A NEW MANAGEMENT SYSTEM FOR GLAUCOMA BASED ON IMPROVEMENT OF THE APPEARANCE OF THE OPTIC DISC OR VISUAL FIELD*

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INTRODUCTION

GLAUCOMA IS A DISEASE OF THE NEURONS EXTENDING FROM THE RETINAL GANglion cells to the geniculate body. The major risk factor for glaucomatous damage is intraocular pressure. Other factors also play important roles. One satisfactory definition of glaucoma is that it is a disease due to intraocular pressure higher than the eye can tolerate.

In primary open-angle glaucoma, or other glaucomas in which there is permanent interference with aqueous outflow, the process responsible for the intraocular pressure which is higher than the eye can tolerate is a continuing one; the process persists for the life of the patient. Therefore, the course of the disease is one of relentless deterioration (Fig 1). The rate of descent and the shape of the course vary from patient to patient (Figs 2 and 3), but the final destination of the journey is pitifully sure—loss of sight.

Some believe that once the optic nerve has become severely cupped, then prevention of continued worsening is difficult, or even impossible. That this should be so *in certain cases* is not surprising when the pathology of glaucomatous optic nerve damage is considered.[1-5] The neurons become compressed by the distorted, posteriorly-bowed lamina and lose

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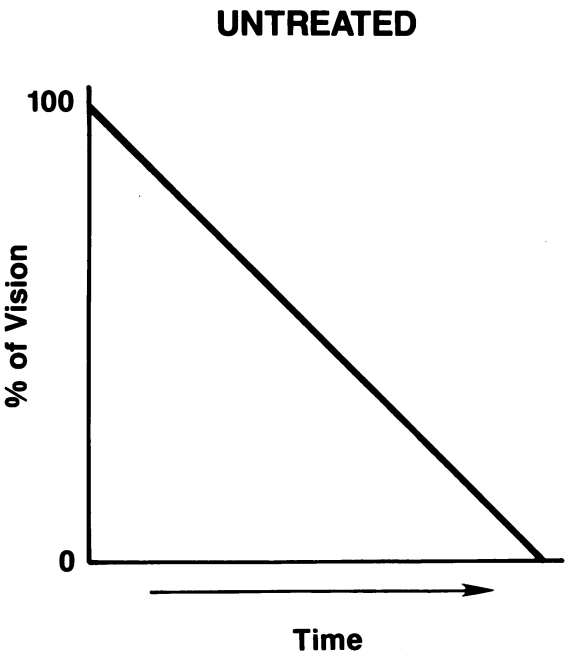

FIGURE 1
Schematic representation of expected deterioration of visual function in a patient with untreated continuing glaucoma. In actuality, course of deterioration is rarely, if ever, in a "straight line" as shown here.

nourishment because of selective ischemia of the badly damaged optic nerve head.[6-8] The laminar distortion in such patients with advanced glaucomatous cupping is permanent. Consequently, the neurons may continue to be damaged, even though the intraocular pressure, the major cause for the distortion of the lamina cribrosa, is lowered. In such a setting the effect of the optic nerve pathology on vision, expressed as visual field loss, decreased color sense, loss of acuity, etc, should continue resulting in further deterioration. This reasoning is supported by several studies that appear to show that visual field loss may continue to progress despite lowering of intraocular pressure in patients with far-advanced glaucomatous cupping.[9,10]

Some have concluded that since there appear to be patients who show further deterioration of vision despite lowering of intraocular pressure, that lowering intraocular pressure is not an effective treatment for glaucoma. But such an observation does not, of course, prove that lowering

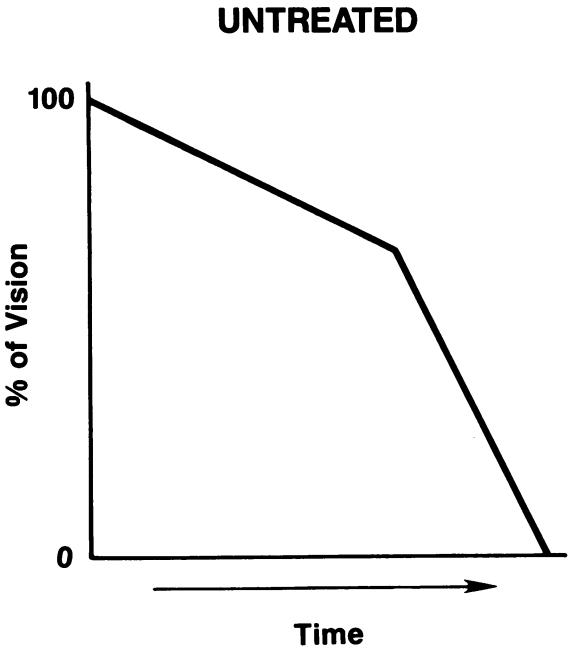

FIGURE 2
Schematic representation of one pattern by which visual field deteriorates in a patient with untreated glaucoma.

intraocular pressure is not effective in preventing further optic nerve damage in patients with glaucoma. In the first place, the phenomenon may be limited only to those with certain types of glaucomatous pathology, especially those with far-advanced disease. For example, it has been shown experimentally that reversal of glaucomatous cupping is possible.[11,12] Furthermore, it may be that in those with advanced glaucomatous damage that a degree of intraocular pressure greater than ordinarily considered necessary may be beneficial. Grant and Burke's[13] retrospective study is illuminating in this regard.

