic ovarian syndrome

Exogenous agents
Chlordecone (kepone)
Corticosteroids (particularly withdrawal)*
Growth hormone
Leuprolerin acetate (LH-RH analogue)
Levothyroxine (children)
Lithium carbonate
Nalidixic acid
Norplant®
Sulfa antibiotics
Tetracycline and related compounds*
  Minocycline
  Doxycycline
Vitamin A and related compounds*
  Accutane
  Vitamin supplements, liver, cod liver oil
  All-trans-retinoic acid (for acute promyelocytic leukemia)

Other medical conditions
Antiphospholipid antibody syndrome
Chronic obstructive pulmonary disease
Polycystic ovary syndrome
Renal failure
Sleep apnea
Systemic lupus erythematosis
Turner syndrome

* common, well-established associations

Table 3. Diagnostic criteria for pediatric IIH [Rangwalla and Liu]

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 H₂O
   Age 8 or above or less than 8 without papilledema: >250 mm H₂O
4. Normal CSF composition except in neonates who may have up to 32 WBC/mm³ 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 transverse 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


Scher AI, Stewart WF, Ricci JA, Lipton RB: Factors associated with the onset and remission of chronic daily headache in a population-based study. Pain 2003;106:81-89


COMMENTARY ON SLIDES

Note: Fundus photos are displayed from the examiner’s perspective – the right fundus is displayed on the left, the left fundus is on the right.

Slide 12
The photo on the right (left eye) shows elevation of the optic nerve head and a partial peri-papillary halo (it appears dark red). There are small hemorrhages and exudates in a radial arrangement off the disc, following the pattern of the retinal nerve fiber layer. Note that all of the vessels cannot be followed along their course from the retina to their “origin” in the optic nerve – this is an important sign, and arises from edema of the overlying nerve fiber layer obscuring our view of them. Ther optic nerves in both eyes are “hyperemic” – the red coloration is from increased vascularity at the optic nerve.
head. Hyperemia is not a reliable sign; some patients with normal optic nerves have fairly red discs.

Slide 14
This patient was in her teens and undergoing treatment for lymphoma, including corticosteroids. Her course was complicated by a superior sagittal sinus thrombosis. Thus, there was more than one possible precipitant of her PTC. She was asymptomatic and the disc edema was found by her pediatric oncologist on a routine examination. Her vision was normal excepting an enlarged blind spot in both eyes. She was treated with acetazolamide and had full recovery of her PTC, lymphoma and sinus thrombosis. At last contact, she was attending nursing school at Johns Hopkins University.

Slide 15
PTC is not a ‘fatal disease’, but in this case it accompanied a fatal illness. This patient was in her 40s and suffered from severe depression for over 10 years. She had “atypical depression” and overate, to the point where she was over 350 pounds. As a result, she developed cor pulmonale and pulmonary hypertension. While in the hospital she complained of visual loss in both eyes. The photos are taken with a portable fundus camera at the bedside (she was too large and too ill to come to the Eye Clinic), so the orientation is a bit tilted. She has bilateral disc edema and has begun to develop optic nerve pallor. The course of some of the vessels cannot be followed over the disc. Her vision was approximately 20/200 in both eyes with marked constriction of her visual fields (tested with a tangent screen at the bedside). Bilateral optic nerve sheath fenestrations were performed under local anesthesia (this procedure is normally done under general anesthesia), as her pulmonologists were concerned that she could not be weaned off of the ventilator postoperatively. Unfortunately, her overall condition deteriorated, she refused intubation, and died.

Slide 16
This 15-year-old girl presented in the late 1980s with typical symptoms of PTC and visual acuities of 20/80 in both eyes. We were struck by her very short stature. She was treated with acetazolamide but missed numerous follow-up appointments because no one could drive her to the office. When she ‘resurfaced’ a couple of months later, her vision had deteriorated to 20/200 in both eyes. She was admitted to the hospital for a lumboperitoneal shunt. Endocrinological evaluation revealed a diagnosis of Turner syndrome. Her photos show bilateral secondary (also called “dirty”) optic atrophy. The margins of the disc look ragged — with most other causes of optic atrophy they are crisp and well delineated. There is gliosis of the nerve fiber layer creating that ‘ratty’ appearance and circumferential remnants of Paton’s lines (“high water marks”) from previous disc swelling. Secondary optic atrophy occurs after papilledema resolves. As Dr. Alfredo Sadun used to tell me during my fellowship, the nerves “look like that because they went down after a fight”.

