Fundoscopy of nerve fiber layer defects in glaucoma

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Early attrition of nerve fiber bundles in glaucoma causes slit-like gaps to appear among the normally uniform, striated arcuate bundles of the retinal nerve fiber layer. The nerve fiber layer thins progressively, and its vessels become exposed as the defects coalesce, deepen, and widen with advancing disease. These changes in the peripapillary retina are exemplified photographically and compared with perimetric findings. We believe that these fundoscopic signs provide the earliest objective evidence of nerve fiber wasting in eyes with chronically elevated intraocular pressure.

Key words: glaucoma, intraocular hypertension, retina, retinal nerve fiber layer, optic disc, examination techniques, ophthalmoscopy, fundus photography.

Attrition of nerve fibers in the anterior visual pathways is reflected directly in the nerve fiber layer of the retina. These retrograde degenerative changes are subtle but they can be seen with an ophthalmoscope and can be photographed with a fundus camera, especially in red-free light. Specific patterns of atrophy in the retinal nerve fiber layer have been identified recently in patients with lesions of the optic nerve1-2 and the optic tract.3,4

The first part of this report gives a schematic outline of the appearance of focal and diffuse axonal loss in the peripapillary retina. The second part exemplifies, by fundus photographs from a pilot study, early, intermediate, and late stages of nerve fiber attrition in eyes with chronically elevated intraocular pressure. These objective retinal signs in glaucoma are correlated with changes in the optic disc and the field of vision.

Fundoscopic appearance of the normal and atrophic nerve fiber layer. The normal peripapillary nerve fiber layer appears slightly opaque with a uniform finely striated radial pattern of superficial light reflexes (Figs. 1A and B). At its thickest portion near the disc, the nerve fiber layer

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has striations that appear coarse and interwoven. The striations can usually be traced peripherally for two to three disc diameters before they gradually fade from view. The opacity of the layer diminishes rapidly with increasing distance from the optic disc and as the thickly packed superior and inferior arcuate bundles blend with para-macular and macular fibers. Proximal trunks of main retinal vessels lie embedded in the nerve fiber layer, causing irregular diffusion of the bright linear highlights from these vessels. Similarly, small vessels within the nerve fiber layer appear faint and crosshatched (Fig. 2).

The peripapillary arcuate nerve fibers add a dull, slightly opaque grey cast to the red of the underlying choroid. When optical imperfections in the eye make nerve fiber striations difficult to see, this dull grey-red appearance of the retina indicates presence of the nerve fiber layer.

Glossy reflexes from the retinal surface in childhood tend to mask the fine striations of the nerve fiber layer. The youthful retina also has other prominent retinal reflexes including Gunn’s dots (pinpoint reflections from Müller cell footplates in the inner-limiting membrane), and broad highlights paralleling major veins and arteries. All of these normal reflexes from the inner-limiting membrane change location and form with each shift of the ophthalmoscopic beam. Prominence of the nerve fiber striations also changes with similar shifts of the beam, but the course, pattern, and location of the striations remain fixed.

Retinal signs of diffuse and focal atrophy of nerve fibers. Both diffuse and focal forms of axon degeneration occur in the retina. The diffuse type is difficult to assess, especially in early stages. Diffuse atrophy
Fig. 2. Schema of normal nerve fiber layer and vessels of the superior temporal arcade close to the optic disc.

increases clarity of vascular light reflexes and exposes small vessels normally obscured by overlying fibers (compare Figs. 2 and 3A). When degeneration of nerve fibers is advanced, the surface of the retina takes on a dark mottled granular appearance, and the vessels stand out in bold relief with unbroken light reflexes and grey streaks outlining their blood columns near the optic disc. At this terminal stage of atrophy smaller vessels shrink or fade from sight (Fig. 3B).