The widespread use of drugs and surgical techniques designed to lower intraocular pressure must indicate that most ophthalmologists believe that lowering intraocular pressure is beneficial in patients with glaucoma, at least those with early or moderate stage of the disease. According to most current thinking, effective intervention results in stability of the optic disc and visual field, and somewhat limits this ability to stabilize the glaucomatous process to those with early or moderate stages of the disease[14] (Fig 4).

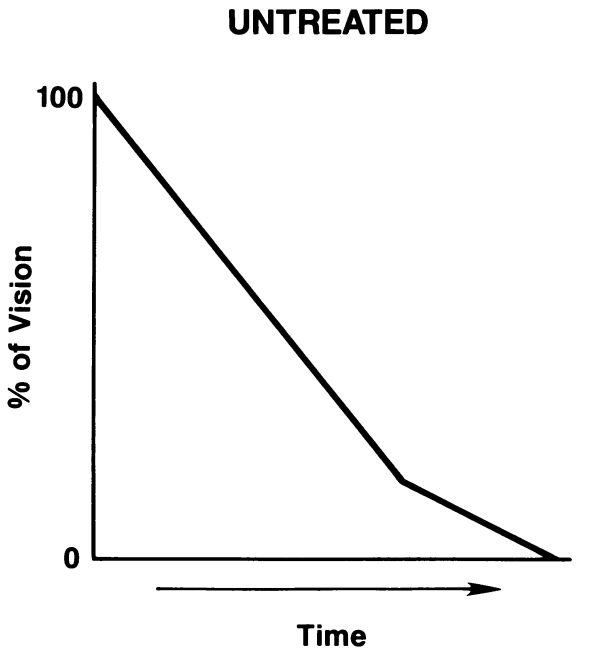

FIGURE 3
Schematic representation of another pattern of visual deterioration in a patient with untreated glaucoma.

There are three basic approaches to the therapy of glaucoma. The first uses intraocular pressure as a predictive indicator of future performance of the disc and visual field. "Glaucoma" is defined in this system as intraocular pressure *above* a specific level: 21, 24, 40 mm Hg, etc. Control is defined as intraocular pressure *below* a specific level, most often 21 mm Hg. The problem with this approach is that the overwhelming majority (some say around 90% to 95%) of those with "elevated intraocular pressure," that is, intraocular pressure greater than 21 mm Hg, never develop optic nerve damage.[15-19] And on the other hand, around one-third of those with glaucomatous cupping have random intraocular pressures less than 21 mm Hg.[20] Now that this lack of correlation between absolute level of intraocular pressure and state of glaucoma is known, and now that it is understood that an intraocular pressure of 30 mm Hg may constitute "control" in patient X and an intraocular pressure of 15 mm Hg may constitute "lack of control" in patient Y, it should be clear that absolute levels of intraocular pressure cannot be used to manage glau-

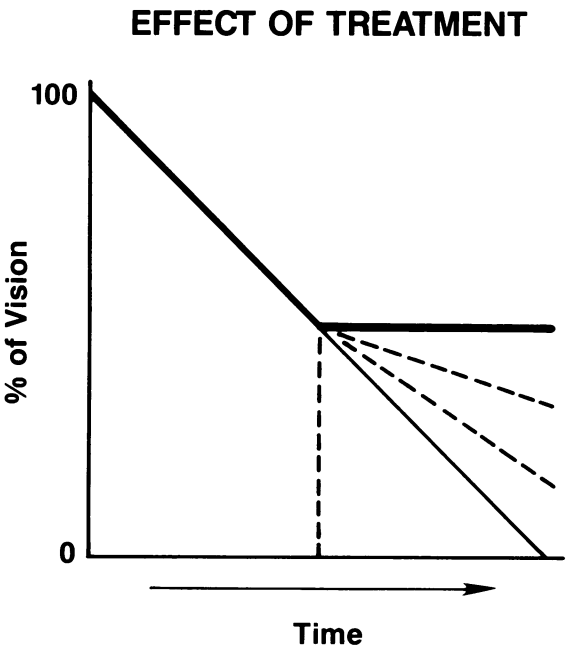

FIGURE 4
Schematic representation of what are generally considered to be effects of treatment on natural history of visual deterioration in a patient with glaucoma. The most effective intervention results in stabilization of field, as shown by *thick line*. If intervention is less successful, rate of deterioration may be slowed, as shown by *dotted lines* between *thick solid line* and *thin solid line*. When such further deterioration is noted, an increase in vigor of therapy may then result in stability of condition, as shown by *thick line*. In occasional cases initiation of treatment may be associated with rapid deterioration of function, as occurs in "wipe-out," a rare complication of glaucoma surgery.

coma.[15-25] Nevertheless, many current articles, especially those dealing with surgery, continue to define glaucoma control as intraocular pressure less than 21 mm Hg.

