Evidence of Early Change in Iris Color With Latanoprost Use

Latanoprost, a 17-phenyl–substituted analog of PGF$_2$$_\alpha$, has been shown to effectively lower intraocular pressure in clinical trials and darken the irides in both subhuman primates and humans. The reported time of onset of the change in iris color has been noted to be as early as 3 months. To our knowledge, this case represents the earliest reported change in iris color following the initiation of latanoprost use.

Report of a Case. A 78-year-old white woman was first seen in 1986 complaining of worsening vision, which was found to be secondary to nuclear sclerosis involving her right eye. She underwent an uncomplicated extracapsular cataract extraction with intraocular lens implantation in December 1988. Prior to surgery, she had intraocular pressure in the midteens and small symmetric cups with healthy neuroretinal rims. In 1992, she had elevated intraocular pressure in the right eye in the high 20s to low 30s. On visual field testing, she demonstrated a nasal step. The patient was then given timolol maleate twice daily in the right eye. Her intraocular pressure was maintained in the high teens to low 20s using this treatment regimen until she was seen in 1993 with evidence of progression of her visual field defect. In 1994, the medical therapy was changed to 1% pilocarpine hydrochloride 4 times daily. During a 3-year period, the optic nerve of her right eye progressed with evidence of vertical elongation and a superior rim defect. In 1996, after a course of dorzolamide hydrochloride was given in the right eye 3 times daily with minimum improvement, the patient was then given latanoprost in the right eye only for a 4-week period. The iris color in the right eye was the same as the left eye at that time. During the 4-week period, the patient’s iris color changed from blue-green to brown-green. Use of the medication was subsequently discontinued (Figure).

Comment. Alm et al$^1$ summarized the results of 198 patients who previously participated in the original phase 3 clinical trials that assessed the safety and efficacy of latanoprost. Photographs of the iris were not taken prior to 2 months after the initiation of treatment. Darkening of the iris occurred in 14 patients (7%) at 6 months and in 24 patients (12%) after 1 year of treatment. The authors noted that nevi or freckles did not increase in size and the likelihood of change was greatest in those patients who had heterogeneous pigmentation at baseline. The adverse effect is likely related to an increase in melanin production in the melanocytes of the iris stroma.

In the case presented herein, the patient was unilaterally treated, thus the slightest change in iris color could be detected early. At baseline, the patient had an iris color with mixed pigmentation, placing her at high risk for the development of this adverse effect. This report differs from previous reports in that the onset of change occurred after 4 weeks of treatment. Previous reports$^2$ in subhuman primates noted the change after at least 6 weeks of treatment. We noted no change in the lashes, which may be related to the short exposure to the drug.$^3$

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Dr Higginbotham was an investigator in the phase 3 clinical trial and is currently an investigator in the combined latanoprost-timolol study, which is sponsored by Pharmacia-Upjohn, Kalamazoo, Mich. Her expenses for

Magnified view of the affected right eye (left) and unaffected left eye (right).
travel to various meetings have also been reimbursed by Pharmacia-Upjohn.

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Bull’s-eye Maculopathy Associated With Chronic Macular Hole

Bull’s-eye maculopathy has been associated with various macular diseases, most notably chloroquine and hydroxychloroquine maculopathy, cone dystrophy, and Stargardt disease (Table).1-4 To our knowledge, bull’s-eye maculopathy associated with chronic macular holes has not been previously reported.

Report of Cases. Case 1. A 71-year-old woman developed progressive visual loss in her left eye in 1990. Examination of the left eye disclosed a macular hole and a visual acuity of 20/200. Seven years later, best-corrected visual acuity was 20/200 OS (Figure 1, left). Fundus photography revealed a bull’s-eye maculopathy, and fluorescein angiography showed a retinal pigment epithelial window defect surrounding a central area of normal fluorescence (Figure 1, right).

Case 2. A 60-year-old man noted central distortion of vision in his left eye after he covered his right eye in 1978. Examination of the left eye disclosed a stage 2 macular hole (Figure 2, left) and a visual acuity of 20/50. Twenty years later, best-corrected visual acuity was 20/200 OS. Fundus photography revealed a characteristic bull’s-eye maculopathy (Figure 2, right).

