

LEO Clinical Topic Update

Neuro-Ophthalmology

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Introduction

Many important advances have occurred in the last 5 years in neuro-ophthalmology in the areas of clinical diagnosis and medical and surgical management. In the area of clinical diagnosis, there are important new uses for proven modalities of sensory testing such as visual fields, color vision testing, and fluorescein angiography. Improved and new neuroimaging techniques that may be of interest to the ophthalmologist include magnetic resonance angiography and other new magnetic resonance imaging sequences. In medical management, important advances have been made in the diagnosis and treatment of optic neuritis, traumatic optic neuropathy, and anterior ischemic optic neuropathy. The efficacy of surgical management (eg, optic nerve sheath decompression and lumboperitoneal shunting) in pseudotumor cerebri is discussed in this Clinical Topic Update and the pathogenesis and epidemiology of pseudotumor cerebri are reviewed.¹⁻⁴

Two important clinical trials are summarized: the Optic Neuritis Treatment Trial⁵ and the Ischemic Optic Neuropathy Decompression Trial.⁶ Relatively new reports of visual field loss following vitrectomy for macular holes are discussed,^{7,8} as well as unusual neuro-ophthalmic conditions, including paraneoplastic retinopathies (eg, cancer-associated retinopathy and melanoma-associated retinopathy) and Leber's hereditary optic neuropathy.⁹⁻¹²

Advances in Clinical Diagnosis

Visual Field Testing

Although manual Goldmann and tangent screen visual field techniques still have application—especially for patients who are uncooperative, unreliable, or have functional visual loss—automated perimetry has gained widespread use and acceptance for neuro-ophthalmic conditions.¹³ An Ophthalmic Procedures Assessment published by the American Academy of Ophthalmology discusses and summarizes the uses of computerized perimetry, and several reports have proposed techniques for the efficient use of perimetry in neuro-ophthalmology.¹⁴ Siatkowski and colleagues reviewed the role of suprathreshold static perimetry in neuro-ophthalmic disease by performing central 30-degree full-threshold and suprathreshold perimetry in 159 consecutive patients, of whom half had neuro-ophthalmic disease.¹⁵ Although sensitivity and specificity were comparable between the two perimetry techniques, the mean time required for full-threshold testing was 14.8 minutes compared with 3.5 minutes for suprathreshold testing. This time difference may be important for certain neuro-ophthalmic patients with limited attention and decreased reliability in visual field testing. However, these authors emphasized that full-threshold testing was still required for detailed quantification of visual field loss and in follow-up evaluations for conditions such as pseudotumor cerebri or other optic neuropathies.

Wall and colleagues demonstrated long- and short-term variability of automated perimetry results in patients with optic neuritis and in healthy subjects.¹⁶ They caution that because of this variability care should be taken in the interpretation of abnormal results from test to test. Thompson and colleagues reported that with minimal coaching, normal subjects could replicate organic-

appearing visual field abnormalities—including enlargement of the blind spot and quadrantic, hemianopic, and altitudinal visual field loss—on both manual and automated perimetry.¹⁷ Paracentral and cecocentral defects were much more difficult to replicate, however. As would be expected, they reported that the level of visual field technician experience is an important factor in differentiating organic from nonorganic visual field loss on manual testing.

Visual field testing may be performed in children. Safran and colleagues reported on 42 female patients ages 5 to 8 years who underwent three successive automated perimetry tests.¹⁸ All but one 5-year-old child were able to complete the testing with a relatively low false-positive and false-negative response rate. The authors suggest that automated perimetry is feasible in children as young as 5 years old with appropriate familiarization and instruction.

Other Tests of Afferent Function

Trobe and colleagues described the measures of visual function in the Optic Neuritis Treatment Trial.¹⁹ These authors found that a normal result on either Pelli-Robson contrast sensitivity, mean deviation on Humphrey visual field testing, or Farnsworth-Munsell 100-hue color vision testing—in addition to normal Snellen visual acuity—was predictive of normal Snellen visual acuity at 6 months. The Pelli-Robson contrast sensitivity test was found to be the most sensitive indicator of visual dysfunction at 6 months.

Color testing is useful for patients with unexplained visual loss who are suspected of harboring an underlying optic neuropathy. Aroichane and colleagues reported a prospective study of 178 consecutive patients who were tested with Hardy-Rand-Rittler and Ishihara color plates.²⁰ These authors believe that the Hardy-Rand-Rittler plates are more likely than Ishihara plates to detect a color vision defect (particularly if the visual acuity is 20/25 or better) but that neither test is sensitive enough to be used as the sole criterion for the diagnosis of optic neuropathy. Color comparison between the two eyes may be more useful than the absolute responses, particularly in unilateral disease.

Arnold and colleagues report that fluorescein angiography may be a useful technique in the evaluation of ischemic and nonischemic optic disc edema.²¹ These authors compared fluorescein angiography from 22 patients who had nonischemic optic disc edema with age-matched controls who had nonarteritic anterior ischemic optic neuropathy (NA-AION). They found a significant delay in prelaminar optic disc filling of at least 5 seconds in 76% of patients with NA-AION as compared with nonischemic controls.

Ice Test

Golnik and colleagues reported a novel method of testing for myasthenic ptosis called the ice test.²² Twenty patients with myasthenia gravis and ptosis and 20 control patients with nonmyasthenic ptosis were evaluated. Palpebral fissures were measured before and immediately after a 2-minute application of ice to the ptotic eyelid. A positive ice test was noted in 16 of 20 (80%) patients with myasthenia gravis and in none of 20 patients without myasthenia gravis. The ice test may prove to be a simple, short, specific, and relatively sensitive test for myasthenic ptosis.

