Can an Eye in Phthisis Be Rehabilitated? A Case of Improved Vision With 1-Year Follow-up

Phthisis bulbi implies, in clinical terminology, a shrunken globe, usually from ceased aqueous humor formation (phthisis meaning “wasting away”). The intraocular pressure approaches 0 mm Hg. As a consequence, the cornea becomes distorted and can develop edema and scarring, and the lens develops cataracts. Both seem to occur due to the lack of nutrition by the aqueous. In addition, edema can develop in the macula and the optic nerve head and vision suffers accordingly. Finally, cyclitic membranes and proliferative vitreal retinopathy can develop, resulting in total retinal detachment and scar formation. The cause of phthisis is often uveitis, either long-term or following trauma, surgery, or end-stage, heavily treated glaucoma.

Treatment of phthisis is generally considered hopeless. Aggressive treatment of intraocular inflammation in uveitis or avoiding too much cyclodialysis or severe cyclitic membranes, a surgical approach has been reported to be of some value. In general, however, if the intraocular pressure is close to 0, the eye is collapsed, the cornea is edematous, the lens is cataractous, the ocular volume is reduced to half or one third of the normal volume, and the ocular layers are correspondingly thickened, no treatment has, to our knowledge, been effective in restoring vision.

Any proposed treatment of phthisis must be surgical, if for no other reason than to restore the clarity of the cornea. In this respect, standard corneal transplantation is ineffective, since the source of nutrition, a healthy flow of aqueous, is absent. With the advent of more advanced techniques for keratoprosthesis surgery and more long-term, postoperative stability, there may be new hope for eyes going into phthisis. Initial attempts in this direction have been made in the past, but there was no success in restoring vision. In this report, we describe a patient with a chemical burn that led to a shrunken eye, no palpable intraocular pressure, an opaque cornea (due in part to the direct effect of the alkali), and an attached retina, who regained substantial vision following keratoprosthesis surgery and was followed up for 1 year.

Report of a Case. The patient, a citizen of Ghana, had alkali thrown in his face 9 months prior to the referral. The burn was extremely severe (Figure 1). Ophthalmic examination in April 1997 showed both eyes to be totally soft and collapsed. In the right eye, the upper eyelid margin was fused to the lower part of the cornea (Figure 2). Visual acuity was light perception only, with reasonably accurate projection. B-scan ultrasonography showed that the retina and choroid were attached and the vitreous cavity contained some low reflective debris and probably posterior vitreous detachment. An A-scan ultrasonogram showed a 15.5-mm distance between the posterior surface of the cornea and the anterior surface of the retina.

We tried keratoprosthesis, preceded by a buccal mucosal graft that was carried out by Jeffrey Green, MD. The keratoprosthesis surgery was done 2 months later, using a Dohlman-Donan II device (Massachusetts Eye and Ear Infirmary, Boston). It was inserted into a 9.5-mm corneal graft from a frozen-stored donor eye in a previously described manner. After taking down the buccal mucosal graft to bare the cornea, the intraocular pressure was again evaluated by indentation and it seemed to be extremely soft by palpation. The distance from the corneal back surface to the retina was 15.5 mm.

Figure 1. The patient suffered a severe alkali burn 9 months prior to surgery. Visual acuity was light perception OD.

Figure 2. The right eye seemed collapsed and the intraocular pressure was extremely soft by palpation. The distance from the corneal back surface to the retina was 15.5 mm.
pension (to discourage tissue necrosis and melt) and an antibiotic was given 4 times daily, reduced to 2 times daily after 6 months. One month postoperatively, the anterior chamber hardly exhibited any inflammatory reaction, only a rare cell; however, 40 mg of triamcinolone was injected once through the lower eyelid.

Visual acuity was 20/100 OU 1 week after the operation and gradually rose to 20/60 OU during the ensuing 5 months (Figure 3). This required a spectacle correction of +10.00 diopters (D) due to a miscalculation in the choosing of the prosthesis. The optic disc was difficult to see due to an overhanging vitreous veil, but the macula was without edema and showed no abnormalities. The visual field showed an enlarged blind spot and a suggestion of a nasal step, most likely due to a short period of high pressure soon after the burn. One year after the keratoprosthesis surgery the situation seems stable.