A second method of management is retrospective, based on stability of the optic disc and visual field. This school aims to halt the deterioration. The intraocular pressure is lowered to a predetermined level, at which time the optic disc and visual field are re-examined. If they are stable, then the glaucoma is considered "controlled." But loss often occurs gradually and imperceptibly, and what appears to be "control" is often found at a later date to be inadequate when further deterioration is documented. The intraocular pressure at that point is then considered too

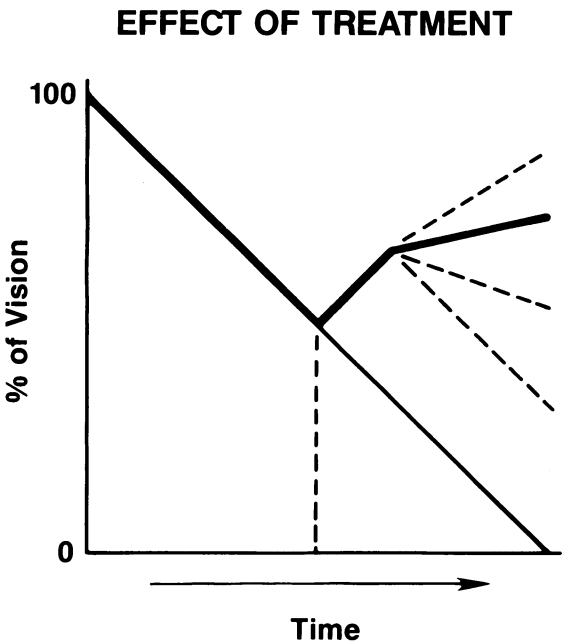

FIGURE 5
Schematic representation of course of glaucoma and effect of treatment, as discussed in the present report. This maintains that effective intervention may be associated with an improvement in visual function, as seen with *thick solid line*. This improvement may continue, stabilize, or stop, allowing further deterioration. The other lines in Fig 5 represent the same possibilities as shown in Fig 4.

high, the glaucoma out of control, and attempts are made to lower the pressure to a yet lower baseline level. The process is repeated again and again until hopefully no further deterioration is noted. At this time the patient is once again considered controlled and that new level of intraocular pressure considered adequate for control. This appears to be the method most glaucoma specialists employ today. One indication of this is that it forms the basis of the therapeutic approach for the National Eye Institute-sponsored Glaucoma Laser Trial.

A third system of treatment is the primary substance of this report. It is a new approach. It is based on improvement in the optic disc or visual field. This school states that both the disc and the visual field can improve when intraocular pressure is lowered (Fig 5). It does not state that the disc or field return to normal. It does not state such improvement occurs in every patient. It does contend that, with proper examination tech-

niques and adequate pressure lowering, improvement will often be seen. The ophthalmologist lowers the intraocular pressure and looks critically for improvement of the disc or visual field; if real improvement becomes apparent, the pressure associated with such improvement is considered to represent "control." If such improvement is not noted after lowering intraocular pressure, the ophthalmologist then considers what is necessary to lower the intraocular pressure still further and weighs the risks of more aggressive treatment against the potential benefits. Obviously, dead neurons don't recover, and blown-out optic nerve heads don't return to normal-appearing discs. The goal is not return *to* normal, but return *toward* normal. This third system of treatment avoids the inevitable under- and over-treatment of the first method, where control is based on intraocular pressure, and prevents the deterioration that is an essential part of the second system, where control is determined by the level of intraocular pressure associated with stability of disc and field.

There is increasing evidence that there is, in fact, improvement of disc and field in patients with glaucoma. Apparent improvement in the appearance of the optic disc was first noted in 1869 by von Jaeger[26] and illustrated in his beautiful atlas published just 19 years after Helmholtz gave us the ophthalmoscope. It has been well documented in children and adults since.[27-47] The frequency with which such optic nerve change occurs is not known, but an indication that it is common was presented at the 1985 meeting of the Association for Research and Vision in Ophthalmology.[37] Katz and co-workers[37] performed a controlled, masked study of pre- and posttreatment photographs of the eyes of glaucoma patients using masked observers and random allocation design. Three groups were chosen: two controls and one study group. Photographs of 100 glaucomatous eyes were selected for evaluation. Group 1 consisted of 25 eyes that had two sets of stereoscopic photographs on the same day. Group 2 (24 eyes) and group 3 (51 eyes) had stereoscopic photographs taken before and after glaucoma treatment. Patients in group 2 had less than a 20% decrease in intraocular pressure, while those in group 3 had a greater than 30% drop in intraocular pressure after treatment had been instituted. The pairs of stereoscopic photographs from all three groups were then randomly assigned by a coin toss to be labeled either A or B. The 100 sets of photographs were then randomly assigned to a number 1 to 100.