New technologies, including magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA), are expanding the diagnostic tools available to the ophthalmologist.²³⁻³² One of the most important and potentially life-threatening clinical situations faced by the ophthalmologist is a pupil-involved third nerve palsy due to an underlying posterior communicating artery aneurysm.³³⁻³⁷ Aneurysms compressing the third nerve impair the pupil in 96% of cases, and in the 4% of cases in which the pupil has been spared the ocular motility has been only partially reduced.³⁷ Thus, the possibility of an aneurysm should be considered in all cases of pupil-involved third nerve palsy.

MRA is rapidly emerging as a useful noninvasive imaging modality for vascular disease and may detect up to 95% of cerebral aneurysms that will bleed.^{33,34} Unfortunately, 95% is not 100%, and conventional contrast angiography remains the diagnostic procedure of choice for the detection of aneurysms.³⁷ Nevertheless, experience with MRA continues to grow and the technique may one day reduce the need for exposing patients to the not-insignificant risks of standard contrast cerebral angiography, especially in cases with partial pupil involvement or partial third nerve motor involvement.^{33,34,36} Jacobson and Trobe reviewed the scientific literature to determine the sensitivity of three-dimensional time-of-flight magnetic resonance angiography for detection of aneurysms causing a third nerve palsy. They conclude that a properly performed and interpreted magnetic resonance angiogram would overlook only 1.5% of aneurysms producing a third nerve palsy that would rupture if untreated.³⁸

Frequency-selective fat suppression techniques have improved our ability to visualize orbital anatomy and pathology on T1-weighted MRI scans. Normally, the hyperintense fat signal on pre- and postcontrast enhanced T1-weighted images obscures the underlying orbital detail. Fat saturation techniques allow the fat signal to be suppressed. Unfortunately, however, incomplete fat suppression can create artifacts on MRI that may mimic orbital disease; careful clinical correlation is required.

Newer techniques in MRI have improved evaluation of brain pathology. One technique, fast fluid-attenuated inversion recovery (FLAIR), uses advanced computer software and basic inversion recovery principles to help differentiate between pathology and normal brain parenchyma without interference from the adjacent high-signal cerebrospinal fluid (CSF). FLAIR produces strong T2 weighting but suppresses the CSF signal and thus produces images with significantly increased lesion-to-background contrast, particularly in the subcortical and periventricular regions. Many recent reports have concluded that FLAIR imaging provides additional useful information in a number of neurologic diseases of interest to the ophthalmologist including optic neuritis, multiple sclerosis, metastatic disease, and ischemia.²⁴⁻³²

Although not universally available to all ophthalmologists, the newer imaging studies positron emission tomography (PET) and single proton emission computed tomography (SPECT) may be useful adjunctive noninvasive techniques for patients with retrochiasmal pathway defects. These techniques use a radiolabeled, biologically active tracer to study brain function. In PET scanning, the tracer is labeled as a radioligand with a positron-emitting isotope. As the tracer accumulates in the brain, positrons are emitted that can be detected and imaged on film as gamma ray energy in the form of protons. SPECT scans

use tracers similar to PET, except that the tracers emit only a single photon (rather than two photons).³⁶

Moster and colleagues reported 2 patients with anoxic brain injury, binocular visual loss, and normal pupillary reactions.³⁰ Based on conventional neuroimaging studies (CT and MRI), both patients were thought to have nonorganic disease; SPECT and PET scans in these patients were helpful in documenting organic metabolic and perfusion abnormalities in the visual cortex. In a similar fashion, functional MRI may allow better evaluation of brain function and may give information that structural conventional MRI cannot provide.³⁶ "Functional" in this context refers to brain activity, rather than brain structure, and is unrelated to "functional" meaning nonorganic visual loss. Miki and colleagues described functional MRI in 5 patients with homonymous hemianopsias.²⁹ The authors found asymmetric activation of the visual cortex in these patients and postulate that functional MRI may find use for patients unable to perform standard perimetry.

Advances in Management

Optic Neuritis

New information has emerged about optic neuritis (ON) as a result of the Optic Neuritis Treatment Trial (ONTT).^{5,16,39-62} The ONTT was a National Eye Institute–sponsored, randomized, controlled clinical trial that enrolled 457 patients at 15 clinical centers in the United States between the years 1988 and 1991. The ONTT entry criteria included the following: (1) patients between ages 18 and 46 years; (2) patients presenting signs of an afferent pupillary defect and a visual field defect in the affected eye; and (3) patients examined within 8 days of the onset of visual symptoms of a first attack of acute unilateral ON. Patients were excluded if they had any of the following: (1) previous episodes of ON in the affected eye; (2) previous corticosteroid treatment for ON or multiple sclerosis (MS); or (3) systemic disease other than MS that might be a cause for the ON. The patients were randomly assigned to one of three treatment arms in the study: (1) intravenous methylprednisolone sodium succinate 250 mg every 6 hours for 3 days followed by oral prednisone 1mg/kg per day for 11 days; (2) oral prednisone 1 mg/kg per day for 14 days; or (3) oral placebo for 14 days followed by a short oral taper.³⁹

Based on their results, the authors recommend that treatment with oral prednisone in standard doses be avoided in ON.³⁹ In addition, their findings suggest that treatment with IV methylprednisolone can be considered for patients with abnormal MRI of the brain or in those with a particular need for rapid visual rehabilitation (such as a monocular patient or an occupational requirement). Beck and colleagues feel that although brain MRI may not be necessary for diagnosis of ON, MRI is valuable for prognostic purposes. Although patients with multiple signal abnormalities on MRI most clearly benefited from IV methylprednisolone in terms of the slowing of development of MS, the rate of development of MS was too low in the patients with normal MRI to assess treatment benefit in this group.^{40-42,45-47,57,60}

In the ONTT, all patients underwent testing for collagen vascular disease (eg, antinuclear antibody [ANA]), serologic testing for syphilis (FTA-ABS), and a

chest radiograph for sarcoidosis. Lumbar puncture was optional.³⁹ Rolak and colleagues analyzed the cerebrospinal fluid (CSF) of 83 patients with clinically isolated ON who underwent lumbar puncture.⁵⁸ No patients had their diagnosis or management altered by the CSF results and these authors conclude that CSF analysis may not be necessary in the routine evaluation of typical ON. Oligoclonal banding in the CSF, present at baseline in 11 of 13 patients who developed MS, did predict progression to clinically definite MS, but this was not independent of MRI abnormalities.