Comment. The definition of ocular phthisis is vague. Severe hypotony due to overfiltration after glaucoma procedures or extensive traumatic cyclodialysis is usually not labeled as phthisis. In such situations, the aqueous formation is grossly intact and therefore provides adequate nutrition to the cornea and the lens is provided, keeping these tissues transparent. If, on the other hand, the ciliary body is destroyed and the aqueous secretion has ceased, the damage is permanent and the cornea and the lens suffer accordingly. This state is labeled by most clinicians as “phthisis.” Some ophthalmic pathologists further restrict the term phthisis to describe shrunken eyes that also show generalized disorganization of the intraocular contents. In our case, the standard clinical definition of phthisis will be used—referring to to irreversible cessation of the aqueous humor formation, near 0 mm Hg intraocular pressure, and a shrunken eye, without consideration of the status of the retina or other intraocular structures.

Our patient had the clinical appearance of a phthisical eye: no detectable intraocular pressure, the bulb collapsed to a much reduced axial length, a swollen and opaque cornea, and a ciliary body that looked totally atrophic on ophthalmic examination. No retinal detachment had occurred and there was no obvious macular edema (the optic nerve could not be well evaluated). The lack of macular edema might be attributable to a low residual, non-detectable, intraocular pressure. Palpation is a crude way of estimating the intraocular pressure but the only one available with this type of keratoprosthesis.

In general, phthisis seems to initially affect the cornea and the lens. Removal of a cataractous lens constitutes no particular clinical problem, but restoring corneal transparency is a more formidable challenge since standard transplantation is impossible. Technique and follow-up regimens for keratoprosthesis, however, have developed to a level where it seems reasonable to try it even in a phthisical situation. The follow-up time of our case is short (only 1 year), and long-term problems may still occur, as in many other keratoprosthesis cases. Still, our study does show that some vision can be restored, at least temporarily, in an eye with close to 0 mm Hg intraocular pressure and an intraocular volume reduced to less than half that of a normal eye.

Retinal detachment is a common end point in phthisical eyes, especially when chronic intraocular inflammation is prominent. In such cases, a keratoprosthesis has to be combined with methods to splint or reattach the retina—obviously a formidable task. Filling the vitreous cavity with a clear substance that exerts a mild, mechanical pressure outward may be a future possibility. The synthesis of a clear hydrogel, glyceryl methacrylate, has been interesting in this regard. This hydrogel was tested for lack of toxic reaction in the vitreous and in the cornea. It was also found that a dried pellet of this material placed in the eye of an animal could swell up, replace the vitreous, and exert a desired intraocular pressure. Our clinical experience with this hydrogel has so far been disappointing, however, because the hydrogel seems to be easily impregnated by proteins that render it opaque. Silicone oil can be used (D. R. C. Caldwell, MD, oral communication, November, 1994), which is optically clear, but does not exert a swelling pressure and is difficult to handle. Prevention or treatment of retinal detachment in phthisical eyes will clearly be the next frontier.

Our patient is, to our knowledge, the first report of a phthisical eye with severely opaque cornea who had substantial vision restored—at least during this short follow-up period.

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Figure 3. Appearance after buccal mucosal graft, followed up 2 months later by keratoprosthesis and vitrectomy. Visual acuity was 20/60 after a 1-year follow-up.
Good Visual Outcome Following Laser Therapy for Proliferative Radiation Retinopathy

Radiation retinopathy is a potentially severe complication of radiation therapy for orbital disease. Findings range from intraretinal hemorrhages, cotton-wool spots, and macular edema (nonproliferative radiation retinopathy) to extensive retinal capillary ischemia leading to neovascularization and vitreous hemorrhage (proliferative radiation retinopathy). Kinyoun et al.1 reported that eyes with proliferative radiation retinopathy had poor visual prognosis despite treatment with panretinal photocoagulation. We report a case of a man with proliferative radiation retinopathy treated with laser therapy who retained excellent vision for 5 years.

