NONCONTACT TRANSSCLERAL ND:YAG CYCLOPHOTOCOAGULATION: A LONG-TERM FOLLOW-UP OF 500 PATIENTS*

BY *M. Bruce Shields,* MD, AND (BY INVITATION) *Sarah E. Shields*

THERE ARE CERTAIN GLAUCOMA PATIENTS WITH WHOM THE OPHTHALmologist is very familiar because of their poor response to standard medical and surgical therapy. They may have one of the more difficult glaucomas to treat, such as neovascular glaucoma, glaucoma in aphakia or pseudophakia, or glaucoma associated with active inflammation, or they may have had multiple failed filtering procedures for any form of glaucoma. These patients are often desperate because their glaucoma may be about to take whatever vision they have left.

A number of surgical procedures have been tried for patients in this high-risk population. Some surgeons have utilized a modified filtering procedure, such as a laser sclerostomy. Others have employed adjunctive agents to modify wound healing, such as 5-fluorouracil or mitomycin C, with either a modified or standard filtering procedure. Still others have turned to drainage implant devices, such as the Molteno implant. Each of these operations is designed to lower the intraocular pressure by increasing the rate of aqueous outflow. An alternative approach is to reduce aqueous production by one of the cyclodestructive procedures, such as transscleral cyclophotocoagulation.

At present, there is insufficient evidence to claim superiority for any one of these operations over the others. Surgeons have continued to evaluate one or more of the surgical options in the hope of finding the best help for these desperate patients. In the mid-1980s, we began evaluating transscleral cyclophotocoagulation because we felt that it might have the most to offer for at least some of the patients in this high-risk population.

Following a series of laboratory experiments, which were used to estab-

*From the Duke University Medical Center, Department of Ophthalmology, Durham, North Carolina.

lish preliminary treatment parameters, we began a clinical trial of noncontact transscleral Nd:YAG cyclophotocoagulation in August 1987.[1,2] We report herein our long-term experience with the first 500 patients in this trial.

MATERIALS AND METHODS

The 500 patients in this study were treated consecutively in the Glaucoma Service of the Duke University Eye Center by the senior author or under his direct supervision. Records were maintained on each patient in a prospective manner and have been entered into a computer database for retrospective analysis. For cases in which our records contained less than 6 months' follow-up, we contacted the patient's referring ophthalmologist to update our database. For patients who received bilateral cyclophotocoagulation, we analyzed and report only the first eye that was treated.

Selection criteria for patients in this trial included uncontrolled glaucoma, which had failed to respond to medical therapy and to standard laser and incisional surgical procedures, or in which such procedures were not possible or were felt to have a low chance of success. No forms of glaucoma were excluded from the study, although the most common were neovascular glaucoma, glaucomas in aphakia or pseudophakia, glaucomas associated with active inflammation, or any form of glaucoma with multiple failed filtering or other glaucoma procedures. There was no exclusion for age in the study, although it was necessary for the patient to be old enough and sufficiently cooperative to allow retrobulbar anesthesia in the office and to sit up at the slit lamp during the procedure.

A portion of these 500 patients have been previously reported in one of three series with shorter follow-up.[3-5] The first 100 patients were treated under a protocol approved by the Investigational Review Board, in which the investigative nature of the procedure was explained.[3] These patients were given the option of cyclophotocoagulation or cyclocryotherapy, the latter of which was the standard cyclodestructive procedure at that time. Subsequently, with the advent of Food and Drug Administration approval, cyclophotocoagulation was recommended to the patient as the procedure of choice. In most cases, however, the alternative of a filtering procedure was also explained.

All procedures in this study were performed on a single Nd:YAG laser (Microruptor II, HS-Meridian, formerly Lasag). This is a noncontact laser, which uses slit-lamp delivery. For cyclophotocoagulation, it is operated in a thermal, pulsed mode of 20 msec and can reach energy levels of up to 9 J. It has a HeNe aiming beam, which can be offset from the Nd:YAG therapeutic beam, so that the latter can be focused internally at a preset distance when

the aiming beam is focused on the conjunctiva.