ANA tests in the ONTT were positive in a titer of less than 1:320 in 13% of patients and in a titer of 1:320 or greater in 3% of patients. Only one patient was eventually diagnosed with a collagen vascular disease. Visual and neurologic outcomes in these patients were no different than the other ONTT patients. The FTA-ABS was positive in 6 patients (1.3%), but none had syphilis. A chest radiograph did not reveal sarcoidosis in any patient. The ONTT study group recommends that chest radiograph; laboratory tests such as syphilis serology, collagen vascular disease, serum chemistries, complete blood counts, and lumbar puncture are not necessary for typical ON.³⁹

Neuroimaging studies in the ONTT disclosed an alternative etiology for visual loss in only one patient with a pituitary adenoma; a second patient had an ophthalmic artery aneurysm that was not detected on the initial MRI scan. The ONTT authors conclude that neuroimaging is of limited value in establishing the diagnosis of ON, but they feel that MRI of the brain is a powerful predictor of MS and should be considered to assess the risk of future neurologic events of MS and for treatment decision making.^{39-42,45-47,57,60}

The major conclusions of the ONTT related to treatment are summarized below. High-dose IV followed by oral corticosteroids accelerated visual recovery (particularly in regard to visual field defects; $p = 0.0001$), but provided no long-term benefit to vision. Standard dose oral corticosteroid alone did not improve the visual outcome and was associated with an increased rate of new attacks of ON. IV followed by oral corticosteroids reduced the rate of development of clinically definite MS during the first 2 years, particularly in patients with signal abnormalities on brain MRI, but by 3 years the treatment effect had subsided.^{46,57} Treatment was well tolerated with few major side effects.

Intravenous immunoglobulin has also been reported to improve visual acuity in an uncontrolled study of 5 patients with definite MS who had unilateral or bilateral but stable demyelinating ON.⁶¹ These results will need to be replicated on a larger scale before any recommendation on the use of IV immunoglobulin can be made.

Most patients with ON retain good to excellent visual function in the 5 years following an attack of ON (even if recurrent). Recurrences were more frequent in patients with MS and in patients treated with oral corticosteroids alone. The 5-year risk of MS after optic neuritis was 30% and MRI was a strong predictor of clinically definite MS. The 5-year follow-up data have not altered the management recommendations that were made based upon the original results.⁴⁸

For patients with optic disc edema, a macular star figure of exudate, and a normal brain MRI, the etiology of the ON almost always—if not always—is an etiology other than MS.^{48,53} In fact, infectious etiologies such as cat scratch disease or syphilis are more likely in this setting. Demyelinating ON would not be expected to cause a secondary macular star figure of exudate. In the ONTT, excluding patients with severe optic disc edema, retinal or disc hemorrhages, and macular exudates increased the life-table analysis estimate of 5-year risk of MS

from 30% to 32% in the full cohort. The rate of MS increased from 16% to 19% for patients without an MRI lesion at the time of diagnosis of ON.

Traumatic Optic Neuropathy

Traumatic optic neuropathy (TON) is a clinical diagnosis that is characterized by a history of impact injury to the head, face, or orbit that is presumably transmitted directly or indirectly to the optic nerve. TON results in variable loss of visual acuity (ranging from 20/20 to no light perception) and/or loss of visual field; an afferent pupillary defect in unilateral or bilateral but asymmetric cases; and a (commonly) normal or (less commonly) swollen optic nerve that later develops optic atrophy.

Once the clinical diagnosis of TON is made, neuroimaging should be performed. Computed tomography (CT) scans may be the preferred modality in the setting of trauma for the evaluation of the emergent patient with TON; for detailed examination of bone fractures and bone anatomy; and for the detection of acute hemorrhage.

The natural history of TON is unknown. There is no large, well-controlled, randomized, prospective body of data regarding the treatment of TON due to variations in clinical presentation; treatment modalities (corticosteroids alone, corticosteroids with surgery, surgery alone); surgical techniques and approaches; inclusion criteria; recruitment bias; small sample sizes; and outcome measures.^{63–71} However, in 1996 Cook and colleagues reviewed all cases of TON published in the English language literature, as well as some additional cases, to perform a meta-analysis of treatment.⁶⁸ Patients who underwent treatment showed greater improvement than patients who had observation alone. No significant difference in improvement, however, was noted among patients treated with corticosteroids alone, surgical decompression alone, or a combination of these modalities. Recovery of vision was better for patients without orbital fractures and was better for patients with anterior rather than posterior fractures.⁶⁸

Although the mainstay of medical treatment for TON has been corticosteroids, there are no prospective data to support the efficacy of treatment or the validity of any specific corticosteroid preparation, dosage, or duration of therapy. Because of this lack of treatment data, many authors have advocated extrapolating data on the use of higher-dose methylprednisolone from central nervous system (CNS) injury.^{63–66} The first National Acute Spinal Cord Injury Study (NASCIS 1) was a non–placebo-controlled study. This study concluded that there was no beneficial effect of methylprednisolone 1000 mg bolus followed by 1000 mg per day for 10 days ("high dose") as compared with methylprednisolone 100 mg bolus followed by 100 mg per day for 10 days ("standard dose"). NASCIS 2 was a multicenter, placebo-controlled, randomized, double-masked study of acute spinal cord injury that showed that treatment within 8 hours with a methylprednisolone 30 mg/kg bolus followed by 5.4 mg/kg/hour for 24 hours resulted in significant improvement in motor and sensory function as compared with placebo. However, methylprednisolone delivered after 8 hours did not improve neurologic outcome.^{63–66}