Focal axonal degeneration in the retina causes characteristic changes in the appearance of the nerve fiber layer. Dark slits or grooves appear among the arcuate bundles approaching the optic disc superiorly or inferiorly. These slits are usually found about one to one and one-half disc diameters from the nerve head but sometimes they are more obvious two to three disc diameters away. Narrow slits fade from sight as adjacent fiber bundles converge toward the disc. Arcuate slits may be narrow but multiple, producing a raked appearance of the nerve fiber layer (Fig. 4A). Wider grooves take the form of arcuate wedges.

The broad wedges of more advanced nerve fiber degeneration are easily overlooked. They are only slightly darker than the adjacent retina (Fig. 4B). The border contrast is faint when a wedge is surrounded by a diffusely atrophic nerve fiber layer. Contrast can be enhanced in red-free illumination.

Retinal reflexes mimicking focal nerve fiber degeneration. Occasionally arc-like highlights are seen near the main trunks of the superior temporal vessels (Figs. 5A and B). These reflexes from the internal-limiting membrane can be confused with edges of broad, wedge-shaped defects of the nerve fiber layer. However, such reflexes
Fig. 3A. Schema of diffusely degenerated and thinned nerve fiber layer.

Fig. 3B. Schema of retinal surface with total atrophy of the nerve fiber layer.
Fig. 4A. Schema of early nerve fiber bundle degeneration.

Fig. 4B. Schema of advanced atrophy of arcuate fibers in a diffusely degenerated and thinned nerve fiber layer.
Fig. 5. Pseudodefects in the nerve fiber layer. A. Bright arcuate reflexes delimit a wide wedge in the superior arcuate bundle. There is a reflex discontinuity at a vein branch (solid arrow). The superior reflexes are spotty and split in two branches (open arrow), showing that they do not arise from nerve fiber bundles. The pseudodeflect is no darker than neighboring areas of the retina, and its nutrient vessels are blurred to a normal degree by overlying nerve fibers. B. The bright reflexes differ from the smooth arcs of nerve fibers. (Fundus photographs from a 35-year-old healthy Iranian woman.)

are bright, discontinuous, and nonstriated. In contrast to the borders of a genuine nerve fiber defect, these reflexes tend to meander from the smooth arcuate path of the nerve fiber bundles, sometimes forking or fusing together. With each shift of the ophthalmoscopic beam they change form and position. A pseudoneuron fiber bundle defect bordered by two of these streak-like reflexes has the striations and color of normal retina.

Materials and methods

The photographs in this study were obtained from patients under observation in the Glaucoma Clinic. Patients were selected whose chronically elevated intraocular pressure was confirmed on many visits to the clinic and whose standard perimetric examinations in the clinic had indicated stages of nerve fiber attrition ranging from none to advanced. All patients had clear optical media.

Clinical data for each patient, including charts of the visual fields, is provided with the figures. Perimetric examinations were repeated by both kinetic and static methods.

Clinical observations of the nerve fiber layer were performed with a direct ophthalmoscope that emitted bright red-free light. Factors aiding visualization of the nerve fiber layer were a dilated pupil and clear optical media. Fine details were more difficult to see and to photograph in some of our elderly patients, and in patients with sparse retinal pigmentation.

Fundus photographs were obtained with the Zeiss Oberkochen fundus camera using the 2× magnification attachment. Three to five exposures were usually sufficient to cover the area of the optic disc and the peripapillary arcuate nerve fibers. In some cases the fundus was recorded directly on Kodak Plus-X black and white film, using a Wratten No. 65 (green) filter to enhance the contrast of gaps in the nerve fiber layer. In others the fundus was recorded on Kodachrome II film and the color transparencies were then copied on Plus-X film using the same green filter.

The black and white negatives were printed on Kodak Ektamatic SC paper using suitable contrast filters. Final magnification ranged between 20 to 40×.
Findings

Early stage of nerve fiber atrophy in glaucoma.