Before the laser procedure, the patients received retrobulbar anesthetic consisting of 4 ml of lidocaine 4% and bupivacaine 0.75% in equal parts with hyaluronidase 150 USP units. The patient was then taken to the laser room and seated at the slit lamp. In the first series of 100 patients, the lids were separated by the surgeon, and the aiming beam was focused directly on the conjunctiva. In the second series and in all subsequent patients, cyclophotocoagulation was performed with a special contact lens, which has been previously described.[4] This lens separates the lids, compresses and blanches the conjunctiva, and provides etch marks for measuring the position of the laser beam from the limbus.

Laser settings for all patients consisted of the thermal, pulsed mode (20 msec), a maximum offset of 9 between the aiming and therapeutic beam (3.6 mm in air), and the Multiple Mode (multiple point source of the therapeutic beam, as compared with a single focal point with the Fundamental Mode). An energy level of approximately 8 J was used in the first two series. In the third series, patients were randomized between 4 and 8 J.[5] On the basis of information gained from this study, the energy level for the remaining patients was set between 4 and 8 J, with lower levels for patients with lower baseline intraocular pressures and better visual potential. With the eye in approximately the primary position, the aiming beam was positioned 1.5 mm from the limbus at the 12-o'clock position, and 30 evenly spaced laser lesions were applied for 360 degrees. The distance from the limbus was tapered to 1 mm at the 3- and 9-o'clock positions.

In some patients, retrobulbar anesthesia was insufficient, which was most often in the temporal quadrant. If it was possible to treat at least three quadrants, the remaining applications were placed between the previous laser applications, for a total of 30, sparing the inadequately anesthetized quadrant. When it was not possible to treat at least three quadrants because of inadequate anesthetic, supplemental retrobulbar anesthesia was administered.

At the end of the procedure, 0.5 ml of dexamethasone was injected subconjunctivally and the eye was dressed with atropine ointment and a light gauze dressing. No additional medication was given before or after the procedure on a routine basis to avoid postoperative intraocular pressure elevations. The patients were examined 2 hours later. They were then instructed to continue all current glaucoma medications, except for miotics, and to add atropine 1% twice daily and an antibiotic-steroid combination or prednisolone 1% four times a day for approximately 10 days. (The antibiotic-steroid combination was used initially because of occasional conjunctival disruption that occurred prior to use of the contact lens. With the contact

lens, however, these conjunctival disruptions are rarely seen, and antibiotic prophylaxis is not felt to be necessary.)

The patients were instructed to return on the first postoperative day. If they were doing well at that time, they were asked to return in 1 month. They were followed thereafter every 3 to 4 months, or more frequently as their situation required. The glaucoma medicines were gradually reduced or eliminated as the reduction in intraocular pressure permitted.

Patients who were not controlled with the first cyclophotocoagulation procedure usually received one or more subsequent treatments. An effort was made to wait at least 1 to 2 months between treatments, although some patients with dangerously high pressures required subsequent treatment sooner than this. For most patients, the protocol for repeated therapy was identical to that for the initial treatment. In some patients, however, whose pressures were dangerously high or who had repeatedly failed to respond to the standard protocol, a modified protocol was employed in which two rows of applications 1 and 2 mm from the limbus were applied for a total of 40 to 50 applications.

RESULTS

The patients ranged in age from 11 to 91 years (mean, 63.1 years). There were 344 white and 156 black patients (241 men and 259 women) in the trial. Table I summarizes the distribution of glaucoma types, which were primarily glaucoma in pseudophakia (161 patients), neovascular glaucoma (130), and glaucoma in aphakia (124). Thirty-two patients had chronic open-angle glaucoma for which glaucoma filtering surgery had repeatedly failed or in which the visual potential was so poor that the laser procedure was felt to be a better option for the patient. Forty-one patients, most of whom were in the aphakic or pseudophakic categories, had also undergone penetrating keratoplasty.

The preoperative visual acuity was 20/400 or better in 229 patients, 32 of whom were 20/30 or better. The mean visual acuity for these 229 patients was 20/193.4. Among the remaining 271 patients, the vision was counting fingers in 98, hand movement in 113, light perception in 47, and no light perception in 13. Indication for cyclophotocoagulation in the latter group was intractable pain, and most of this was in the earlier years of the trial. The preoperative intraocular pressure ranged from 18 to 80 mm Hg (mean, 38.7 mm Hg).