In addition, methylprednisolone in the 15–30 mg/kg dose range apparently has a different pharmacologic effect on CNS injury parameters such as blood flow, calcium homeostasis, energy metabolism, and clinical outcome. The traditional dose calculation for an equivalent dose of dexamethasone compared with methylprednisolone has been based upon the glucocorticoid potency of 5:1.

Steinsapir and Goldberg have emphasized that the potency ratio for dexamethasone to methylprednisolone in CNS injury may be closer to 2:1 and therefore that dexamethasone 15 mg/kg may be required (as compared to the dose of 3–6 mg/kg recommended by previous authors) for the adequate treatment of TON.⁷⁰ The following TON treatment protocol is offered by Steinsapir and Goldberg: (1) Diagnose TON appropriately; (2) Perform canthotomy or cantholysis if the orbit is tense; (3) Drain subperiosteal hematoma if present; (4) Begin methylprednisolone (30 mg/kg IV bolus, then 5.4 mg/kg/hour IV for 48 hours); (5) If vision improves on IV methylprednisolone after 48 hours, then start rapid oral taper of prednisone; (6) If there is no clinical response after 48 hours or if the patient's vision deteriorates during the corticosteroid taper, then offer surgical decompression of the optic canal.

Joseph and colleagues reported variable success in a retrospective, nonconsecutive study on 14 patients with TON who were treated with transthemoidal-sphenoidal optic canal decompression and with dexamethasone pre- and postoperatively.⁶⁹ Levin and colleagues reported a comparative nonrandomized interventional study of TON with the following concurrent treatment groups: (1) untreated; (2) corticosteroid; or (3) optic canal decompression surgery.⁷² They conclude that there was no clear benefit for either corticosteroid therapy or optic canal decompression surgery. The number of patients in the study was adequate to exclude major effects in the treatment groups, although the authors acknowledge that clinically relevant effects in specific subgroups could have been missed. These authors believe that neither corticosteroids nor optic canal decompression surgery should be considered the standard of care for TON.

Pseudotumor Cerebri

Pseudotumor cerebri (PTC), also called idiopathic intracranial hypertension, is a disease that usually occurs in young-adult obese females.^{1–4} PTC can occur in children but there is no gender predilection, obesity is less frequent, and other associated secondary conditions are more common than in adults.³ PTC is defined clinically by the following criteria: (1) signs or symptoms related specifically to increased intracranial CSF pressure (eg, headache, papilledema, sixth nerve palsy); (2) a normal neuroimaging study (usually MRI of the head); and (3) a normal CSF content with an elevated opening pressure on lumbar puncture.

Sugerman and colleagues performed a nonrandomized, prospective study of intra-abdominal pressure (estimated from urinary bladder pressure) and central obesity (measured by sagittal abdominal diameter) in 6 females with PTC.⁴ These authors found evidence that central obesity raises intra-abdominal pressure, increasing pleural pressure and cardiac filling pressure, impeding venous return from the brain, and leading to increased intracranial venous pressure and intracranial CSF pressure.

Medical therapy with acetazolamide (in conjunction with weight loss therapy) has been used with success for patients with PTC. Patients with progressive visual loss due to papilledema or with intractable headache who fail to or are intolerant to or noncompliant with medical therapy may require surgical treatment. Lumboperitoneal shunting (LPS) and optic nerve sheath fenestration (ONSF) are the mainstays of surgical treatment for PTC. Burgett and colleagues

retrospectively reviewed 30 patients who had LPS for PTC and visual loss.¹ Of 14 eyes with poor visual acuity, 10 (71%) improved by at least 2 lines of vision, and 18 of 28 eyes with impaired visual field (64%) improved their visual field. The major drawback of LPS is shunt failure. Goh and colleagues reviewed 29 eyes of patients with progressive visual field loss due to PTC who were treated with ONSF.² Of the 21 patients with adequate follow-up, visual fields improved in 10 of these eyes (48%), were unchanged in 8 eyes (38%), and worsened in 3 eyes (14%).

Important Clinical Trials

Anterior Ischemic Optic Neuropathy

Anterior ischemic optic neuropathy (AION) is the most common acute optic neuropathy among adults over age 50 years.^{6,73-84} AION may be caused by giant cell arteritis (arteritic AION) or it may be associated with vasculopathic risk factors (nonarteritic AION). Hayreh and colleagues reported that the clinical features of jaw claudication, neck pain, advanced age, and elevated erythrocyte sedimentation rate and C-reactive protein level are suggestive of biopsy-proven giant cell arteritis.⁷⁹ NA-AION is characterized clinically by acute loss of vision and a visual field defect resulting from an optic neuropathy; an ipsilateral afferent pupillary defect; and a swollen optic nerve in an older patient who often has underlying vasculopathic risk factors (eg, hypertension and diabetes).⁸¹