Report of a Case. A 39-year-old man with a history of pineoblastoma had decreased vision in his left eye. The patient received 45 Gy of external beam irradiation in November 1992 (dose fraction, 1.8 Gy; 25 treatments in 36 days). Seventeen months later an examination revealed visual acuities of 20/25 OD and 20/40 OS, nonproliferative radiation retinopathy in the right eye, and neovascularization with vitreous hemorrhage and clinically significant macular edema confirmed by contact lens examination in the left eye. Fluorescein angiogram of the left eye demonstrated severe capillary nonperfusion and diffuse cystoid macular edema (Figure 1, A and B). The patient received grid laser treatment and panretinal photocoagulation in the left eye (Figure 1, C). He required a pars plana vitrectomy for nonclearing vitreous hemorrhage. Visual acuity improved to 20/25 OU with resolution of the macular edema and vitreous hemorrhage. The patient has had no recurrence of proliferative radiation retinopathy or macular edema in the left eye (Figure 2), and his visual acuity after cataract extraction 1 year later has remained stable at 20/20 OU for 3 years. A fluorescein angiogram performed 47 months after development of proliferative radiation retinopathy demonstrated intact foveal capillaries and no retinovascular leakage in the left eye. Early proliferative radiation retinopathy was present in the right eye.

Comment. Head and neck irradiation can cause ophthalmic complications including cataracts, optic neuropathy, and radiation retinopathy.1 Radiation retinopathy has been reported in radiation doses as low as 11 Gy, but is infrequent below the dose of 45 Gy.2,3 Our patient received 45 Gy of irradiation. While visual prognosis in patients receiving laser therapy for radiation-induced macular edema is favorable, poor visual outcome is reported for patients treated for proliferative radiation retinopathy, presumably due to severe capillary nonperfusion and ischemia of the macula.4

Kinyoun et al.1 documented that panretinal photocoagulation halted new vessel formation in eyes with proliferative radiation retinopathy;

Figure 1. A, Venous phase fluorescein angiogram of the left eye demonstrating extensive capillary nonperfusion. B, Late-phase angiogram of same eye shows diffuse macular edema. C, Color fundus photograph of the same eye after grid and panretinal photocoagulation laser treatment showing vitreous hemorrhage.

Figure 2. A, Venous phase fluorescein angiogram of the left eye 5 years after first visit with proliferative radiation retinopathy. B, Perifoveal capillaries are patent and macular edema is not evident in the late phase of the angiogram. C, Color fundus photograph of the left eye at 5-year follow-up showing grid and panretinal photocoagulation laser and without evidence of active proliferative radiation retinopathy or macular edema.
however, 86% of patients developed visual acuities less than 20/200 OU and no eyes had visual acuity better than 20/50 OU after a mean follow-up time of 75 months. Ninety-three percent of their patients with proliferative radiation retinopathy also had optic neuropathy, 86% had macular edema, and 100% had macular ischemia. Our patient, who had no signs of optic neuropathy, had regression of neovascularization, resolution of macular edema and capillary nonperfusion, and restoration of a visual acuity of 20/20 OU after laser therapy. We agree that patients receiving head and neck irradiation need to be screened for radiation retinopathy. However, it is possible that proliferative radiation retinopathy itself does not confer a poor visual prognosis if other irreversible forms of vision loss such as optic neuropathy and macular ischemia are not present. Indeed, early detection of proliferative radiation retinopathy and treatment with laser may improve visual acuity.

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A Confocal Microscopic Study of Advancing Wavelike Epitheliopathy

Advancing wavelike epitheliopathy was first described by D’Aversa et al1 In their study, 11 eyes of 7 patients were seen with well-demarcated, centripetally advancing waves of irregular epithelium and subepithelial haze, originating from the upper aspect of the limbus. Identified risk factors included the use of topical antiglaucoma medications or contact lens care solutions, contact lens wear, past ocular surgery, acne rosacea, and atopic dermatitis. The condition was reported to respond to 1% silver nitrate applied to the superior aspect of the limbus. To our knowledge, no other cases have been documented. We describe a patient with advancing wavelike epitheliopathy and the confocal microscopic findings.