Slide 17
A 19-year-old overweight nurse developed the worst headaches of her life with photosensitivity, rendering her bedridden and unable to work. She noticed dark spots in her vision and was ultimately referred when she developed diplopia. Her exam showed good central vision, an inferior acuate field defect in the left eye and an enlarged blind spot in both eyes, a left afferent papillary defect and bilateral VI nerve palsies. Her photos show acute, high-grade papilledema. The margins of the optic nerves cannot be
discerned. There are nerve fiber layer hemorrhages, exudates and that ominous sign – inability to follow all of the vessels as they cross over the disc margin. She had a left optic nerve sheath decompression with partial resolution of her arcuate defect.

Slide 20
Automated perimetry (Humphrey 24-2) in a patient with PTC. For those readers who are not familiar with this type of visual field, it tests the retinal sensitivity in the central 24 degrees of vision. The perimeter flashes a light of variable intensity in a pre-determined pattern and the patient responds by pressing a button each time they see the light in their peripheral vision. When looking at the printout, the patient is looking where the lines intersect. The lighter the grayscale, the better the vision. The darker the gray tone, the worse vision is at that location. Unlike fundus photos, visual fields are always displayed as the patient sees the world (if you pretend you are the patient, that’s what you would see) – the left eye is on the left side, the right eye is on the right side.

This patient has enlarged physiologic blind spots in both eyes (located temporal to fixation) and inferior field loss in both eyes, moreso on the left. (Overall, the retinal sensitivity is depressed – the background should be lighter.)

Slide 21
Patients with PTC may have superimposed non-organic (“functional”) visual loss. This young lady used to drive 2.5 hours to her office visits and was an avid golfer. She had well-documented PTC in the past. Her vision was 20/20 in both eyes with bilateral optic nerve pallor. Her automated visual fields consistently looked like this picture. Note that the remaining visual field is square – this is not physiologic, our visual field is not square. A person with only 5 degrees of central field would not be driving or playing golf! Kinetic perimetry confirmed functional visual field loss, with crossing of the isopters and failure of the field to expand with a larger target.

Slide 24
Sagittal view of the orbit shows typical signs of papilledema. The optic nerve sheaths are distended and tortuous (the optic nerve is light gray, the CSF in the subarachnoid space is black). There is protrusion of the optic nerve head into the vitreous and flattening of the posterior sclera (it should be round).

Slide 34
The optic discs are small and tilted – the temporal aspect of the nerve protrudes more than the nasal aspect, which might look like optic disc swelling with the direct ophthalmoscope. There is no tortuosity or engorgement of the vessels, as would be seen in true papilledema, and the vessels smoothly cross the disc.

Slide 35
Optic disc drusen are calcifications that arise in the substance of the nerve, and tend to migrate to the anterior surface of the nerve over time. They give the optic nerve head a “lumpy, bumpy” appearance with an irregular contour. Drusen may be buried, or visible, as in the photo on the right, which shows a prominent drusen at 6:00 on the edge of the optic nerve head. The elevation of the nerve produced by drusen can be mistaken for true papilledema, especially when the drusen are buried. Sometimes optic disc edema and drusen co-exist in the same patient.
Slide 51
When the optic nerve sheath is fenestrated (retracted in the photo), the surgeon sees a “gush of fluid” as the CSF is released. In reality, the “gush” is usually only a few drops to a milliliter of CSF, magnified under the operating microscope.

Slide 56
Smooth walled stenosis of the transverse sinuses may be present on MRV, as in the images on top. The stenosis resolved after the intracranial pressure was lowered, either by lumbar puncture or shunt (bottom images).

Slide 61
Stained glass panel from the University of Rochester Eye Institute.
Questions

1. The fastest growing segment of the population being diagnosed with PTC is:
   a. Obese women
   b. Children
   c. **Obese Men**
   d. Persons over age 45 years
   e. Teenagers

Comment: Recent population studies show that the incidence of PTC has increased overall since the initial studies from 1988. Men are being diagnosed with PTC in larger percentages than previously reported.