Although older age, male sex, presence of hypertension, lack of pain, and less improvement in visual acuity are seen more commonly in NA-AION than in optic neuritis, none of these characteristics are pathognomonic for either disorder. In fact, there may be significant overlap between the two conditions. The major concern for patients with AION is whether or not the visual loss is caused by giant cell arteritis, and the evaluation should be aimed at excluding this possibility (eg, erythrocyte sedimentation rate, temporal artery biopsy).⁷⁹ Gordon and colleagues emphasized the broad spectrum of visual loss in NA-AION in a report of 2 patients with asymptomatic disc edema. These authors reiterated that NA-AION may occur sequentially within a 5-year period at a rate of up to 25% to 50% of cases.⁷⁶ WuDunn and colleagues reviewed 31 records of sequential or bilateral NA-AION and reported that except for the possibility of better visual acuity in the affected second eye in older patients, visual function and the pattern of visual field loss could not be reliably used to predict fellow eye outcome.⁸⁴

The Ischemic Optic Neuropathy Decompression Trial (IONDT). A well-designed, masked, prospective, randomized clinical trial was performed to study the safety and efficacy of optic nerve sheath fenestration in NA-AION.⁶ The study inclusion criteria were a clinical syndrome consistent with NA-AION, age greater than 50 years, and visual symptoms for less than 14 days. The baseline clinical characteristics of patients in the study were 62% male, mean age 66 years, 42% with hypertension, 24% with diabetes, 10% reporting pain, 49% with visual acuity of 20/64 or better at baseline, and 34% with 20/200 or worse vision.^{6,73,74,77,78,80} Patients were randomized to either surgery (optic nerve sheath decompression) or control (observation). After 6 months, 32.6% of the surgery group had improved 3 lines or more compared with 42.7% of the control group;

in addition, 23.9% of the surgery group had lost 3 or more lines compared with only 12.4% of the control group. Visual field data likewise confirmed a lack of treatment effect for surgery. The authors concluded that surgery is not effective and may be harmful.⁶

Medical Treatment of Nonarteritic Anterior Ischemic Optic Neuropathy.

Although experimental therapies such as levodopa and heparin-induced extracorporeal LDL/fibrinogen precipitation (HELP) have shown variable but limited success, other treatments such as hyperbaric oxygen have not been helpful.^{73,77,82} There remains no proven effective treatment for NA-AION.

Beck and colleagues performed a retrospective cohort study of 431 patients to assess the benefit of aspirin in NA-AION.⁷⁴ At 2 years of follow-up, the cumulative probability of developing NA-AION in the fellow eye was lower in the aspirin group (7%) compared with the no aspirin group (15%), but this difference was not present at 5 years (17% versus 20%, respectively). Of interest, the overall 5-year risk was 19%, lower than the previously reported 24% to 48% risk of a fellow eye attack. In a retrospective review of 131 patients, Kupersmith and colleagues reported that aspirin given two or more times per week reduced the incidence (17.5% vs 53.5%) and relative risk (RR = 0.44, $p = 0.0002$) of fellow eye involvement of NA-AION.⁸³ Aspirin use does not seem to improve visual outcome, however, after NA-AION.⁷⁵

New Diseases/Syndromes

Cancer- and Melanoma-Associated Retinopathy

Dysfunction of the retina and consequent visual loss due to paraneoplastic disease has received considerable attention recently.⁹⁻¹¹ Melanoma-associated retinopathy is characterized by night vision impairment, abnormal electroretinography, and selective antibody to rod bipolar cells in a patient with distant melanoma. Cancer-associated retinopathy is another paraneoplastic syndrome characterized by rapidly progressive bilateral visual loss, retinal arteriolar narrowing, an abnormal electroretinogram, and optic atrophy due to an underlying neoplasm (often small cell carcinoma of the lung).

Leber's Hereditary Optic Neuropathy

Leber's hereditary optic neuropathy is characterized clinically by an acute, often bilateral (simultaneous or sequential) optic neuropathy with a central scotoma, severe visual loss (usually 20/200 or less), and apparent edema (peripapillary telangiectasias may be seen) of the optic nerve head in young (typically male) patients. The prognosis is usually poor, although some patients experience spontaneous recovery. The major mutations in mitochondrial DNA that cause Leber's hereditary optic neuropathy are mutations at nucleotide position 11778 (80%), but mutations also occur at positions 3460, 14484, and 15257. The 14484 mutation may have a higher incidence of spontaneous visual recovery than the other mutations.¹²

Visual Field Loss After Vitrectomy for Macular Hole Surgery

A number of reports have documented visual field loss following otherwise uncomplicated vitrectomy for macular hole surgery. A number of theories have been proposed to explain this newly recognized complication,^{7,8} including traction on the optic nerve or peripapillary retina during cortical vitreous peeling, elevated intraocular pressure, or intraoperative mechanical traction during vitreous suction. Unfortunately, none of these theories have been proven or studied prospectively.

References

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1. Burgett RA, Purvin VA, Kawasaki A: Lumboperitoneal shunting for pseudotumor cerebri. *Neurology* 1997;49:734–739.
2. Goh KY, Schatz NJ, Glaser JS: Optic nerve sheath fenestration for pseudotumor cerebri. *J Neuro-Ophthalmol* 1997;17:86–91.
3. Scott IU, Siatkowski RM, Eneyni M, et al: Idiopathic intracranial hypertension in children and adolescents. *Am J Ophthalmol* 1997;124:253–255.
4. Sugerman HJ, DeMaria EJ, Felton WL: Increased intra-abdominal pressure and cardiac filling pressures in obesity-associated pseudotumor cerebri. *Neurology* 1997;49:507–511.
5. Beck RW, Cleary PA: Optic Neuritis Trial: one-year follow-up results. *Arch Ophthalmol* 1993;111:773–775.
6. Ischemic Optic Neuropathy Decompression Trial Research Group: Optic nerve decompression surgery for nonarteritic anterior ischemic optic neuropathy is not effective and may be harmful. *JAMA* 1995;273:625–632.
7. Bopp S, Lucke K, Hille U: Peripheral visual field loss after vitreous surgery for macular holes. *Graefes Arch Clin Exp Ophthalmol* 1997;235:362–371.
8. Ezra E, Arden GB, Riordan-Eva P, et al: Visual field loss following vitrectomy for stage 2 and 3 macular holes. *Br J Ophthalmol* 1996;80:519–525.
9. Ing EB, Augsburger JJ, Eagle RC: Lung cancer with visual loss. *Surv Ophthalmol* 1996;40:505–510.
10. Thirkill CE: Lung cancer-induced blindness. *Lung Cancer* 1996;14:253–264.
11. Wolf JE, Arden GB: Selective magnocellular damage in melanoma-associated retinopathy: comparison with congenital stationary night blindness. *Vision Res* 1996;36:2369–2379.
12. Yamada K, Mashima Y, Kigasawa K, et al: High incidence of visual recovery among four Japanese patients with Leber's hereditary optic neuropathy. *J Neuro-Ophthalmol* 1997;17:103–107.