Report of a Case. A 49-year-old white woman was referred for evaluation of corneal abnormalities. Her chief complaint was ocular discomfort and photophobia in both eyes for 1 month, and she had a history of daily soft contact lens wear in both eyes for 1 year. Her medical history was unremarkable. Best-corrected visual acuity was 20/20 OU. Slitlamp examination showed the presence of coarse irregular epithelium plaques originating from the superior aspect of the limbus in both eyes into the superior aspect of the cornea (Figure 1). At the subepithelial level, a diffuse haze was noted. The remainder of the ophthalmic examination, including examination of the conjunctiva, showed no abnormalities. The patient was examined using a prototype, white-light, tandem scanning, confocal microscope (LSU Eye Center, New Orleans, La) using a ×24/0.60 contact objective (Tandem Scanning Corp, Reston, Va). Ophthalmic examination was performed with liquefied hydroxypropyl methylcellulose as a coupling gel. Confocal microscopy showed the presence of atypical, elongated, and centripetally oriented cells with easily recognizable nuclei at the level of the abnormal epithelium in both eyes (Figure 2, left). At the subepithelial level, confluent hyperreflective images were detected (Figure 2, right). The areas adjacent to the plaques of irregular epithelium showed no abnormalities. The patient was treated with 1% silver nitrate applied to the superior aspect of the limbus. Subsequently, the symptoms subsided rapidly and complete resolution was noted clinically 1 month after the treatment. Few abnormal epithelial...
cells could still be demonstrated at the limbus in both eyes by confocal microscopy; however, the patient remained asymptomatic during the following 6 months and further treatment was not necessary.

Comment. The clinical presentation of our patient is similar to that described by D’Aversa et al and could be easily differentiated from superior limbic keratoconjunctivitis and corneal pannus. Rapid response to 1% silver nitrate made the possibility of corneal epithelial dysplasia or carcinoma very unlikely.

D’Aversa et al postulated that abnormal limbal cells proliferate and migrate to the cornea. They disclosed parakeratotic alterations and underlying mononuclear cell infiltration in the limbal conjunctiva; however, they did not demonstrate cytological alterations in the corneal epithelium. Using the confocal microscope, we could identify the presence of highly atypical cells at the level of the epithelium. The subepithelial hyperreflective layer probably corresponds to the hazy structure seen on slitlamp examination and is compatible with fibrous tissue. Further studies are necessary to investigate its exact composition.

Our case supports the existence of the clinical entity described by D’Aversa et al and endorses that treatment with silver nitrate may be clinically effective. Confocal microscopic findings of remaining abnormal epithelial cells after the treatment may account for the need of repeated treatments in some patients, as described by D’Aversa et al. Confocal microscopy enables noninvasive in vivo examination of the cornea and may allow diagnosis of advancing wavelike epitheliopathy by demonstrating the atypical elongated cells.

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Traumatic Enucleation From a High-Pressure Water Jet

This article describes an unusual case of enucleation from a high-pressure water jet. Treatment is described and an etiologic hypothesis is presented.

Report of a Case. A 37-year-old man was seen in the emergency department with a traumatic injury to his right orbit. The patient, not wearing protective eyewear, was tightening a high-pressure industrial pipe that began to leak. Owing to a sudden malfunction, a high-pressure water jet was directed into his right orbit. The right globe was found approximately 45 m (50 yd) from the scene of the injury by emergency personnel. Ophthalmic examination of the right orbit showed relatively clean, soft tissue with conjunctival chemosis and an anophthalmic socket. Gross and histopathologic examination findings of the eye revealed an intact globe with no readily identifiable sites of scleral rupture and 15 mm of optic nerve present (Figure 1). The extraocular muscles were avulsed through their insertions on the globe. A computed tomographic scan of the orbits confirmed the anophthalmic socket. The extraocular muscles were in their normal anatomical positions and intact (Figure 2). Ophthalmic examination of the left eye, including confrontation visual fields, showed no abnormalities.

The patient underwent right socket and orbital debridement and a moderate amount of ecchymotic nonviable tissue was removed. The...
orbit was explored extensively and the recti muscles were isolated. The muscle ends were pulled anteriorly and sutured to a 20-mm, scleral-wrapped, hydroxyapatite implant through scleral fenestrations.

Six months after the initial injury and surgery, the patient showed excellent cosmetic results, with a well-healed right orbit and excellent socket motility. Nuclear medicine imaging revealed a well-vascularized, hydroxyapatite implant.