Comment. The term bull’s-eye maculopathy refers to the ophthalmoscopic appearance of a central area of retinal pigment epithelial depigmentation surrounded by relatively normal retinal pigment epithelium giving a “bull’s-eye” appearance to the macula. This appearance is shared by a relatively large group of unrelated conditions.1 The 2 patients described herein demonstrate that chronic macular holes should be included in the differential diagnosis of bull’s-eye maculopathy. Selective depigmentation of the retinal pigment epithelium may occur under the cuff of subretinal fluid that surrounds a chronic macular hole. The retinal pigment epithelial pigmentation underlying the macular hole is usually preserved and corresponds to the center of the bull’s-eye pattern.

Several historical and clinical features aid in the specific diagnosis of a patient with bull’s-eye maculopathy. Certainly, a history of chloroquine or hydroxychloroquine use would lead the clinician to suspect toxicity from systemic medications. Patients with cone dystrophy or Stargardt disease generally have symptoms of visual loss within the first 2 decades of life and may report a family history of ocular disease.2 In contrast, patients with idiopathic macular holes generally have normal vision until the sixth through eighth decades of life and have no family history of macular disease. The bull’s-eye maculopathy associated with chronic macular holes generally has very sharp borders between the depigmented macular area and the surrounding normal retinal pigment epithelium.

Differential Diagnosis of Bull’s-eye Maculopathy*

- Age-related macular degeneration
- Bardet-Biedl syndrome
- Benign concentric annular macular dystrophy
- Chloroquine and hydroxychloroquine maculopathy
- Clofazimine retinopathy
- Cone dystrophy
- Cone-rod dystrophy
- Fenestrated sheen macular dystrophy
- Hallervorden-Spatz syndrome
- Idiopathic central serous choriotretonopathy
- Leber congenital amaurosis
- Lipofuscinosis
- Sorsby central areolar choroidal dystrophy
- Stargardt disease

* Differential diagnosis of bull’s-eye maculopathy listed in alphabetical order.1

Figure 1. Case 1. Left, Macular hole in the left eye associated with bull’s-eye maculopathy. Right, Fluorescein angiogram demonstrates retinal pigment epithelial window defect surrounding a circular area of intact retinal pigment epithelium in the central macula.
Acute Macular Edema Associated With an Infected Scleral Buckle

Exposure or infection of a scleral buckle is an unusual complication of retinal detachment surgery. It has been reported in 0.5% to 18.0% of all procedures. Patients may be seen with ocular irritation, pain, discharge, redness, and sometimes visual loss. Reported causes of visual loss include uveitis with vitreous clouding, recurrent retinal detachment secondary to proliferative vitreoretinopathy, and macular distortion. \(^1\)\(^4\) Case report describes angiographically documented diffuse macular edema associated with acute visual loss in a patient with an infected and extruded scleral buckle.

Report of a Case. A 77-year-old white man was referred to our clinic with a 2-week history of new-onset visual blurring in the left eye. The patient had an ocular history notable for severe myopia and retinal detachments in both eyes. The patient’s medical history was noteworthy only for controlled hypertension. He underwent scleral buckling procedures with silicone explants in the late 1960s. He had cataract extractions in 1984 (left eye) and 1991 (right eye), resulting in bilateral aphakia. In 1993, the patient first was seen by his ophthalmologist with redness, discharge, and ocular irritation in the left eye. At that time, he had an exposed area of conjunctiva superiorly over his scleral buckle. The buckle was still thought to be well positioned, and the patient was treated using topical ciprofloxacin. He was seen periodically and was thought to be doing well with vision of 20/25 OS with conservative management. In August 1996, the patient had acute painless visual loss to 20/60 OS. Examination revealed an exposed scleral buckle superiorly with purulent discharge (Figure 1). Funduscopic examination revealed diffuse macular and retinal edema. There was no intraocular inflammation. A fluorescein angiogram was obtained, revealing diffuse macular hyperfluorescence consistent with the macular edema noted clinically (Figure 2). There was no evidence of vasculitis. The patient was given oral cefazolin, 250 mg 4 times daily, for 4 days and topical ciprofloxacin drops 4 times daily and subsequently underwent surgical removal of the scleral buckle through the superior conjunctival opening. An encircling band and tire were removed. Cultures of these elements were negative for organisms. Marked scleral thinning was noted beneath the scleral buckle site at the time of surgery (Figure 3). The conjunctiva was closed over this area. Subconjunctival vancomycin, 50 mg, was injected at the end of surgery. The patient was given polymixin-
trimethoprim drops 4 times daily and continued to use oral cefazolin for a total of 7 days. Two weeks after surgery, the vision had improved to 20/25 OS. Funduscopic examination revealed no appreciable residual macular thickening. Further follow-up at 10 months revealed no changes, with vision remaining at 20/25 OS.