13. Reitner A, Tittl M, Ergun E, et al: The efficient use of perimetry for neuro-ophthalmic diagnosis. *Br J Ophthalmol* 1996;80:903–905.
14. American Academy of Ophthalmology: Automated perimetry [Ophthalmic Procedures Assessment]. Reprinted from *Ophthalmology* 1996;103:1144–1151.
15. Siatkowski RM, Lam BL, Anderson DR, et al: Automated suprathreshold static perimetry screening for detecting neuro-ophthalmologic disease. *Ophthalmology* 1996;103:907–917.
16. Wall M, Johnson CA, Kutzko KE, et al: Long- and short-term variability of automated perimetry in patients with optic neuritis and healthy subjects. *Arch Ophthalmol* 1998;116:53–61.
17. Thompson JC, Kosmorsky GS, Ellis BD: Fields of dreamers and dreamed-up fields: functional and fake perimetry. *Ophthalmology* 1996;103:117–125.
18. Safran AB, Laffi GL, Bullinger A, et al: Feasibility of automated visual field examination in children between 5 and 8 years of age. *Br J Ophthalmol* 1996;80:515–518.
19. Trobe JD, Beck RW, Moke PS, et al: Contrast sensitivity and other visual tests in the Optic Neuritis Treatment Trial. *Am J Ophthalmol* 1996;121:547–553.
20. Aroichane M, Pieramici DJ, Miller NR, et al: A comparative study of Hardy-Rand-Rittler and Ishihara colour plates for the diagnosis of nonglaucomatous optic atrophy. *Can J Ophthalmol* 1996;31:350–355.
21. Arnold AC, Hepler RS: Fluorescein angiography in acute nonarteritic anterior ischemic optic neuropathy. *Am J Ophthalmol* 1994;117:222–230.
22. Golnik KC, Pena R, Lee AG, et al: An ice test for the diagnosis of myasthenia gravis. *Ophthalmology* 1999;106(7):1282–1286.
23. Biousse V, Newman NJ, Carroll C, et al: Neuro-ophthalmology of vascular disease. *Neurology* 1998;50:258–265.
24. Davis SL, Newman NJ: Advances in neuroimaging of the visual pathways. *Neurol Clin* 1996;14:201–222.
25. Fillipi M, Yousry T, Baratti C, et al: Quantitative assessment of MRI lesion load in multiple sclerosis: a comparison of conventional spin-echo with fast fluid-attenuated inversion recovery. *Brain* 1996;119:1349–1355.
26. Hoisington L, Miller RA, Vreibel B: Fast FLAIR techniques in MR imaging of the brain. *Radiolog Technol* 1998;69:351–357.
27. Jackson A, Sheppar S, Laitt RD, et al: Optic neuritis: MR imaging combined with fat- and water-suppression techniques. *Radiology* 1998;206:57–63.
28. Kates R, Atkinson D, Brant-Zawadzki M: Fluid-attenuated inversion recovery (FLAIR): clinical prospectus of current and future applications [abstract]. *Top Magn Reson Imaging* 1996;8:389–396.
29. Miki A, Nakajima T, Fujita M, et al: Functional magnetic resonance imaging in homonymous hemianopsia. *Am J Ophthalmol* 1996;121:258–266.
30. Moster ML, Galleta SI, Schatz NJ: Physiologic functional imaging in "functional" visual loss. *Surv Ophthalmol* 1996;40:395–399.
31. Rovaris M, Yousry T, Calori G, et al: Sensitivity and reproducibility of fast-FLAIR, FSE and TGSE sequences for the MRI assessment of brain lesion load in multiple sclerosis: a preliminary study. *J Neuroimaging* 1997;7:98–102.
32. Warach S, Hajnal JV, Rovaris M, et al: The role of techniques characterized by aster acquisition times in the evaluation of multiple sclerosis. *J Neurol Neurosurg Psychiatr* 1998;64(1):S59–S65