Follow-up time ranged from 6 to 75 months, with a mean of 24 months for 458 of the patients in the study. In the remaining 42 patients, follow-up information could not be obtained beyond 1 to 5 months, and these patients

TABLE I: DISTRIBUTION OF GLAUCOMA TYPES

GLAUCOMA TYPES	NO. OF PATIENTS
Glaucoma in pseudophakia	161
Neovascular glaucoma	130
Glaucoma in aphakia	124
Chronic open-angle glaucoma*	32
Glaucoma associated with uveitis	22
Glaucoma following trauma	17
Chronic angle-closure glaucoma	5
Developmental glaucoma	4
Glaucoma associated with neoplasia	3
Iridocorneal endothelial syndrome	2

*Most cases had multiple failed filtering surgery.

were not included in the final analyses.

At the 2-hour postoperative examination, most patients had moderate conjunctival hyperemia. In the initial series in which the contact lens was not used, there was typically a prominent white conjunctival burn at each treatment site. This was occasionally associated with superficial tissue disruption, especially in patients with conjunctival pigmentation. With the subsequent use of the contact lens, the conjunctival burns were smaller and tissue disruption was rare. Even without the use of the contact lens, however, the conjunctival burns were usually not apparent after 24 to 48 hours.

Slit-lamp examination 2 hours after cyclophotocoagulation typically revealed an anterior chamber reaction of 1 to 2+ flare and cell. A 3+ flare and cell reaction or a 4+ reaction with fibrin was seen in 12% of the cases. A small hyphema was observed in four patients, all of whom had neovascular glaucoma.

The intraocular pressure 2 hours after the procedure was unchanged in 52 patients (10%). The pressure was reduced from baseline in 355 patients (71%). This reduction ranged from 1 to 55 mm Hg (mean, 12.5 mm Hg). Ninety-three patients (19%) had a rise in pressure at the 2-hour check, which ranged from 1 to 30 mm Hg (mean, 5.97 mm Hg).

On the first postoperative day, the patients were questioned regarding the degree of pain they experienced after the retrobulbar anesthesia had worn

off. Twenty-two percent of the patients reported either no pain or a mild ache that did not require pain medication. Sixty-six percent indicated that they had a mild to moderate ache around and behind the treated eye, which was relieved by aspirin or equivalent and was gone by the following morning. Twelve percent reported a more severe pain, which required an analgesic stronger than aspirin. Even in the latter group, however, the pain rarely persisted the following day.

Examination of the eye on postoperative day 1 typically revealed mild to moderate conjunctival hyperemia. In most cases, the only evidence of previous conjunctival laser burns was a slight focal increase in conjunctival hyperemia. The anterior chamber reaction was 1 to 2+ flare and cell in 55%, 3+ flare and cell in 33%, and a fibrin reaction in 12%.

The intraocular pressure on the first postoperative day was lower than the preoperative level in 90% of patients. This pressure reduction ranged from 1 to 60 mm Hg (mean, 17.8 mm Hg). Those patients who had a pressure that was higher than the baseline had an increase between 1 and 23 mm Hg (mean, 8 mm Hg).

By the 1-month check, the conjunctiva was typically white, except for those cases in which the hyperemia was felt to be related to topical medications, underlying disease process, or persistent pressure elevation. The anterior chamber reaction in almost all patients was a 1+ flare with a rare cell. This low-grade anterior chamber reaction persisted permanently in most patients.

The intraocular pressure after 1 month was reduced from baseline in 81% of the patients. This pressure reduction ranged from 1 to 68 mm Hg (mean, 19 mm Hg). In 62% of the total population, this pressure reduction was considered to be adequate to protect the optic nerve head in eyes with visual potential or to relieve pain in the remaining cases. Among those patients whose pressure was higher than baseline at 1 month, the range was 1 to 25 mm Hg (mean, 9.6 mm Hg).