Three ophthalmologists independently graded each set of stereoscopic photographs in numerical sequence. Each pair was reviewed in an A-B order. Criteria for comparison included stereoscopic cup appearance, neuroretinal rim area, and vessel displacement. The observers made one of three choices: stereoscopic photograph pair A appearing better than

TABLE I: APPEARANCE OF POSTTREATMENT DISC

	BETTER	NO CHANGE	WORSE	TOTAL
Control 1*	0	25	0	25
Control 2	0	23	0	23
Study group	17	32	2	51
Total	17	80	2	99

*Eyes in this group received no treatment. Stereoscopic photographs are from the same day.

pair B, stereoscopic photograph pair B appearing better than pair A, or no observable difference between the two pairs.

In 13 of the 51 eyes in group three, all three observers independently graded the disc as improved. In four additional eyes in group three, two of the three observers were in agreement that an improvement had occurred (Table I). The agreement among the observers was high (Table II). There was no significant difference in agreement among the observers between the three groups.

No discs in either control group (group 1 or 2) were considered by at least two observers to have improved or to have deteriorated. The difference in frequency of improvement in the study group in comparison to either of the two control groups was highly significant ($P < 0.003$).

There was no significant difference between the three groups in race or sex. Of the 17 patients whose discs improved, 10 have primary open-angle glaucoma, 3 secondary glaucoma, 3 juvenile glaucoma, and 1 primary open-angle glaucoma. Age and preoperative and postoperative intraocular pressure are shown in Table III.

In this study, then, one third of the patients having a decrease in pressure of 30% or more (17 of 51 cases) showed an apparent improvement in the appearance of the optic nerve head.

If the appearance of the optic disc has improved, it seems logical to conclude that the intraocular pressure has been lowered below the level

TABLE II: AGREEMENT AMONG OBSERVERS FOR EACH GROUP

	CONTROL 1	CONTROL 2	STUDY GROUP	TOTAL
3 of 3 agreement	24	20	38	82
2 of 3 agreement	1	3	13	17
None	0	1	0	1
Total	25	24	51	100

TABLE III: AGE AND INTRAOCULAR PRESSURES (IOPs) OF EACH GROUP

			STUDY GROUP	
	CONTROL 1	CONTROL 2	IMPROVED DISCS	NONIMPROVED DISCS
Age range (yrs)	60 (22-73)	51 (30-71)	52 (17-80)	42 (24-76)
Average pre IOP (mm Hg)	—	18.5	29.7	33.2
Average post IOP (mm Hg)	—	20.6	15.9	11.4

responsible for the development of glaucomatous cupping. Presumably, this level of intraocular pressure should be low enough to prevent further damage. In patients with early or moderate glaucomatous cupping, it seems reasonable to assume that this will reflect stability of the disease. This conclusion is based on the assumption that whatever is responsible for the resistance of the disc and neurons to damage remains relatively constant with time. This is an assumption. It may be that a level of intraocular pressure tolerable at one point of the patient's history may at a later date become intolerable. It is also recognized that, as discussed earlier, visual field deterioration may continue despite an intraocular pressure which is lower than that required initially to cause damage to the optic nerve. Improvement in the appearance of the optic disc, especially in a patient with far-advanced disease, does not mean that the patient will necessarily have an improved or stable visual field. If apparent improvement in the appearance of the optic disc is noted, yet visual field deterioration continues, it seems logical to conclude that further lowering of intraocular pressure will not be beneficial. This also appears to be a new concept, with important implications for the management of patients. In patients showing further deterioration of vision despite apparent improvement in the appearance of the optic nerve, it would seem logical not to attempt to lower the intraocular pressure still further despite the presence of the continuing visual field loss, as one would not expect any further improvement in a clinical course from a lower intraocular pressure.

In early or moderate glaucoma it appears reasonable to expect that improvement in the appearance of the optic disc will be associated with improvement in visual function; our clinical impression supports such a correlation. However, it should *not* be concluded that improvement in the appearance of the optic disc is necessarily going to be associated with improvement in visual function in all cases, especially in those with advanced disease. In fact, in patients with advanced glaucomatous nerve

damage, apparent improvement in the optic disc may be an unfavorable observation, as concerns visual function. As the anatomy of the optic disc is altered the already badly damaged optic neurons may suddenly become even more damaged. Conceivably this structural rearrangement that takes place at the time intraocular pressure is lowered may be the mechanism responsible for "wipe-out."[36]