Fig. 6. Early nerve fiber layer defects in an eye with chronically elevated intraocular pressure. Note parallel dark slits below the main trunk of the superior retinal vein (arrows). The slits can be followed proximally from just beyond a vertical line through the macula (to the left of the figure), to where they fade out in the thick fiber layer above the disc. The axial light reflexes from major vascular trunks are continuous, indicating absence of overlying nerve fibers. This suggests diffuse reduction of superficial nerve fibers in addition to the localized nerve fiber bundle defects. The disc tissue appears to be well vascularized but the optic cup, though relatively small, is deep and elongated vertically. Perimetric evidence of nerve fiber abnormality was obtained only with a 2/2,000 mm. white test object. The field defect consisted of spotty, relative scotomas and on-and-off blinking in the lower nasal half of the Bjerrum area. The blind spot was normal in size. (The patient was a 17-year-old boy, who had been followed for three years for chronically elevated intraocular pressure, without treatment. The pressure ranged between 28 and 35 mm. of mercury by applanation. Both his mother and his maternal grandfather had glaucoma.)
Fig. 7. Early defects in the nerve fiber layer in glaucoma. The wedge within open arrows contains multiple dark slits (solid arrows). The cup of the optic disc is small in diameter but deep. (This is the left fundus of the patient described in Fig. 6. The tonometric and perimetric findings were similar to those of the right eye.)
Fig. 8. Early nerve fiber layer defects in glaucoma. The superior arcuate bundle gaps (between solid arrows) coalesce beneath the superior temporal vein and cross the disc margin as a dark band (open arrows). The optic cup is vertically elongated, particularly above. Patchy scotomas and blinking of the 2/2,000 mm. white stimulus were present in the nasal portion of the Bjerrum zone. The blind spot was normal in size. (This 36-year-old woman was followed for five years for chronically elevated intraocular pressure. Pressures ranged between 30 and 38 mm. of mercury by applanation. No treatment had been given.)
Fig. 9. Early nerve fiber layer defects in glaucoma. Multiple narrow dark bands (between arrows) enter the disc superiorly, and several wider but less dark bands approach it inferiorly. Note the blurring of the axial light reflex of the inferior temporal artery, indicating the presence of superficial nerve fibers. The optic cup is elongated vertically, more above than below. Relative Bjerrum area defects were demonstrated above and below with the 2/2,000 mm. white test object. The blind spot was normal. (This is the left fundus of the patient described in Fig. 8. The intraocular pressure range was the same as in the right eye.)
Fig. 10. A. At larger magnification the nerve fiber bundle defect in Fig. 8 can be recognized as a dark band approaching the disc above (between arrows). B. This magnified view of the optic disc in Fig. 9 shows dark radial bands just beyond the disc margin (arrows). These may represent proximal ends of superior nerve fiber bundle gaps. C. Optic disc with a large cup in an eye without elevated intracocular pressure or field defect. Compare the uniform appearance of the nerve fiber tissue surrounding and covering the disc margin with the areas designated by arrows in Figs. 10A and B.

Fig. 11. Moderately advanced glaucomatous nerve fiber layer defect. The nerve fiber layer striations are visible superiorly but indistinct temporally. The defect (between solid white arrows) appears as a dark scimitar-like wedge joining the disc margin at 1 o'clock. Note how the borders of the wedge conform precisely to the course of the temporal arcuate bundles. Also note how the small vessels are exposed and better defined within the wedge (as at a) but partially obscured by a more normal complement of overlying nerve fibers at the borders of this area (b). In this eye, the granular appearance throughout the retina is an effect of diffuse axonal attrition. The area above the disc is dark; this is partly due to the high-contrast photographic paper used to enhance the arcuate defect. The optic disc shows marked cupping. The neurological rim is indented at a point corresponding to the wedge defect in the nerve fiber.
Intermediate stage of nerve fiber atrophy in glaucoma.