One hundred seven patients (21%) underwent one or more repeated procedures. The time from the initial procedure to the first repeat ranged from 2 weeks to 3 years. The majority of the repeated procedures, however, were performed during the first 6 months after the initial procedure. A second repeated procedure was required in 22 patients (4%). Five patients underwent a third repeated procedure, and one patient each received 4, 5 and 6 repeated procedures. Early postoperative pressures, inflammation, and pain were similar to that experienced after the initial procedure.

At the final examination, following one or more cyclophotocoagulation procedures, 94% of the patients had an intraocular pressure that was lower than the preoperative level. The pressure reductions in this group ranged

from 1 to 74 mm Hg (mean, 24 mm Hg). This degree of pressure reduction was sufficient to achieve the therapeutic goal of protecting the optic nerve or preventing pain in 87% of the patients. In the remaining patients with inadequate pressure control, no further treatment was performed because patients either no longer had a potential for useful vision or refused further surgery. However, no patient refused repeated treatment because of pain from the surgery, other than that associated with the retrobulbar anesthesia.

Hypotony, which was defined as an intraocular pressure of 7 mm Hg or less with associated visual reduction, was seen in 8% of the patients, although phthisis was documented in only six individuals. These complications did not correlate with the frequency of repeated procedures.

The mean final intraocular pressure reduction was 25.9 mm Hg among patients 40 years of age or younger, compared with 24.3 mm Hg in those older than 40 years. However, 25 of the 59 patients in the younger group (43%) required one or more repeated procedures, compared with 18% in the older age-group. Black patients had a mean final pressure reduction of 25.6 mm Hg, and 19% required repeated procedures, compared with 23.8 mm Hg and 22.7%, respectively, for white patients. Patients with neovascular glaucoma had a final mean pressure reduction of 33.5 mm Hg, and 15% required repeated procedures, compared with 18.9 mm Hg and 22.8% in patients with glaucoma in pseudophakia and 13.8 mm Hg and 26% in patients with glaucoma in aphakia. Patients in the neovascular glaucoma group also had a higher mean baseline intraocular pressure, 51.7 mm Hg, compared with 32.4 mm Hg and 31.9 mm Hg in the pseudophakia and aphakia groups, respectively. Patients with neovascular glaucoma were also more likely to develop hypotony or phthisis.

At the time of the final examination, the visual acuity in the treated eye was reduced by two or more lines on the Snellen chart or by one or more low vision categories in 39% of the patients. In most cases, the visual loss did not exceed 3 lines on the Snellen chart or one low vision category (eg, from counting fingers to hand movements). A greater degree of reduced visual acuity, however, was documented in 36 patients, with 8 patients progressing to no light perception. All but one of the latter patients had hand movement or light perception vision preoperatively. Among the 32 patients with a preoperative visual acuity of 20/30 or better, 12 lost 2 or more lines on the Snellen chart, and 5 of these patients lost 5 to 10 lines of vision. The percentages for visual loss among the major diagnostic categories were 46%, 38%, and 34% for neovascular glaucoma and glaucomas in aphakia and pseudophakia, respectively.

In at least half of the patients with reduced vision, there were additional factors that could explain progressive visual loss, such as corneal edema,

cataract, progression of an underlying retinal disorder, corneal graft rejection, or progressive glaucomatous optic atrophy in those with inadequate pressure reduction. It was difficult to determine the percentage of patients whose visual loss was due to the laser treatment, but the timing of the loss in relation to the treatment and the absence of other apparent causes suggest that the cyclophotocoagulation was most likely the cause of the reduced vision in at least half of the cases. In some cases, macular edema was documented as the apparent cause of the treatment-related visual loss. Fluorescein angiography was not performed on all patients with reduced vision, and it is assumed that this was the mechanism in many of the patients who suffered visual loss. In other cases, the mechanism may have been hypotony or phthisis, following the laser procedure.

Of the 41 patients in the study who had penetrating keratoplasty prior to the cyclophotocoagulation, 30% had clouding or graft rejection following the laser procedure. Most patients were aphakic or pseudophakic prior to the laser procedure. Among the 123 phakic patients, significant progression of the cataract was documented in 13 eyes. Among the pseudophakic patients with an intact posterior capsule, clouding of the capsule following the laser procedure was observed in seven eyes. A vitreous hemorrhage shortly after the laser procedure was seen in three patients. Other than the previously noted macular edema or sequelae of hypotony or phthisis, no treatment-related changes were seen in the retina. Specifically, there were no cases of sympathetic ophthalmia in this study.