Comment. This case demonstrates diffuse macular edema associated with an infected scleral buckle resulting in acute visual loss. Prompt removal of the infected scleral buckle may result in rapid visual recovery, as noted in our patient. The macular edema is likely the result of the infection and associated scleritis. This inflammatory process can extend from the sclera and result in several ocular complications, including uveitis. Although no intraocular inflammation was seen during our examination, it is also possible that prior inflammation existed and led to the development of macular edema. In addition to macular edema, long-standing uveitis may also cause cataracts and glaucoma that can also result in visual loss.

Our patient’s infection occurred nearly 30 years after the procedure. Most infections occur much earlier, with a mean of 2 months in one series and 8 months after initial surgery in another series. Our patient had a dramatic return of visual acuity with normalization of the fluorescein angiogram. Visual acuity results after removal of an infected scleral buckle are rarely reported in the literature. Retinal detachment is the most common cause of poor vision after removal of scleral buckles. Late detachment rates range from 45% to 39%, with the highest percentage occurring when the buckle has been in place for less than 6 months. Most detachments occur within the first 6 months after removal. In our patient, the retina has remained attached at 10 months after surgery. Scleral thinning, as seen in our patient, has been reported after infection and removal of scleral buckles as well. One series showed that this occurred in nearly 30% of the cases. Macular edema may be difficult to detect in these patients with infected or extruded scleral buckles because discharge may affect corneal clarity and the patient may be photosensitive. The use of fluorescein angiography may be a useful adjunct to making the diagnosis. Recognition of macular edema may encourage earlier removal of the buckle so as to avoid complications of chronic macular edema.

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Supported in part by an unrestricted grant from Research to Prevent Blindness Inc, New York, NY, and by core grant EY01931 from the National Institutes of Health, Bethesda, Md.
Hemolytic Uremic Syndrome Associated With Purtscher-like Retinopathy

Purtscher reported the findings of cotton-wool spots, hemorrhages, and edema in the posterior fundus of 2 patients who experienced severe head trauma. Later, angiopathica retinai traumatica, or Purtscher retinopathy, was described following long-bone fractures, rapid deceleration injuries, and compressive injuries to the trunk. Subsequently, Purtscher-like retinopathy was observed in atraumatic cases such as pancreatitis, collagen vascular disease, amniotic fluid embolism, retrolubar anesthesia, chronic renal failure, and thrombotic thrombocytopenia purpura. We report a case of Purtscher-like retinopathy in a patient with hemolytic uremic syndrome (HUS).

Report of a Case. A 31-month-old boy was admitted to a hospital with a history of pallor, lethargy, and oliguria preceded by gastroenteritis. After experiencing 2 brief tonic-clonic seizures, he was transferred to the pediatric intensive care unit where examination revealed a leptatic child with scattered petechiae and periorbital and peripheral edema. The child was anuric. Computed tomography of his brain was normal on admission. Laboratory findings revealed microcytic hemolytic anemia (hemoglobin, 68 g/L; mean corpuscular volume, 72.5 mm³), thrombocytopenia (platelets, 33 × 10⁹/L), and acute renal failure (creatinine, 407 µmol/L [4.6 mg/dL]). Stool culture yielded Escherichia coli (0157:H7). Diagnosed as having HUS, the patient underwent plasmapheresis and hemodialysis. Three days after admission to the pediatric intensive care unit, a repeated computed tomographic scan revealed bilateral infarctions of the basal ganglia (Figure 1). The patient had not experienced any trauma, cardiopulmonary resuscitation, assisted ventilation, or further seizures. On the fourth day of his intensive care admission, an ophthalmic evaluation disclosed sluggishly reacting pupils without relative afferent pupillary defect and moderate conjunctival chemosis. Funduscopic examination revealed ischemic retinal whitening in both posterior poles, most prominently in the peripapillary area. Retinal arteriolar attenuation and scattered intraretinal hemorrhages were also present bilaterally. Additionally, a preretinal hemorrhage and peripapillary nerve fiber layer hemorrhage were noted in the left eye (Figure 2).