Fig. 11 cont’d.

layer (n). The visual field defects, recorded on the Tubingen perimeter, consisted of a relative scotoma in the Bjerrum area with in-and-out blinking of the test object at its proximal end, represented by ⊗, a dense scotoma peripherally, and a nasal step, all recorded by kinetic perimetry. Static profiles at the 337 degree meridian (below right) show a general depression and the dense scotoma at 15 degrees of eccentricity. A corresponding depression was found at the 240 degree meridian (below left). (The patient was a 50-year-old man with chronic elevation of the intraocular pressure, detected 10 years earlier. The anterior chamber angle was open.)
Advanced stage of nerve fiber atrophy in glaucoma.

Fig. 12. Advanced nerve fiber layer defects in chronic glaucoma. In this fundus a sector of the retina (between white arrows) contains striations indicating presence of nerve fibers. Above and below this sector the retina is darker and devoid of striations. The nasal borders of the denuded areas cannot be seen in the photograph but the blurred nasal disc margin indicates the presence of nerve fibers in the nasal sector. The optic cup extends vertically to the disc margin (small arrows) where neuroglial tissue is absent. These notches in the neuroglial rim correspond to the apices of the two defects in the nerve fiber layer. Note also the peripapillary halo. The visual field contained double absolute Bjerrum scotomas between the blind spot and the nasal periphery. In other sectors the field was generally depressed. Corrected visual acuity was 20/20. (This patient was a 60-year-old man with recently detected, open-angle glaucoma. The intraocular pressure was about 32 mm. by applanation.)

Discussion

Our pilot studies of the peripapillary nerve fiber layer in eyes with chronically elevated intraocular pressure establish that glaucomatous nerve fiber defects can be seen with an ophthalmoscope and in fundus photographs. Importantly, these retinal changes can be detected at a stage in the disease when abnormality of the optic disc and the visual field would be regarded as marginal. As Figs. 6 through 10 illustrate, glaucomatous atrophy first appears as multiple, fine, shallow grooves or slits in the arcuate bundles of the peripapillary nerve fiber layer. These slits represent effects of nerve fiber bundle degeneration. Striated reflexes paralleling such slits appear normal, not coarse and indistinct as occurs with some types of optic neuropathy. The length of slits is usually 2 to 3 disc diameters. They are sometimes traceable to the disc margin, but more often they fade out ½ to 1 disc diameter before reaching the disc (Figs. 6 and 7).

Three of the four eyes with early retinal signs of glaucomatous nerve fiber atrophy (Figs. 6, 8, and 9) had small but vertically oval optic cups; in two the oval cup was closer to the superior margin of the disc corresponding with the defects in the
Fig. 13. Advanced nerve fiber layer attrition in chronic glaucoma. Evidence of nerve fibers is difficult to discern beneath the lines defined by solid arrows. Above these lines the nerve fiber layer appears intact. Note how the arteries and veins stand out in relief inferiorly. The walls of the inferior vein are visible as grey lines. Blurred nutrient vessels of the nerve fiber layer can be seen above but not below. Arcuate bundle defects in the superior portion of the fundus were seen ophthalmoscopically but lie beyond the field covered by this photograph. The optic cup is markedly enlarged and excavated. The neuroglial rim ends abruptly (black arrow) where nerve fibers are lacking. There was an absolute defect in the superior half of the visual field. The inferior half was generally depressed and contained scotomas within the arcuate zone. The corrected visual acuity was 20/20. (This patient was a 62-year-old black male with poorly controlled chronic open-angle glaucoma.)

Contrast at the border of such defects is low, making them difficult to see. Where the apex of the wedge meets the disc margin, there is an indentation or notch in the neuroglial rim of the glaucomatous cup (Figs. 11 and 12).