Comment. Systemic high-pressure injection injuries have been documented in the literature since the 1930s. Most of these have occurred in industrial settings and have involved a variety of high-pressure greases, air, and water machines that cause systemic trauma. These pipes contain water at pressures of between 6000 and 8000 psi, whereas pressures of only 100 psi are necessary to penetrate skin. A break in the closed system can propel water at speeds of up to 600 ft/s—close to the muzzle velocities of some rifles. Similar injuries to the eyes and adnexa are much less common. Holds et al. described 8 patients with hydraulic orbital injection injuries. No patient lost vision permanently as a sequelae of the initial trauma.

To our knowledge, this is the first reported case of a hydraulic orbital injection injury resulting in enucleation. The proposed mechanism of injury in this patient involved a high-pressure jet of water transecting the conjunctiva, traveling to the retrobulbar space, and then building up enough posterior pressure to rupture all of the connective tissue support, the 4 recti near their insertions, and the optic nerve. Orbital trauma associated with anterior pressure alone usually results in globe rupture. The pathologic condition in our patient is similar to that reported in psychiatric patients, where a finger or instrument is placed behind the globe and force is applied outward, resulting in enucleation. This is not a common pathophysiological mechanism of injury, but considering the velocities attainable with pressurized fluids, one that should not be surprising.

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A Hereditary Chiasmal Optic Neuropathy

Rarely is a nonneoplastic disorder responsible for a bitemporal visual field defect, and in those cases, mechanical or radiation injury, inflammation, infection, demyelination, intoxication, infarction, or hypoplasia of the optic chiasm are the mechanisms. We have encountered a family in which 3 siblings had a unique, presumably hereditary neuropathy manifested by a chiasmatic visual field defect.

Report of Cases. The 3 white patients whose histories are presented below represent all of the children of a nonconsanguineous marriage between a healthy mother of Puerto Rican descent and a healthy father of Irish descent.

Case 1. A healthy 28-year-old woman was advised to have an ophthalmic examination because an abnormality in her sister’s optic nerves had been discovered. The patient’s only eye problem had been fully correctable myopia and astigmatism. Her neurological and endocrine histories showed no abnormalities and an ophthalmologist found that her visual acuity was 20/20 OU, but she had pallor of her optic nerves and a bitemporal visual field defect. A computed tomographic scan of the brain showed no abnormalities. She remained asymptomatic and was referred for evaluation at age 35 years.

Her best-corrected visual acuity was 20/15 OU. She missed several of the Ishihara test plates with each eye, but she made no errors when tested with the Farnsworth D-15 panel. There was a bilateral supertemporal quadrantanopsia (Figure 1). Her corneal nerves seemed unusually prominent and there were white dots scattered in the cortex of both lenses. Both optic discs were atrophic but of normal size. Findings from the remainder of her examination showed no abnor-
malities. Magnetic resonance imaging scan of the brain and orbits with gadolinium injection and full-field and foveal electroretinograms showed no abnormalities. Blood test results for 4 of the mitochondrial mutations known to be associated with Leber hereditary optic neuropathy (codons 11778, 14484, 15257, and 3468) were normal. Her condition remains unchanged 5 years later.

Case 2. The older brother of patient 1 was found to have abnormal optic nerves when he went to an optometrist at age 27 years to have his contact lenses checked. He was in good general health and his only eye problem had been myopia and astigmatism that was fully correctable with lenses. An ophthalmologist to whom he was referred found that his visual acuity was 20/20 OU with slight posterior subcapsular cataracts and pale optic discs. Automated perimetry revealed defects near fixation. Findings from the neurological examination, 100-Hue color testing, magnetic resonance imaging scanning, and pattern visual evoked response testing showed no abnormalities. He was examined again at age 33 years by a neuro-ophthalmologist. Best-corrected visual acuity was 20/20 OU. On Ishihara color plate testing, he missed 2 with his right eye and 1 with his left. Slitlamp examination revealed mildly thickened corneal nerves and posterior subcapsular cataracts in both eyes. There was no relative afferent pupillary defect. Humphrey visual field testing showed central dropout with a superotemporal loss approaching the vertical meridian in each eye (Figure 2). Both optic nerves were pale but of normal size.