The patient experienced cardiovascular and neurologic decline despite intensive management and...
COMMENT. Hemolytic uremic syndrome is the most common cause of acute renal failure in young children and is marked by a prodrome of gastrointestinalitis followed in 5 to 10 days by pallor, irritability, weakness, lethargy, and oliguria. Laboratory findings include microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure of severity varying from mild insufficiency to renal shutdown. Central nervous system manifestations occur in a majority of patients and portend a poorer prognosis. Stool culture frequently yields enterohemorrhagic E coli (0157:H7).3

The gastroenteritis, hematologic abnormalities, and renal failure in HUS result from thrombotic microangiopathy. Escherichiacoli (0157:H7) initiates a pathogenic cascade by elaborating verocytotoxin. This Shigalike exotoxin targets glycolipid GBk, expressed on the endothelial surface of intestinal, renal, and central nervous system arterioles of predisposed individuals. Once internalized by receptor-mediated endocytosis, a toxin subunit inhibits protein synthesis and damages the endothelium. Platelet aggregation and ensuing thrombotic microangiopathy result in target organ ischemia. Erythrocytes suffer mechanical damage as they transit altered vasculature, resulting in hemolytic anemia, while intra-luminal platelet damage and aggregation result in thrombocytopenia.

Purtscher retinopathy and Purtscher-like retinopathy are characterized by multiple patches of retinal whitening, hemorrhages, and arteriolar attenuation in the posterior pole. Siegler et al4 first reported retinal involvement in HUS with features compatible with sequelae of the acute manifestation of retinal infarction seen in our case. The basal ganglia infarcts in our patient and that of Siegler et al are a similarity suggesting Purtscher-like retinopathy in HUS could indicate concurrent ischemia elsewhere in the central nervous system.

The pathogenesis of Purtscher retinopathy remains controversial. Hypotheses have implicated reflux hydrostatic injury, vasospasm, and microembolism of fat, air, fibrin, amniotic fluid, or granulocyte aggregates in retinal arterioles.2 The pathogenesis of HUS suggests the Purtscher-like changes in our patient are a result of thrombotic retinal microangiopathy caused by exotoxin-induced endothelial injury.

Purtscher-like retinopathy in HUS is reported infrequently and its diagnosis in the acute phase is overshadowed by the grave systemic complications of HUS. Awareness of this entity may help explain visual loss in children who recover from acute HUS.

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Supported by an unrestricted fund from the Research to Prevent Blindness Inc, New York, NY.

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Delayed Branch Retinal Artery Occlusion Following Presumed Blunt Common Carotid Dissection

Ischemic events to the eye can occur after cervical carotid dissections.1 Ocular vaso-occlusions usually occur within 1 month after the onset of dissection. We report a case of traumatic common carotid occlusion, presumably caused by dissection, which led to an ischemic event to the right eye 4 months after trauma.

Report of a Case. A 19-year-old woman complained of acute painless visual loss in her right eye 7 days prior to our examination. Four months earlier, she was involved in a motor vehicle crash as a restrained passenger. She sustained sternal and rib fractures and bilateral pneumothoraces, requiring 2 chest tubes. She did not have any neurological or ocular symptoms and was discharged 1 week after the trauma. Her medical history was notable for sickle cell trait and cigarette use of half a pack per day. She had discontinued her oral contraceptives 1 month prior to the motor vehicle crash.