Visual fields can improve when intraocular pressure is lowered.[38-47] How frequently this occurs in patients with glaucomatous disease has not been established. Some studies have indicated no correlation between the fall of intraocular pressure and improvement in the visual field.[48-50] Others appear to find a relationship which is quite definite.[44-47,51] Those failing to show a correlation have usually been shorter-term studies and have usually not defined the populations or analyzed the visual field as selectively as those showing a correlation. It is important to recall that both of the variables being considered, intraocular pressure and visual field change, are highly subject to "noise." While intraocular pressure may be accurately determined for a precise moment in time, how accurately that specific measurement reflects the behavior of intraocular pressure throughout the day and over time is far more uncertain. Although it seems likely that an individual in whom the intraocular pressure is measured at three separate times to be around 30 mm Hg prior to trabeculoplasty, and around 15 mm Hg following trabeculoplasty has actually had a fall of intraocular pressure, such measurements are by no means proof of that. It may simply be that the patient in question was so bothered by the trabeculoplasty that he decided to use his medications prior to his subsequent office visits in order to assure that his intraocular pressure had fallen. Or there may have been marked and prolonged spikes or troughs of intraocular pressure between examinations, and such changes were obviously not able to be recorded by the ophthalmologist. Visual field changes are also subject to variability. Such improvements and deteriorations may be indications solely of the testing event, and not representations of real improvement or deterioration in optic nerve function. Because of this high degree of "noise" both with regard to the intraocular pressure and the visual field, where studies are able to find a high correlation between fall of intraocular pressure and improvement of the visual field, it is reasonable to conclude that the actual correlation is, in fact, even higher. Table IV provides data that suggest a strong correlation between change in intraocular pressure and change in visual field. It is interesting that persons in whom there is advanced visual field loss appear to have decreased ability for the field to improve in association with decrease in intraocular pressure. This is not an unexpected finding.

TABLE IV A & B: RELATIONSHIP BETWEEN CHANGE IN INTRAOCULAR PRESSURE (IOP) AND CHANGE IN VISUAL FIELD IN PATIENTS WHO HAD EITHER TRABECULOPLASTY OR TRABECULECTOMY*

	IV A	
BEHAVIOR OF IOP	WORSE OR ? WORSE	NO CHANGE, ? BETTER, OR BETTER
Not improved	8	1
Improved	8	20
Total	16	21

	IV B	
BEHAVIOR OF IOP	WORSE, OR ? WORSE	? BETTER, OR BETTER
Not improved	8	1
Improved	8	10
Total	16	11

IV A; statistical significance, $P = 0.002$. IV B; statistical significance, $P = 0.025$.

*Information modified from reference 51. Visual field examination with Octopus computerized perimetry prior to and around 3 months following trabeculectomy or trabeculoplasty. Intraocular pressure was also measured at the same time. The table shows in a form designed for chi-square analysis the groupings of patients according to behavior of intraocular pressure and behavior of visual field. Table IV A includes those patients in whom there was no significant change in visual field and patients whose visual field was thought to have improved following surgery. The indication for surgery was deterioration of visual function. It was concluded that if the field stopped deteriorating, there had been a beneficial effect. Table IV B eliminates the patients in whom there was no apparent change in the field, and considers only those in whom the field appeared to continue to deteriorate and those in whom the visual field appeared to improve, and relates the changes to behavior of intraocular pressure.

If indeed improvement in the visual field or the appearance of the optic disc is common following lowering of intraocular pressure, why has it not been observed more frequently in the past? This is an important question that needs to be answered. There are several reasons. Probably the most important is that the phenomenon has simply not been believed to occur and therefore has not been looked for. (The major purpose of this presentation is to change that belief and to encourage studies that will define accurately the frequency or infrequency with which such changes actually occur.) An additional reason is that the changes that occur are in most cases slight and, as such, cannot be detected by techniques which are not

sufficiently sensitive to document small changes. While in some cases the decrease in glaucomatous cupping is truly dramatic, such is not the rule. Unless photographic documentation of the optic nerve head has been obtained, and unless the photographs are carefully examined, small changes will not be noted. It has been disturbing to the senior author of this paper to note how frequently a review of photographs for purposes of a study has shown improvement or deterioration of the optic nerve head that was not noted clinically, even though the photographs of the optic nerve head had been obtained as a routine part of clinical care, specifically for the purpose of noting such changes, and how even more frequently changes were noted in the photographs but had not been observed by ophthalmoscopic examination of the optic disc. The ability to examine the configuration of optic discs quantitatively by using image analysis techniques should dramatically improve the ability to recognize the amount and the pattern of change in the optic disc, change for the better or for the worse.

Similarly, changes in the visual field will not be reliably detected unless the instrument employed has the capability to do so. Just as one cannot see the most distant galaxies with opera glasses, and one cannot see quarks with a microscope, so one cannot find small changes in the optic disc or visual field without appropriate instrumentation. Where the magnitude of noise is greater than the magnitude of change, real alterations occur but will be missed, because of the inability of the system to distinguish them. This may well be the case with regard to the type of visual field changes alluded to in this report. Unless the visual field testing is vigorously standardized, as with automated or computerized perimetry, and unless there is elimination of variables such as pupil size, refractive error, etc, noice cannot be effectively limited. Nor is standardization alone adequate. The technique employed must also be sufficiently sensitive to detect small changes. This requires utilization of programs that will determine threshold accurately, define areas of concern, and provide valid estimates of variability.