33. Futatsuya R, Seto H, Dameai T, et al: Clinical utility of three-dimensional time-of-flight magnetic resonance angiography for the evaluation of intracranial aneurysms. *Clin Imaging* 1994;18:101–106.
34. Horokoshi T, Fukamachi A, Nishi H, et al: Detection of intracranial aneurysms by three-dimensional time-of-flight magnetic resonance angiography. *Neuroradiol* 1994;36:203–207.
35. Jacobson DM: Pupil involvement in patients with diabetes-associated oculomotor nerve palsy. *Arch Ophthalmol* 1998;116:723–727.
36. Lee AG, Tanz C, Cassidy M: Neuroimaging of the ophthalmic patient. *Refinements* Module 10. San Francisco: American Academy of Ophthalmology; July 1998;1–11.
37. Trobe JD: Managing oculomotor nerve palsy. *Arch Ophthalmol* 1998;116:798.
38. Jacobson DM, Trobe JD: The emerging role of magnetic resonance angiography in the management of patients with third cranial nerve palsy. *Am J Ophthalmol* 1999;128(1):94–96.
39. Beck RW, Cleary PA, Anderson MA, et al: A randomized, controlled trial of corticosteroids in the treatment of acute optic neuritis. *N Engl J Med* 1992;326:581–588.
40. Beck RW: Corticosteroid treatment of optic neuritis. *Neurology* 1992;42:1133–1135.
41. Beck RW, Arrington J, Murtagh FR, et al: Brain magnetic resonance imaging in acute optic neuritis experience of the Optic Neuritis Study Group. *Arch Neurol* 1993;50:841–846.
42. Beck RW, Cleary PA, Trobe JD, et al: The effect of corticosteroids for acute optic neuritis on the subsequent development of multiple sclerosis. *N Eng J Med* 1993;329:1764–1769.
43. Beck RW, Kupersmith MJ, Cleary PA, et al: Fellow eye abnormalities in acute unilateral optic neuritis. *Ophthalmology* 1993;102:1504–1508.
44. Beck RW, Cleary PA, Backlund JC: The course of visual recovery after optic neuritis. *Ophthalmology* 1994;101:1771–1778.
45. Beck RW, Trobe J: What we have learned from the optic neuritis treatment trial. *Ophthalmology* 1995;102:1504–1508.
46. Beck RW: The Optic Neuritis Treatment Trial: three-year follow-up results. *Arch Ophthalmol* 1995;113:136–137.
47. Beck RW: The Optic Neuritis Treatment Trial: putting the results in perspective. *J Neuro-Ophthalmol* 1995;12:131–135.
48. Beck RW, Moke PS, Trobe JD: The 5-year risk of MS after optic neuritis [response to Lee AG, Brazis PW]. *Neurology* 1998;51:1231.
49. Brodsky MC, Beck RW: The changing role of MR imaging in the evaluation of acute optic neuritis. *Radiology* 1994;192:22–23.
50. Cleary PA, Beck RW, Anderson MM, et al: Design, methods, and conduct of the Optic Neuritis Treatment Trial. *Controlled Clin Trials* 1993;14:123–142.
51. Keltner JL, Johnson CA, Beck RW, et al: Quality control functions of the visual field reading center (VFRC) for the Optic Neuritis Treatment Trial (ONTT). *Controlled Clin Trials* 1993;14:143–159.
52. Keltner JL, Johnson CA, Spurr JO, et al: Baseline visual field profile of optic neuritis: the experience of the Optic Neuritis Treatment Trial. *Arch Ophthalmol* 1993;111:231–234.
53. Lee AG, Brazis PW: The 5-year risk of MS after optic neuritis [letter]. *Neurology* 1998;51:1230.

54. Lessell S: Corticosteroid treatment of acute optic neuritis. *N Eng J Med* 1992;326:634–635.
55. Optic Neuritis Study Group: The clinical profile of optic neuritis: experience of the Optic Neuritis Treatment Trial. *Arch Ophthalmol* 1991;109:1673–1678.
56. Optic Neuritis Study Group: Visual function after 5 years: experience of the Optic Neuritis Treatment Trial. *Arch Ophthalmol* 1997;115:1545–1552.
57. Optic Neuritis Study Group: The 5-year risk of MS after optic neuritis: experience of the Optic Neuritis Treatment Trial. *Neurology* 1997;49:1404–1413.
58. Rolak LA, Beck RW, Paty DW, et al: Cerebrospinal fluid in acute optic neuritis: experience of the Optic Neuritis Treatment Trial. *Neurology* 1996;46:368–372.
59. Silberberg DH: Corticosteroids and optic neuritis. *N Eng J Med* 1993;329:1808–1810.
60. Trobe JD: High-dose corticosteroid regimen retards development of multiple sclerosis in Optic Neuritis Treatment Trial. *Arch Ophthalmol* 1994;112:35–36.
61. van Engelen BGM, Hommes OR, Pinckers A, et al: Improved vision after intravenous immunoglobulin in stable demyelinating optic neuritis. *Ann Neurol* 1992;32:834.
62. Wray SH: Optic neuritis: guidelines. *Curr Opinion Neurol* 1995;8:72–76.
63. Bracken MB, Collins WF, Freeman DF, et al: Efficacy of methylprednisolone in acute spinal cord injury. *JAMA* 1984;251:45–52.
64. Bracken MB, Shepard MJ, Hellenbrand KG, et al: Methylprednisolone and neurological function 1 year after spinal cord injury: results of the National Acute Spinal Cord Injury Study. *J Neurosurg* 1985;63:713.
65. Bracken MB, Shepard MJ, Hellenbrand KG, et al: A randomized controlled trial of methylprednisolone or naloxone in the treatment of acute spinal cord injury: results of the Second National Acute Spinal Cord Injury Study. *N Eng J Med* 1990;322:1405–1411.
66. Bracken MB, Holford TR: Effects of timing of methylprednisolone or naloxone administration on recovery of segmental and long-tract neurologic function in NASCIS 2. *J Neurosurg* 1993;79:500–507.
67. Brodsky MC, Wald KJ, Chen S, et al: Protracted posttraumatic optic disc swelling. *Ophthalmology* 1995;192:1628–1631.
68. Cook MW, Levin LA, Joseph MP, et al: Traumatic optic neuropathy: a meta-analysis. *Arch Otolaryngol Head Neck Surg* 1996;122:389–392.
69. Joseph MP, Lessell S, Rizzo J, et al: Extracranial optic nerve decompression for traumatic optic neuropathy. *Arch Ophthalmol* 1996;108:1091–1093.
70. Steinsapir KD, Goldberg RA: Traumatic optic neuropathy. *Surv Ophthalmol* 1994;38:487–518.
71. Volpe N, Lessell S, Kline L: Traumatic optic neuropathy: diagnosis and management. *Int Ophthalmol Clin* 1991;31:142–156.
72. Levin LA, Beck RW, Joseph MP, et al: The treatment of traumatic optic neuropathy: the International Optic Nerve Trauma Study. *Ophthalmology* 1999;106(7):1268–1277.
73. Arnold AC, Hepler RS, Lieber M, et al: Hyperbaric oxygen therapy for nonarteritic anterior ischemic optic neuropathy. *Am J Ophthalmol* 1996;122:535–541.