Visual acuity was 20/40 OD and 20/30 OS, and there was a right relative afferent pupillary defect. Goldmann visual fields showed a supranasal quadrantic defect in the right eye and were full in the left eye. Results of a fundus examination showed a branch retinal artery occlusion of the inferotemporal arcade in the right eye with a partial cherry-red spot (Figure 1). She was complaining of intermittent numbness in her right arm and her radial pulse was decreased on the right side, with asymmetric blood pressures (right arm, 72/51 mm Hg; left arm, 110/61 mm Hg).

Carotid ultrasound examinations showed an occlusive thrombus in the right common carotid artery extending into the internal and external arteries. Angiography confirmed total occlusion of the innominate artery with no demonstrable flow in the right carotid system, even in its supracoaroid portion (Figure 2). The eye was most likely supplied by the external carotid artery by retrograde flow from distal branches of the internal maxillary artery and thyrocervical trunks. Warfarin was used as long-term anticoagulation therapy with no further sequelae.

Comment. Traumatic dissections can result from multiple nonpenetrating injuries such as motor vehicle crashes, chiropractic manipulation, falls, and hanging.1,2 Dissection of the carotid arteries is an important cause of cerebrovascular ischemic events in young adults,3 and embolism is the most commonly presumed mechanism.

Common carotid dissections are almost always traumatic and can re-
sult either from direct trauma or extension of a dissection of the aorta or the innominate artery.3 Our patient most likely had a traumatic innominate and common carotid dissection that led to an internal carotid thrombus and, eventually, an embolus that produced an ocular stroke, even as long as 4 months after trauma.

Of interest in our case was the lack of any cervical pain, headache, or Horner syndrome, the most common symptoms in cervical artery dissections.2,4 Acute, painless, monocular vision loss in a young adult can be caused by carotid dissection, either traumatic or spontaneous. The diagnosis of either common carotid or internal carotid dissection should be entertained when a patient is seen with an ocular stroke, even as long as 4 months after trauma.

Our patient’s ischemic event occurred 4 months after her accident. In a prospective series of 80 patients with internal carotid dissection, Bisousse et al4 reported that the majority of strokes (82%) occurred in the first 7 days, and the latest occurred 31 days after the first symptoms of dissection. In a retrospective series of 21 patients with traumatic carotid dissection, Mokri2 reported ischemic events in 15 patients (71%), 6 of whom had focal cerebral symptoms 2 months to 10 years after the trauma.

Ocular strokes have been reported after carotid dissection. Newman et al1 reported 2 cases of central retinal artery occlusion following previously undiagnosed carotid artery dissection. In 1 of the cases, the patient had been in a motor vehicle crash 1 week prior to his ocular stroke.

Autoimmune Optic Neuropathy

Optic neuritis is a syndrome of visual loss due to inflammation of the optic nerve. It is usually either id-

Figure 1. Fundus photography shows a branch retinal artery occlusion in the inferotemporal arcade of the right eye. Arrows outline the area of edema resulting from the occlusion.

Figure 2. Left, Aortic arch angiogram shows total occlusion of the right innominate artery (arrow). Right, Cerebral angiogram, anteroposterior view, after left internal carotid injection, shows intracerebral flow of right carotid system assumed by the left carotid via the anterior communicating artery and the right posterior communicating artery. The right ophthalmic artery fills from left-sided flow (arrow).
We describe 2 patients with autoimmune optic neuropathy and typical abnormalities on skin biopsy specimens. The first patient is the youngest case of this disorder reported to date and histopathologic findings of the optic nerve are available on the second patient.