A patient with glaucoma in whom there is progressive visual field loss may be assumed to fall into one of three categories: (1) the progressive visual field loss is not due to glaucoma, (2) the neurons have been so mortally wounded by the glaucomatous process that no matter what happens they will continue to deteriorate, or (3) the cause of the damage to neurons has not been corrected; that is, the intraocular pressure is still higher than tolerable. Regarding category 1, it is usually possible to rule out causes other than glaucoma for progressive optic nerve damage and visual field loss. As for category 2, just how badly damaged an optic nerve

needs to be before the damage will continue to progress despite elimination of the causative factor, elevated intraocular pressure, is not known and deserves further study.[13] We contend that in early or moderate disease, and in some patients with advanced disease as well, glaucomatous damage continues because intraocular pressure is higher than the eye can tolerate.

The only *sure* way in which intraocular pressure can be known to have fallen to a level which will be as well tolerated by the eye in question as possible is by seeing an improvement in the disc or in visual function.

The development of quantitative perimetry and quantitative ophthalmoscopy should allow continued improvement in the ability to detect small, definite changes in the visual field and the optic disc.[52] It is hoped that such increased sensitivity and specificity of observation may lead to confirmation of the validity of the concept of management that is presented here and will result in a diminution of the now all-too-large number of patients who become visually incapacitated by glaucoma, a disease that theoretically can be managed so that visual function is preserved.

REFERENCES

1. Emery JM, Landis D, Paton D, et al: The lamina cribrosa in normal and abnormal eyes. *Trans Am Acad Ophthalmol Otolaryngol* 1974; 78:OP290.
2. Fuchs E: *Textbook of Ophthalmology*. New York, Appleton-Century-Crofts, 1982, p 334.
3. ———: Über die Lamina Cribrosa. *Albrecht Von Graefes Arch Klin Exp Ophthalmol* 1916; 91:435-485.
4. Anderson DR: Pathogenesis of glaucomatous cupping: A new hypothesis, in Symposium on Glaucoma. *Transactions of the New Orleans Academy of Ophthalmology*. St Louis, CV Mosby, 1975, p 81-94.
5. Quigley HA, Hohman RM, Addicks EM, et al: Morphological changes in the lamina cribrosa correlated with neural loss in open-angle glaucoma. *Am J Ophthalmol* 1983; 95:673.
6. von Jaeger E: Über Glaucoma und seine Helung durch Iridectomie. *Z Ges Aerzte Wien* 1858; 14:465-474, 484-491.
7. Schwartz B, Reiser JC, Fishbein SL: Fluorescein angiographic defects of the optic disc in glaucoma. *Arch Ophthalmol* 1977; 95:1961-1974.
8. Spaeth GL: *Pathogenesis of Nerve Damage in Glaucoma Contributions of Fluorescein Angiography*. New York, Grune & Stratton, 1977.
9. Kronfeld PC, McGarry HI: Five-year follow-up of glaucomas. *JAMA* 1948; 136:957-965.
10. Werner ED, Drance SM: Progression of glaucomatous field defects despite successful filtration. *Can J Ophthalmol* 1977; 12:275-280.
11. Crapps EE, Levy NS: Displacement of the lamina scleralis with pressure elevation. *Invest Ophthalmol Vis Sci* (Suppl) 1981; 20:82.
12. Quigley HA: The pathogenesis of reversible cupping in congenital glaucoma. *Am J Ophthalmol* 1977; 84:358-370.
13. Grant WM, Burke JF Jr: Why do some people go blind from glaucoma. *Ophthalmology* 1982; 89:991-998.