74. Beck RW, Hayreh SS, Podhajsky PA, et al: Aspirin therapy in nonarteritic anterior ischemic optic neuropathy. *Am J Ophthalmol* 1997;123:212–217.
75. Botelho PJ, Johnson LN, Arnold AC: The effect of aspirin on the visual outcome of nonarteritic anterior ischemic optic neuropathy. *Am J Ophthalmol* 1996;121:450–451.
76. Gordon RN, Burde RM, Slamovits TL: Asymptomatic optic disc edema. *J Neuro-Ophthalmol* 1997;17:29–32.
77. Haas A, Walz M, Jesenik F, et al: Application of HELP in nonarteritic anterior ischemic optic neuropathy: a prospective, randomized clinical trial. *Graefes Arch Clin Exp Ophthalmol* 1997;235:14–19.
78. Hattenhauer MG, Leavitt JA, Hodge DO, et al: Incidence of nonarteritic anterior ischemic optic neuropathy. *Am J Ophthalmol* 1997;123:103–107.
79. Hayreh SS, Podhajsky PA, Raman R, et al: Giant cell arteritis: validity and reliability of various diagnostic criteria. *Am J Ophthalmol* 1997;123:285–296.
80. Ischemic Optic Neuropathy Decompression Trial Research Group: Characteristics of patients with nonarteritic anterior ischemic optic neuropathy eligible for the ischemic optic neuropathy decompression trial. *Arch Ophthalmol* 1996;114:1366–1374.
81. Jacobson DM, Vierkant RA, Belongia EA: Nonarteritic anterior ischemic optic neuropathy: case-control study of potential risk factors. *Arch Ophthalmol* 1997;115:1403–1407.
82. Johnson LN, Gould TJ, Krohel GB: Effect of levodopa and carbidopa on recovery of visual function in patients with nonarteritic anterior ischemic optic neuropathy of longer than six months' duration. *Am J Ophthalmol* 1996;121:77–83.
83. Kupersmith MJ, Frohamn L, Sanderson M, et al: Aspirin reduces the incidence of second eye NAION: a retrospective study. *J Neuro-Ophthalmol* 1997;17:250–253.
84. WuDunn D, Zimmerman K, Sadun AA, et al: Comparison of visual function in fellow eyes after bilateral nonarteritic anterior ischemic optic neuropathy. *Ophthalmology* 1997;104:104–111.

Related Academy Materials

Academy Statements

Automated Perimetry. Ophthalmic Procedures Assessment. 1995.

Basic and Clinical Science Course

Neuro-Ophthalmology. Section 5. Updated annually.

Focal Points: Clinical Modules for Ophthalmologists

Arnold AC: *Differential Diagnosis of Optic Disc Edema*. Vol XVII, Module 2. 1999.

Brazis, PW, Lee, AG. *Neuro-Ophthalmic Problems Caused by Medications*. Vol XVI, Module 11. 1998.

Chung, SM: *Update on Nonarteritic Anterior Ischemic Optic Neuropathy: The Ischemic Neuropathy Decompression Trial*. Vol XVI, Module 6. 1998.

Ellis, BD, Hogg, JP. *Neuroimaging for the General Ophthalmologist*. Vol XVI, Module 8. 1998.

Newman, SA. *Automated Perimetry in Neuro-Ophthalmology*. Vol. XIII, Module 6. 1995.

Siatkowski, RM. *Third, Fourth, and Sixth Nerve Palsies*. Vol XIV, Module 8. 1996.

Tang, RA, Pardo, G. *Ocular and Periocular Pain*. Vol XIV, Module 2. 1996.

Trobe JD: *Neuro-Ophthalmic Diagnoses You Don't Want to Miss*. Vol XVII, Module 9. 1999.

Monographs

Berkow JW, Flower RW, Orth DH, et al: *Fluorescein and Indocyanine Green Angiography: Technique and Interpretation*. Ophthalmology Monograph 5. 1997.

Kline LB, ed: *Optic Nerve Disorders*. Ophthalmology Monograph 10. 1996.

Walsh TJ, ed: *Visual Fields: Examination and Interpretation*. Ophthalmology Monograph 3. 1996.

Wirtschafter JD, Berman EL, McDonald CS: *Magnetic Resonance Imaging and Computed Tomography: Clinical Neuro-Orbital Anatomy*. Ophthalmology Monograph 6. 1992.

Multimedia

AAO/NANOS *Clinical Neuro-Ophthalmology Image Collection for Ophthalmic Practitioners*. 1998.

ProVision Interactive: Clinical Case Studies. Volume 1, Cornea and Neuro-Ophthalmology. 1996.

Savino PJ, Feldon SE, Katz B, et al: *Neuro-Ophthalmology*. LEO Clinical Update Course on CD-ROM. 1997.

Self-Assessment

Skuta GL, ed: *ProVision: Preferred Responses in Ophthalmology*. Series 2. 1996.
Lane SS, Skuta GL, eds: *ProVision: Preferred Responses in Ophthalmology*.
Series 3. 1999.