Report of Cases. Case 1. An otherwise healthy 17-year-old boy noticed loss of vision in his left eye while watching television. After 2 days of worsening vision, he was found to have visual acuity of 20/20 OD and hand motion at 1 ft (30 cm) OS. His left optic disc had moderate edema; the right optic disc was normal. He was treated for 3 days with intravenous methylprednisolone sodium succinate (1 g/d) followed by a 11-day course of oral prednisone (1 mg/kg per day). His vision slowly improved to 20/50 OS. Two weeks after discontinuing the prednisone, the patient experienced a similar episode in his right eye. General medical and neurologic examination results were normal. The following laboratory studies were normal: brain magnetic resonance imaging, chest x-ray films, cerebrospinal fluid analysis, complete blood cell count, liver function tests, angiotensin-converting enzyme levels, antinuclear antibodies, antineutrophilic cytoplasmic antibodies, erythrocyte sedimentation rate, human immunodeficiency virus serology, VDRL, FTA-ABS, CH50, Lyme titers, blood cultures, and urinalysis. The patient was again treated with the same course of corticosteroids with substantial improvement in his vision; visual acuity improved during treatment to 20/50 OU. Ten days after treatment was stopped, his vision again worsened and he was referred to the Neuro-ophthalmology Unit of the Department of Ophthalmology and Visual Sciences at the University of Iowa, Iowa City.

At that time, his visual acuity was 20/80 – 1 OD and 20/50 – 1 OS with a spherical correction of −6.50 OD and −6.00 OS and there was a small relative afferent pupillary defect (0.5 log unit) in the right eye. There was moderate bilateral optic disc pallor, more in the right eye. A magnetic resonance image of the orbit and brain showed mild enhancement of the retrobulbar right optic nerve. Laboratory measurements of the previously listed tests were again normal, including a repeated cerebrospinal analysis for immunoglobulins, oligoclonal bands, and myelin basic protein. In addition, assays for anticardiolipin antibody, rheumatoid factor, lupus anticoagulant, and mitochondrial DNA screening for most common mutations found in Leber hereditary optic neuropathy were negative. Within 1 week, the patient’s visual acuity decreased to less than 20/200 OU and results of a visual field examination found markedly depressed vision bilaterally. The presence of a dense inferior altitudinal defect in the right eye and a loss of the I2e isoper in the left eye were accompanied by a 0.6–log unit relative afferent pupillary defect in the right eye. The optic disc appearance and findings of the remainder of the ophthalmologic examination were unchanged. A 4-mm punch biopsy specimen of non–sun-exposed buttock skin was obtained by the dermatology service.

The hematoxylin-eosin-stained frozen section showed a mild mononuclear perivascular infiltrate within the dermis and no leukocytoclastic response. Direct immunofluorescent staining was positive for IgM and C3 in a granular pattern in the walls of small blood vessels within the superficial papillary dermis. In addition, IgM and C3 were found at the demodermal junction in a granular to fibrillar staining pattern (Figure 1). No specific staining was seen for IgA. These results indicated the presence of immune complex deposition, and the diagnosis of autoimmune optic neuropathy was made.

The patient again received identical methylprednisolone treatment. His visual acuity began to improve on day 3 of this regimen, as did results of his kinetic perimetry examination. Ten weeks later, his visual acuity had improved to 20/25 OD and 20/30 OS. Both eyes had regained the ability to see the I2e isoper and the inferior altitudinal de-
fect in the right eye had resolved. The patient continued to take 80 mg/d of oral prednisone for 8 additional weeks and his dose was then tapered over a year. His examination findings remained stable for 2 years.

Case 2. A 25-year-old woman experienced rapidly progressive visual loss in her right eye approximately 5 months prior to referral. The visual loss was accompanied by pain with eye movement but no other symptoms. She was diagnosed as having optic neuritis and was treated with the same regimen as patient 1. She experienced recovery of vision to 20/25 OD over the following 7 weeks. She then experienced the same symptoms in the right eye 1 month later. A magnetic resonance image showed a small scarlike lesion in the thalamus. She underwent a detailed evaluation similar to that of patient 1, with normal results. The patient was again treated with an identical regimen of intravenous and oral corticosteroids and experienced improvement of visual function in her right eye.

She had a mild episode of arthritis as a child and had occasional migraine headaches. She had a brother and paternal aunt with systemic lupus erythematosus.

Following a third episode of visual loss in her right eye, the patient was referred to us. Visual acuity was 6/200 OD and 20/15 OS and there was a 1.8-log unit relative afferent pupillary defect in the right eye. Goldmann perimetry showed a large central scotoma with an enlarged blind spot in the right eye. Results of the visual field examination of the left eye were normal. Her examination was otherwise unremarkable except the right optic disc showed temporal pallor, while the left optic disc was normal. Her general medical and neurologic examination findings were otherwise normal.