14. Leydhecker W: Is glaucoma therapy useless?, in GK Krieglstein, W Leydhecker (eds): *Glaucoma Update II*. Berlin, Springer-Verlag, 1983, pp 95-102.
15. Kass MA, Kolker AE, Becker B: Prognostic factors in glaucomatous visual field loss. *Arch Ophthalmol* 1976; 94:1274.
16. Linner E, Strömberg U: Ocular hypertension: A five year study of the total population in a Swedish town and subsequent discussions, in W Leydhecker (ed): *Glaucoma: Tutzing Symposium*. Basel, S Karger 1967, p 187.
17. Wilensky JT, Podos SM, Becker B: Prognostic parameters in primary open angle glaucoma. *Arch Ophthalmol* 1974; 91:200.
18. Armaly MF: Ocular pressure and visual fields: A ten year follow-up study. *Arch Ophthalmol* 1969; 81:25.
19. Bankes JLK, Perkins ES, Tsolokis S, et al: Bedford glaucoma survey. *Br Med J* 1968; 1:791.
20. Hollows FC, Graham PA: Intra-ocular pressure, glaucoma, and glaucoma suspects in a defined population. *Br J Ophthalmol* 1966; 50:570.
21. David R, Livingston DG, Luntz MH: Ocular hypertension: a long-term follow-up of treated and untreated patients. *Br J Ophthalmol* 1977; 61:667-676.
22. Jenson JE: Glaucoma screening: A 16-year follow-up of ocular normotensives. *Acta Ophthalmol* 1984; 62:203-209.
23. Schwartz B, Talusan AG: Spontaneous trends in ocular pressure in untreated ocular hypertension. *Arch Ophthalmol* 1980; 98:105-111.
24. Anderson DR: The management of elevated IOP with normal disc and visual field: I. The disc-field status as a risk predictor. *Surv Ophthalmol* 1977; 21:479-489.
25. Quigley HA: The challenge of when to treat in glaucoma, in Symposium on the Laser in Ophthalmology and Glaucoma Update. *Transactions of the New Orleans Academy of Ophthalmology*. St Louis, CV Mosby, 1985, pp 1-9.
26. von Jaeger E: *Ophthalmoskopischer Hand-Atlas*. Wien, KK Hof-und Staatsdruckerei, 1869.
27. Shaffer RN: The role of astroglial cells in glaucomatous disc cupping. *Doc Ophthalmol* 1969; 26:516-525.
28. Neumann E, Hyams SW: Intermittent glaucomatous excavation. *Arch Ophthalmol* 1973; 90:6466.
29. Shaffer RN, Hetherington J Jr: The glaucomatous disc in infants; a suggested hypothesis for disc cupping. *Trans Am Acad Ophthalmol Otolaryngol* 1969; 73:929-935.
30. Shoise Y, Danda T: Quantitative analysis of "optic cup" and its clinical application. II. Consideration of clinical cases. *Jpn J Clin Ophthalmol* 1974; 28:367-374.
31. Hetherington J Jr, Shaffer RN, Hoskins HD Jr: The disc in congenital glaucoma, in R Etienne, GD Paterson (eds): *XXII Congres International d'Optalmologie, Interantional Glaucoma Symposium*. Albi, France, May 20-24, 1974. Marseille, Diffusion Generale de Librairie, 1975, pp 127-151.
32. Iwata K, Sobue K, Imai A, et al: On the reversibility of the glaucomatous disc cupping and the visual field. *Jpn J Clin Ophthalmol* 1977; 31:759-765.
33. Spaeth GL, Fernandes E, Hitchings RA: The pathogenesis of transient or permanent improvement in the appearance of the optic disc following glaucoma surgery. *Doc Ophthalmol Proc Ser* 1980; 22:111-126.
34. Pederson E, Herschler J: Reversal of glaucomatous cupping in adults. *Arch Ophthalmol* 1982; 100:426-431.
35. Wax MB, Ridley ME, Magargal LE: Reversal of retinal and optic disc ischemia in a patient with sickle cell trait and glaucoma secondary to traumatic hyphema. *Ophthalmology* 1982; 89:845-851.
36. Greenidge KC, Spaeth GL, Traverso CE: Change in the appearance of the optic disc associated with lowering of intraocular pressure. *Ophthalmology* 1985; 92:897-903.
37. Katz LJ, Spaeth GL, Cantor LB, et al: Frequency of reversibility of optic disc cupping in adults with glaucoma. *Invest Ophthalmol Vis Sci* (ARVO Suppl) 1985; 26:223.

38. Niesel P, Flammer J: Correlations between intraocular pressure, visual field, and visual acuity, based on 11 years of observations of treated chronic glaucomas. *Int Ophthalmol* 1980; 3:331-335.
39. Greve EL, Furuno F, Verduin WM: The clinical significance of reversibility of glaucomatous visual field defects. *Doc Ophthalmol* 1979; 19:197-203.
40. Hirsch J: Reversible field loss in glaucoma: A preliminary report. *Presented at the 1st North American Octopus Users Conference*, July 1982.
41. Luntz MH, David R: Reversibility of glaucomatous visual field defects: Three cases with different causes. *Glaucoma* 1981; 3:205-212.
42. Paterson G: Effect of intravenous acetazolamide on relative arcuate scotomas and visual field in glaucoma simplex. *Proc R Soc Med* 1970; 63:865-869.
43. Phelps CD: Visual field defects in open angle glaucoma: Progression and regression. *Doc Ophthalmol* 1979; 19:187-196.
44. Spaeth GL: Regression of optic nerve and visual field defects in glaucoma, in GK Krieglstein, W Leydhecker (eds): *Glaucoma Update II*. Berlin, Springer-Verlag, 1983, pp 81-82.
45. Spaeth GL, McAllister JA, Traverso CE, et al: Lowering intraocular pressure alters the course of glaucoma: The effect of trabeculectomy on intraocular pressure and visual fields. *Br J Ophthalmol.* In press
46. Starita RJ, Traverso CE, Spaeth GL, et al: Short and long term effects of argon laser trabeculoplasty on the relationship between intraocular pressure and visual field. *Invest Ophthalmol Vis Sci* (ARVO Suppl) 1985; 26:41.
47. Yassur Y, Lusky M, Grunewald E, et al: Regression of optic disc excavation and visual field damage following glaucoma surgery in eyes with long-standing glaucoma. *Glaucoma* 1984; 6:202-207.
48. Heijl A, Bengtsson B: The short-term effect of a laser trabeculoplasty on the glaucomatous visual field: A prospective study using computerized perimetry. *Acta Ophthalmol* 1984; 62:705-714.
49. Holmin C, Storr-Paulsen A: The visual field after trabeculectomy: A follow-up using computerized perimetry. *Acta Ophthalmol* 1984; 62:230-234.
50. Holmin C, Bauer B: Laser trabeculoplasty in open angle glaucoma—A short term study using computerized perimetry. *Acta Ophthalmol* 1984; 62:337-341.
51. Spaeth GL: The effect of change in intraocular pressure on the natural history of glaucoma: Lowering intraocular pressure in glaucoma can result in improvement of the visual field. *Trans Ophthalmol Soc UK* 1985; 104:256-264.
52. Takamoto T, Schwartz B: Reproducibility of photogrammetric optic disc cup measurements. *Invest Ophthalmol Vis Sci* 1985; 26:814-817.