In later stages of glaucoma (Figs. 12 and 13), the wedge-shaped defects in the nerve fiber layer expand to sector-shaped areas in which the retina is devoid of all visible nerve fiber detail. Retina adjacent to these sectors may contain sparse striations from the thin partially atrophic nerve fiber layer. Contrast at the borders of these...
sectors is low (Figs. 12 and 13). Corresponding with the sector defects in the retinal nerve fiber layer there are portions of the disc margin that are clearly exposed by the loss of overlying neuroglial tissue.

The overall correlation of fundoscopic and perimetric findings in the glaucomatous eyes comprising this study was good. Most slits or gaps in the nerve fiber layer had perimetric corollaries equaling or exceeding the area of fundoscopic abnormality. The areas of greatest functional deficit were always located more distally along the arcuate bundles than the areas of visible nerve fiber atrophy; the densest portions of the perimetric defects thus occurred in the nasal part of the Bjerrum area rather than close to the blind spot. Our perimetric findings in the eyes with early glaucoma (Figs. 6 through 9) suggest that the first nerve fibers to degenerate belong to the arcuate bundles and originate from ganglion cells in the temporal hemiretina. In fundus photographs the position of these fibers appears to be superficial in the nerve fiber layer.

This observation on the retinotopic lamination of the peripapillary nerve fiber layer agrees with recent fundoscopic findings in homonymous hemiretinal degeneration with optic tract lesions. Here too, retained visual fibers in the eye opposite the lesion take origin in the temporal hemiretina and arc toward the disc in the superficial lamella of the nerve fiber layer. The retinal nerve fibers in the eye on the side of the lesion take their origin in the nasal hemiretina and reach the disc in the deep lamella.

In the eyes with early signs of nerve fiber degeneration (Figs. 6 through 9), field defects were most easily demonstrated on the tangent screen and were more difficult, often impossible, to find with the Goldmann or Tübingen perimeters. The defects were never recorded or suspected from routine examinations on previous visits to the Glaucoma Clinic. Only when our fundoscopic findings prompted detailed exploration of the appropriate Bjerrum area were subtle defects detected. During testing of these areas, each patient reported narrow zones in the nasal half of the Bjerrum area in which small objects (2/2000 mm. white) blinked or dimmed in and out (Figs. 3 through 6). These scotomas are not angioscotomas. They were never found in normal portions of our patient's fundi. The scotomas were always broader and more easily demonstrated than angioscotomas. They were never located close to the blind spot where angioscotomas are ordinarily demonstrated.

At advanced stages of the glaucomatous process, atrophic retinal sectors correspond with dense broad arcuate defects in the field of vision. Wedges or sectors of atrophic bundles in the peripapillary nerve fiber layer correlate with arcuate scotomas having their densest zones nasally in the Bjerrum area. When the rim of the optic cup is denuded of neuroglial tissue at the apex of such a wedge, we could reliably predict that the corresponding arcuate defect would merge with the blind spot.

The pathogenesis of the nerve fiber layer changes in glaucoma remains unclarified in many of its details. The same pattern of nerve fiber loss may occur with other types of optic nerve disease in which focal retrograde axonal degeneration occurs, e.g., as sequelae of optic neuritis. Therefore, at this time, we do not consider the focal nerve fiber bundle changes that we have described in incipient glaucoma to be specific for this disease.

A final conclusion regarding the clinical value of nerve fiber layer examination in glaucoma cannot be made from the selected cases comprising this study. This will have to await simplified high-resolution photographic techniques, their application together with ophthalmoscopy in prospective clinical studies, and comparison with fundoscopic findings from methods in current use for evaluation of the ocular effects of chronically elevated intraocular pressure. The value of any objective method for assessment of early and continuing effects of glaucoma is self-
evident. As exemplified in our studies, red-
free fundoscopy of the retinal nerve fiber
layer provides greater diagnostic sensitivity
in the detection of glaucomatous atrophy
than any current methods. More important
still, this report describes a new and pre-
cise clinical tool for the identification and
evaluation of diseases that cause degenera-
tion of axons in the anterior visual path-
ways.

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