2. The most sensitive parameter to follow visual function in PTC patients is:
   a. visual acuity
   b. **perimetry**
   c. visual evoked potentials
   d. confrontation visual fields
   e. pupillary reactions

Comment: Visual acuity is not sensitive to peripheral visual field loss, which is the type most frequently found in PTC. Perimetry, either Goldmann kinetic perimetry or automated perimetry (e.g., Humphrey), is the best way to assess visual function in PTC patients. Visual evoked potentials are not sensitive, and will not be abnormal until a significant amount of optic nerve damage is present. Color vision is not sensitive, confrontation visual fields are inadequate and the pupillary reactions may be symmetrical in the setting of bilateral optic neuropathy.

3. All of the following medications have been associated with PTC except:
   a. Oral contraceptives
   b. Minocycline
   c. Human growth hormone
   d. Accutane™
   e. Corticosteroid withdrawal

Comment: Oral contraceptives have not been shown to be directly associated with PTC, although they may predispose to cerebral venous sinus thrombosis which is a secondary cause of PTC.

4. There is an increased rate of developing PTC during pregnancy compared to the non-gravid state.
   a. True
   b. **False**

Comment: A case-control study showed no increase of PTC developing during pregnancy in patients vs. age-matched controls. [Digre]

5. All of the following agents are acceptable to use for treatment of PTC during pregnancy except:
   a. Acetazolamide (Diamox™)
b. Corticosteroids
c. Optic nerve sheath fenestration
d. Repeated lumbar punctures
e. Topiramate (Topamax™)

Comment: Acetazolamide has not been linked to adverse effects on the mother or fetus and can be used after the first trimester. Corticosteroids, which are generally not recommended for treatment of PTC, may be given during pregnancy if needed. Optic nerve sheath fenestration and repeated lumbar punctures are not contraindicated. Frequent lumbar punctures and acetazolamide are often sufficient to treat women during pregnancy. Topiramate should not be used during pregnancy, and is not considered a first-line treatment for PTC in any case.

6. The most common symptom of PTC is:
   a. Headache
   b. Transient visual obscurations
c. Diplopia
d. Pulsatile tinnitus
e. Neck pain

Comment: All of the selections may be symptoms of PTC but headache is the most common, present in over 90% of patients.[Wall & George]

7. What percentage of body weight loss is associated with improvement in papilledema?
   a. 3%
b. 6%
c. 10%
d. 17%
e. 20%

Comment: When we counsel obese patients to lose weight as part of their treatment regimen, the immediate goal is 6% of body weight. This is generally perceived as an achievable goal and may be better accepted by the patient than a general statement to “lose weight”. It is uncertain whether the weight loss causes papilledema to improve, or whether it is a manifestation of the disorder improving overall.

8. A case-control study found a statistically significant correlation between this factor and the development of PTC:
   a. Tetracycline use
   b. Irregular menses
c. Recent weight gain
d. Vitamin A intake
e. Oral contraceptives

Comment: The only case-control study of risk factors for PTC showed that obesity and a recent weight gain were significantly different in patients vs. control subjects.[Ireland]

9. Neuroimaging findings that are characteristic of PTC include:
   a. Slit ventricles
b. Transverse venous sinus stenosis

c. Empty sella

d. Distention of the optic nerve sheaths

e. Flattening of the posterior sclerae

Comment: While some patients with PTC may have small ventricles, the ventricular size in PTC is considered normal, and no different than in healthy age-matched control subjects.[Jacobson]. One should not discount the diagnosis of PTC if the ventricles are normal; however, they should not be enlarged. Venous sinus stenosis, an empty sella, distention of the optic nerve sheaths, flattening of the posterior sclerae and protrusion of the optic nerve head into the globe are useful signs. Patients with PTC may have some or all of these findings.

10. Which of the following surgical procedures used in the treatment of PTC has the highest failure rate (requiring repair or re-treatment)?
   a. Ventriculoperitoneal shunt
   b. **Lumboperitoneal shunt**
   c. Ventriculoatrial shunt
   d. Optic nerve sheath fenestration

Comment: The large experience from Johns Hopkins found that lumboperitoneal shunts were most likely to fail, upwards of 50% over three years. Patients with a headache duration of 3 years or more were least likely to improve, regardless of shunt patency.[McGirt] The failure rate of ventriculoperitoneal shunts, ventriculoatrial shunts, and optic nerve sheath fenestration is somewhat lower.