DISCUSSION

The findings in this study are felt to support the claim that transscleral cyclophotocoagulation is superior to cyclocryotherapy and is presently the cyclodestructive procedure of choice. Compared with other cyclodestructive operations, cyclophotocoagulation has the advantages of less transient pressure elevation, less pain, and less ocular inflammation.[6-8] These observations may be explained by the fact that the laser lesion is more focal, with less damage to adjacent structures, compared with other cyclodestructive procedures. Histologic studies have shown minimal changes in the sclera or ciliary muscle, with most of the tissue change occurring when the laser energy is absorbed by the ciliary epithelium.[1,2] Other cyclodestructive procedures, which cause more damage to adjacent structures, may cause transient intraocular pressure elevation owing to shrinkage of the sclera or further compromise of the trabecular meshwork. The severe pain, which is experienced with the other cyclodestructive procedures, especially with cyclocryotherapy, may be due to the increased amount of damage and

inflammation to the ciliary muscle. This increased damage to the ciliary body and adjacent iris may also explain the increased degrees of anterior uveitis associated with the other cyclodestructive procedures.

With regard to intraocular pressure reduction, cyclophotocoagulation appears to be at least as good as the other cyclodestructive procedures. Some patients appear to respond better than others. Younger patients (≤40 years) had a final mean pressure reduction that was similar to the remainder of the study population (25.9 mm Hg and 24.3 mm Hg, respectively), but one or more repeated procedures were required in 47% of the patients, compared with 18% in the older age-group. This difference is probably due to the normal involutional changes of ciliary tissue in older eyes, rendering them more susceptible to laser damage. Black patients may respond slightly better than whites, with mean final pressure reductions of 25.6 mm Hg and 23.4 mm Hg and repeated procedures in 19% and 22.7%, respectively. This is consistent with the observation that eyes with increased uveal melanin absorb more laser energy and consequently have more tissue response to comparable laser settings.[9] The type of glaucoma may also influence the results, in that patients with neovascular glaucoma had a mean final pressure reduction of 33.5 mm Hg, compared with 18.9 mm Hg and 13.8 mm Hg for patients with glaucomas in pseudophakia and aphakia, respectively. However, the neovascular glaucoma patients had a higher mean baseline pressure, 51.7 mm Hg, compared with 32.4 mm Hg and 31.9 mm Hg in the other two groups, respectively. Furthermore, the patients with neovascular glaucoma were more likely to develop postoperative hypotony or phthisis and had a worse visual outcome (visual loss in 46% of patients, compared with 34% and 38% in patients with glaucomas in pseudophakia or aphakia, respectively).

The fact is that any of the cyclodestructive procedures can have a high success rate with regard to pressure reduction, if the ciliary body is sufficiently damaged by either heavy treatment or multiple repeated treatments. The problem with all of these operations, however, is preserving the patient's vision while obtaining the pressure reduction. In this regard, cyclophotocoagulation appears to have some advantage over the other cyclodestructive procedures. However, visual loss is still a major concern, with 39% of the patients in the present study experiencing some additional reduction in vision after the surgery. It is hard to know how many of these were a direct result of the cyclophotocoagulation, although it is estimated that the treatment was responsible for at least half the cases of visual loss.

The principal mechanism for reduced vision with cyclophotocoagulation appears to be macular edema. Whether this is due to the treatment-induced inflammation or is a direct effect of the laser energy reaching the posterior

pole is unclear. Efforts to reduce visual loss from cyclophotocoagulation should consider both possibilities.