DISCUSSION

DR DOUGLAS R. ANDERSON. Our thanks to Doctor Spaeth for sharing his observations and thoughts with us.

In this discussion, reversibility of cupping and field loss need to be discussed separately, as they seem to be two different phenomena.

Reversibility of cupping is most often observed in children. Doctor Spaeth's group has documented that a detectable amount of "filling in" of the cupping also occurs in one-third of adults whose antiglaucoma therapy achieves a 30% lowering of pressure. A major portion of the reversibility must be due to an elastic relaxation of the posterior bowing of the lamina cribrosa and relaxation of the stretching of the peripapillary sclera. This elastic relaxation occurs right away. For example,

in a recent infant aniridic patient fo mine, there was opportunity to examine the fundus immediately at the completion of surgery, and the cup had already filled in. There are undoubtedly fluid shifts and changes in cytoplasmic volume that may also occur over a longer period of time, but presumably axon regeneration or proliferation of other tissue elements does not occur.

The mechanism of visual recovery is different. Only some of the lost vision is potentially reversible, and specifically that due to axon drop-out is surely not. However, there is evidently a stage of damage in which axons do not conduct nervous impulses but are viable and can recover function—even alternately losing and regaining function. For example, I have seen at the two ends of the spectrum (1) a case of early glaucoma with a single dense paracentral scotoma that could easily be demonstrated on some occasions and could not be detected at all on other occasions, and (2) a case of end-stage glaucoma with no light perception on some occasions but 20/50 acuity in a small seeing island on other office visits. Thus there is hope that successful control of the pressure may allow return of some part of the lost visual function.

It is difficult to judge how often and to what degree real recovery of optic nerve function occurs after control of the intraocular pressure. In some of the studies of Doctor Spaeth's group, certain confounding variables were specifically eliminated—for example, cases in which an improved field might have been due to a larger pupil postoperatively, and cases in which a poorer field might have resulted from a media opacity with reduced acuity. In fact, they were so careful about obtaining pure examples that more cases were eliminated from the study than were retained, because so many cases had features that could have affected visual function in ways other than by improved optic nerve function. The practitioner who thinks he is observing an example of improvement in visual field must consider whether or not potential confounding factors might be present, such as a larger pupil now or development of a "learning effect" in a patient upon performing a second or third field examination.

Scientific interpretation of the data is difficult because of the fact that there are physiologic fluctuations of visual function from one test to another, and because of "regression to the mean." This statistical phenomenon enters the data in two ways. First, surgery will tend to be done immediately after a visual field test that was worse than the previous test. Even without actual improvement in optic nerve function, the postoperative field will tend to be better to whatever degree the preoperative worsening was simply due to the physiologic variation in visual function and its testing. Second, variability is greater in defective areas, and points that are particularly bad on any one examination will tend to be better the next time simply because some of the badness of some of these points will have been due to the physiologic variability. Contrariwise, points at which the variation happened to be in the direction of better sensitivity will tend to be in the more normal areas of the field and will tend to worsen slightly on the next examination. The effect of this "regression to the mean" is small, but so are the changes in the field being reported here.

Although further work is needed to know how frequently and how much true field improvements occurs, the clinical philosophy advocated by Doctor Spaeth is most instructive. Certainly the emphasis in management of glaucoma must continue to be on the status of the optic nerve and visual field, not simply the intraocular pressure. We can feel more comfortable that the management has achieved satisfactory control in patients that manifest a reversal of cupping or improved sensitivity scores on visual testing. Of course, the control may also be considered satisfactory in the larger number of patients who have substantial lowering of intraocular pressure even without evident reversal of cupping or field loss, as long as continued monitoring proves the progress of the disc damage and the field loss have been halted.

DR GEORGE SPAETH. I thank you, Doctor Anderson, for your thoughtful comments.