Case 3. The younger sister of patient 1 allegedly had poor vision since childhood and a “lazy eye” that was treated with exercises. Migraine headaches had been present since age 15 years. As early as age 27 years she was noted to have elevated prolactin levels but no endocrine symptoms. Ophthalmic examination then revealed a visual acuity of 20/25 OD and 20/20 OS, 9 of 14 Ishihara color plates correct with each eye; enlarged blind spots and loss of superotemporal visual field and bilateral optic atrophy on kinetic visual field were noted during testing. Computed tomographic scans showed no abnormalities at ages 27 and 30 years. At age 32 years, Humphrey visual field testing showed superotemporal defects respecting the vertical meridian. Magnetic resonance imaging revealed a small, hyperintense, intrasellar lesion in the left side of the pituitary gland without suprasellar extension, presumed to be a pituitary cyst. When examined by a neuro-ophthalmologist at age 37 years, her visual acuity was 20/25 OU. She correctly identified 2 of the 14 Ishihara color test plates with each eye. There were bitemporal visual field defects on static visual field testing and both optic discs were atrophic but of normal size. A second magnetic resonance imaging scan showed no abnormalities.

She was examined by a neuro-ophthalmologist 2 years later. Her best-corrected visual acuity was 20/25 OD and 20/20 OS. On color vision testing, she correctly identified 3.5 of the 14 plates with her right eye and 2.5 of the 14 plates with her left. Slit-lamp examination showed no abnormalities. Humphrey visual fields revealed bilateral superotemporal field defects (Figure 3). The mean deviation was unchanged compared with the automated visual fields done at age 32 years. There was diffuse optic nerve pallor of both optic nerve heads with temporal excavation. The optic discs were normal sized.

The father’s family history is notable only for cataracts. The mother’s family history is notable for siblings who died at ages 14 and 12 years of a neurological disease characterized initially by stuttering and loss of balance, progressing to bed confinement, and aphasia. Further details of their illnesses are unavailable. Both parents were free of systemic disease, had normal corrected visual acuities, Humphrey automated visual field results, color vision (Ishihara color plates), and optic nerve heads. Patient 1 has 2 daughters, a 12-year-old and a 9-year-old, both of whom are healthy. Both had neuro-ophthalmic examinations, testing visual acuity, color vision, and
visual fields, as well as visualization of the optic nerves, all of which showed no abnormalities. The older daughter of patient 1 had strabismic amblyopia that was successfully treated with patching. Patient 2 has an 18-month-old son, who is healthy, and patient 3 has a 9-year-old son and a 2-year-old daughter, both of whom are healthy.

Comment. We suspect that the 3 siblings described in this article have a unique optic neuropathy that is manifested exclusively or predominantly at the level of the optic chiasm based on the presence of typical chiasmatic visual field defects, and is probably inherited as an autosomal recessive trait. While we recognize that centrocecal scotomas can be mistaken for chiasmatic bitemporal defects and that automated perimetry can give the false impression that a temporal defect comes to, but does not cross, the vertical midline, nevertheless we are confident that our patients’ defects were chiasmatic. Centrocecal defects would not give a defect confined to the superior quadrant and would not be likely to spare Snellen visual acuities in every patient. The issue of the midline boundary can be resolved in 2 of the patients because testing on several occasions with Goldmann perimetry demonstrated that their visual field defects “respected” the vertical meridian. Two of the siblings had a pure median chiasmal syndrome when first evaluated and their visual acuity and color sense during many years of observation showed no abnormalities. Although the visual field defect in patient 3 is bitemporal, her slightly reduced visual acuity in 1 eye and her bilateral dyschromatopsia imply that she also has some involvement of uncrossed axons.

It is highly unlikely that the disorder was not inherited as a mendelian dominant trait since neither parent was affected. Only in the event that an affected man other than the putative father sired all 3 siblings could this conclusion be founded. An illness involving an entire sibship but sparing the parents could be genetically or nongenetically inherited. Nongenetic, static, congenital optic neuropathies in multiple siblings can, albeit rarely, result from an abnormal uterine environment. Segmental optic nerve hypoplasia in the offspring of mothers with diabetes mellitus is one of the few examples of this phenomenon; however, nongenetic inheritance of this kind cannot be ruled out in our cases. Mutations in mitochondrial DNA can be transmitted through unaffected maternal carriers as in Leber hereditary optic neuropathy. Leber hereditary optic neuropathy was ruled out in patient 1 and, without special molecular investigations and extensive information about multiple generations of the family, this possibility cannot be evaluated. Autosomal recessive mendelian inheritance would be the mechanism most likely to explain the occurrence of the optic neuropathy in this family.