Factors related to inflammation may include the energy level, duration of exposure, number of applications per session, and wavelength of the laser. A comparison of 4 J and 8 J with noncontact transscleral Nd:YAG cyclophotocoagulation revealed more inflammation with the higher energy level, although the final visual result was the same with the two energy levels.[5] Clinical experience with transscleral cyclophotocoagulation using a contact, fiberoptic, continuous-wave Nd:YAG laser (Surgical Laser Technology) revealed a lower incidence of visual loss of 7%, compared with our experience of 39%.[10] The explanation for this difference may be the duration of exposure, which was 700 msec with the continuous-wave laser, compared with 20 msec in our study. The duration of exposure has been shown to influence the type of tissue reaction in the ciliary body, with the shorter duration causing a more explosive disruption of tissue, while the longer duration causes a contraction and coagulation of the tissue with less disruption.[11] Preliminary studies in rabbits suggest that the tissue reaction associated with the shorter duration creates significantly more inflammation.[12]

At present, we do not have sufficient information with lasers of alternative wavelengths to determine what effect this may have on inflammation and vision. Preliminary experience with the semiconductor diode laser has revealed less visual loss than was observed in our study.[13] However, the diode laser operates in the longer-duration, continuous-wave mode, and it is not possible to determine whether it is the wavelength or the duration of exposure that may be responsible for the different clinical results. It should also be noted that the clinical trial with the diode laser was limited to 18 applications for 270 degrees, and number of applications is another factor that requires further study.

The use of anti-inflammatory agents postoperatively may be another way to reduce the loss of vision associated with inflammation following cyclophotocoagulation. We have recently begun using ketorolac tromethamine postoperatively in patients with central vision. While this may offer some benefit, it is too early to make any conclusions at this time. Nevertheless, the postoperative modulation of inflammation is another area that requires continued study.

Preventing laser energy from reaching the posterior retina may be more difficult than controlling for postoperative inflammation. With the transscleral delivery of laser energy, there is undoubtedly light that reaches the posterior pole. The transpupillary and intraocular routes of delivery, in which the laser energy is applied directly to ciliary processes, do seem to have lower rates of visual loss. However, these procedures have their own

sets of problems and most likely will not replace transscleral cyclophotocoagulation in the majority of cases.

Another way to reduce laser energy from reaching the posterior pole might be to use a photosensitizing agent that is relatively specific for the ciliary body, to reduce the amount of light energy required to produce cyclodestruction. This concept was actually used in one of the first reports of cyclophotocoagulation in animals.[14] We have also explored this possibility in our laboratory (unpublished data), and it appears to be another area in which continued research is indicated.

While the search continues for the optimum form of cyclophotocoagulation, the other important question is how current techniques of cyclophotocoagulation compare with alternative treatments for the high-risk glaucoma population. Comparisons of drainage implant devices with transscleral cyclophotocoagulation have shown a slight advantage of the former with regard to preservation of vision, although the implant surgery also required more repeated procedures.[15] In eyes with penetrating keratoplasties, the cyclophotocoagulation may have the advantage of a lower rate of graft failure.[16,17] In any comparison of cyclophotocoagulation and drainage implant surgery, it must be kept in mind that the former is a brief, outpatient procedure, while the latter is a significantly more involved incisional operation.

The use of adjunctive medications to modulate wound healing does appear to significantly increase the success rate with trabeculectomies in eyes with glaucoma in aphakia or pseudophakia and is probably the operation of choice in these patients, especially those with a potential for good central vision.[18,19] However, these operations are also associated with significant complications, including prolonged hypotony, and more clinical experience is needed before the relative merits of cyclophotocoagulation and filtering surgery with modulation of wound healing can be determined.

SUMMARY

Long-term experience with transscleral cyclophotocoagulation in 500 patients suggests that this operation is the cyclodestructive procedure of choice. It offers a reasonable surgical option in the high-risk glaucoma population, which includes patients with neovascular glaucoma, glaucomas with active uveitis, glaucomas in aphakia or pseudophakia, and other cases in which filtering surgery has failed or is felt to have a low chance for success. Satisfactory intraocular pressure reduction was achieved in 62% of the patients with one treatment session. After one or more repeated procedures in 21% of the study group, the final intraocular pressure was below baseline

in 94%, with a mean final reduction of 24 mm Hg, which was judged to be adequate for 87% of the patients.

However, visual loss remains a significant postoperative complication, with some degree of reduced vision occurring in 39% of the study population. Patients with neovascular glaucoma had the greatest percentage of visual loss at 46%, compared with 34% and 38% for patients with glaucomas in pseudophakia and aphakia, respectively. While it is hard to know how many of these cases of visual loss were a direct result of the cyclophotocoagulation, the procedure should be used with caution in eyes with a potential for good central vision.