A magnetic resonance image at that time showed mild enhancement of the right intraorbital optic nerve and both lacrimal glands appeared mildly enlarged (Figure 2). A laboratory evaluation, again similar to that of patient 1, was repeated and showed no abnormalities. In addition, sarcoidosis was suspected and bilateral conjunctival biopsies were performed, results of which were normal. A lacrimal gland biopsy was performed through an anterior orbitotomy with the specimen showing no signs of inflammation.

A trial of oral prednisone was then initiated with some subjective improvement after the third day of treatment. However, the patient experienced mania with psychotic features due to the prednisone, which was then discontinued. Nine days later, with her visual acuity at hand motion in the temporal visual field of the right eye, a medial orbitotony and optic nerve biopsy was performed, which showed chronic perivasculitis or optic nerve necrosis (Figure 3). No immune complex staining was performed on the optic nerve specimen.

Later, an assay for antiphospholipid antibodies showed elevated IgM (12.6 IgM phospholipid units, normal value, <11 units). An assay for IgG was normal. In addition, a 4-mm punch biopsy specimen of non–sun-exposed (buttock) skin was obtained, which showed direct immunofluorescent microscopy findings suggestive of autoimmune connective tissue disease, specifically IgM and C3 granular staining of the dermal–epidermal junction and focal granular deposits in small vessel walls. Her visual acuity remained at light perception in the right eye and 18 months later she developed progressive visual loss over a 6-day period in her left eye. Visual acuity worsened to 20/40 OS and Goldmann perimetry revealed inferonasal depression and a cecocentral scotoma.

She was pretreated with lithium carbonate to prevent mania and then given the methylprednisolone and prednisone regimen described above. Her visual acuity improved to 20/20 OS over 2 months. Results of Goldmann visual examination returned to normal during this same time. She is currently being treated with a very slow prednisone taper while taking lithium.

Comment. Autoimmune retrobulbar optic neuropathy, now more...
commonly called autoimmune optic neuropathy, was first described by Dutton et al. They described a disorder characterized by progressive visual loss and serologic evidence of an autoimmune disorder. Long-term corticosteroid or immunosuppressive therapy seemed to promote visual recovery and prevent further attacks. Affected patients had laboratory evidence of an autoimmune phenomenon but lacked the clinical manifestations of a systemic collagen vascular disease. Several groups have attempted to identify reliable laboratory markers (antinuclear antibodies, anticardiolipin antibodies, skin biopsies with immunofluorescent staining) to allow earlier diagnosis and treatment. Use of these markers is complicated by negative results when prior pulses of corticosteroids have been given.

Abnormal skin biopsy findings were the most consistent markers of autoimmune optic neuropathy according to Bielory et al. Hematoxylin-eosin staining typically showed a perivascular infiltration by lymphocytes and neutrophils, which was found in the biopsy specimens from both of our patients. Direct immunofluorescence microscopy showed IgM, IgG, IgA, or complement in immune complex deposition around dermal blood vessels and at the dermal-epidermal junction. Both patients displayed a similar IgM and C3 staining pattern. For non–sun-exposed skin, the rate of immune complex deposition around blood vessels is between 0% and 1.7%.

Autoimmune optic neuropathy should be considered whenever a patient with optic neuritis has an atypical recurring course. This usually is seen as recurrent bouts of visual loss as treatment is tapered or stopped. Our first patient was initially seen at age 17 years, and is to our knowledge the youngest reported patient in the literature with this condition. Our second case is important for 2 reasons. First, it shows the importance of long-term, slow tapering of immunotherapy. Second, this case provides the first histopathologic study of optic nerve tissue affected by autoimmune optic neuropathy. It implies autoimmune optic neuropathy is a disorder characterized by chronic perivascular nongranulomatous inflammation. These cases remind us that autoimmune optic neuropathy can be difficult to diagnose unless it is suspected and it is appropriately evaluated.

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This study was supported in part by grants from Research to Prevent Blindness Inc, New York, NY, and a Department of Veterans Affairs Merit Review.

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