It is impossible to determine if the visual defects were congenital or acquired. In all 3 patients, the neuroophthalmic abnormalities were discovered incidentally when each patient was asymptomatic. Two of the patients had normal findings on routine examinations (without perimetry) many years before discovery of the optic disc pallor, but it is possible that the pallor was present but missed. None of the siblings has shown a decline in visual function under observation following discovery of the defect. In certain congenital optic neuropathies, the optic disc is hypoplastic. None of our patients had discernible hypoplasia, but subtle degrees of hypoplasia can be hard to recognize. If acquired postnatally, the latest the disorder could have begun was in the third decade of life.

Bitemporal visual field defects have been identified in hereditary optic neuropathies. Raaf and Bair1 described the findings in patients from a family with Leber hereditary optic neuropathy. Two siblings, both with impaired visual acuity, had visual field defects with bitemporal characteristics. Weiner et al2 reported a sporadic case of Leber hereditary optic neuropathy in a woman whose first symptom was a temporal blur. On her initial examination she had reduced visual acuity in one eye but normal visual acuity in the other with a bitemporal visual field defect, densest adjacent to fixation. Manchester and Calhoun3 reported bitemporal visual defects in several members of 2 generations of a family with dominantly inherited optic atrophy. Although 2 of the patients were asymptomatic, all of them had subnormal visual acuity. Votruba et al,4 in their extensive and intensive evaluation of patients with dominantly inherited optic atrophy, found that 33 of 50 study patients had superotemporal visual field defects when tested with automated perimetry. It is impossible to determine if any them were asymptomatic or had a pure chiasmatic syndrome.

How might a congenital bitemporal visual field defect eventuate from a genetic disorder? Recent research has revealed several possible molecular bases for chiasmal maldevelopment.5-12 Retinal ganglion cell axons are believed to respond to specific cues in their environment during development as they migrate toward the optic chiasm. Cell surface proteins on neurons or glia in the chiasmal region may help...
to direct axonal processes to their appropriate destinations in the ipsilateral or contralateral optic tract and lateral geniculate nucleus. The loss of signals and/or growth factors that maintain the survival of fibers destined to cross in the chiasm may lead to their selective loss and subsequently to bitemporal visual field defects. There are even cell surface proteins such as the protein product of the gene roundabout that are believed to repel axons from crossing midline structures. It is possible that the absence of this protein at a stage where retinal ganglion cell axons from the inferonasal regions of the ipsilateral and contralateral eyes are approaching the midline structures of the optic chiasm may preclude survival of the retinal ganglion cells. Alternatively, loss of factors that maintain or influence neuronal metabolism or synaptic connections between retinal ganglion cells and then postsynaptic targets in the lateral geniculate nucleus may be responsible for selective loss of inferonasally located retinal ganglion cells.

We believe that the siblings described in this article have a novel hereditary chiasmal optic neuropathy that is recessively inherited. Although there are several possible mechanisms for selective loss of crossing axonal fibers in the optic chiasm, it is unclear which may be affected in this hereditary optic neuropathy. Current research in progress studying the molecular cues involved in the control of axonal crossing at midline structures may contribute to the identification and treatment of the hereditary genetic defect responsible for this phenotype.

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From the Archives of the ARCHIVES

A look at the past . . .

Chochrjakow ligated the ureters in a number of dogs and rabbits and killed some of them after the appearance of uremic symptoms (second day), and some were allowed to die of uremia (second to fourth day). In another series he removed the ligature and killed the animals intervals, letting them live from a week to two months. The microscopic preparations of the retina were stained by the Ehrlich-Dogiel methylene-blue method. There were found general edema of the retina, with vacuole formation in and about the ganglion cells, in the nuclear and reticular layers, in the varicose thickening of the nerve fibres and Müller's fibres, as well as swelling of the vascular endothelium and enlargement of the perivascular spaces. All these changes appeared in from 2 to 7 days and disappeared, after restoring the permeability of the ureters, within two months. Similar changes were found in the eyes of persons dead of uremia. The author believes uremic blindness with negative ophthalmoscopic findings to be due to the changes he describes in the retina.