Further study is needed to determine the relative indications for transscleral cyclophotocoagulation and the various operations to increase aqueous outflow in the management of patients in the high-risk glaucoma population.

ACKNOWLEDGMENTS

We gratefully acknowledge the assistance of Ms Robin Goodwin, who helped collect and tabulate follow-up data from referring ophthalmologists, and Mr Nick Hernandez, who helped with the computer analyses of the data. The following surgeons performed some of the cyclophotocoagulation procedures: Drs Marino Blasini, David A. Echelman, Sharon F. Freedman, Kevin N. Miller, Ruthanne B. Simmons, and Mark H. Wilkerson.

REFERENCES

1. Hampton C, Shields MB: Transscleral neodymium:YAG cyclophotocoagulation: A histologic study of human autopsy eyes. *Arch Ophthalmol* 1988;106:1121-1123.
2. Blasini M, Simmons R, Shields MB: Early tissue response to transscleral neodymium:YAG cyclophotocoagulation. *Invest Ophthalmol Vis Sci* 1990;31:1114-1118.
3. Hampton C, Shields MB, Miller KN, et al: Evaluation of a protocol for transscleral Nd:YAG cyclophotocoagulation in 100 patients. *Ophthalmology* 1990;97:910-917.
4. Simmons RB, Shields MB, Blasini M, et al: Transscleral Nd:YAG laser cyclophotocoagulation with a contact lens. *Am J Ophthalmol* 1991;112:671-677.
5. Shields MB, Wilkerson MH, Echelman DA: A comparison of two energy levels for noncontact transscleral neodymium:YAG cyclophotocoagulation. *Arch Ophthalmol* 1993; 111:484-487.
6. Caprioli J, Strang SL, Spaeth GL, et al: Cyclocryotherapy in the treatment of advanced glaucoma. *Ophthalmology* 1985;92:947-954.
7. Brindley G, Shields MB: Value and limitations of cyclocryotherapy. *Graefes Arch Klin Exp Ophthalmol* 1986;224:545-548.
8. Coleman DJ, Lizzi FL, Driller J, et al: Therapeutic ultrasound in the treatment of glaucoma: I. Clinical applications. *Ophthalmology* 1985;92:347-353.
9. Coleman AL, Jampel HD, Javitt JC, et al: Transscleral cyclophotocoagulation of human autopsy and monkey eyes. *Ophthalmic Surg* 1991;22:638-643.

10. Schuman JS, Puliafito CA, Allingham RR, et al: Contact transscleral continuous wave neodymium:YAG laser cyclophotocoagulation. *Ophthalmology* 1990;97:571-580.
11. Prum BE Jr, Shields SR, Simmons RB, et al: The influence of exposure duration on transscleral Nd:YAG cyclophotocoagulation. *Am J Ophthalmol* 1992;114:560-567.
12. Echelman DA, Nasisse MP, Shields MB, et al: Influence of exposure duration on inflammatory response to continuous-wave neodymium:YAG cyclophotocoagulation in rabbits. *Arch Ophthalmol* 1994;112:977-981.
13. Gaasterland DE, Abrams DA, Belcher CD, et al: A multicenter study of contact diode laser transscleral cyclophotocoagulation in glaucoma patients. *Invest Ophthalmol Vis Sci* (suppl) 1992;33:1018.
14. Vucicevic ZM, Tsou KZ, Nasarian IH, et al: A cytochemical approach to the laser coagulation of the ciliary body. *Bibl Ophthalmol* 1969;79:467.
15. Noureddin BN, Wilson-Holt N, Lavin M, et al: Advanced uncontrolled glaucoma. Nd:YAG cyclophotocoagulation or tube surgery. *Ophthalmology* 1992;92:430-437.
16. Sherwood MB, Smith MF, Driebe WT Jr, et al: Drainage tube implants in the treatment of glaucoma following penetrating keratoplasty. *Ophthalmic Surg* 1993;24:185-189.
17. Hardten DR, Brown JD, Holland EJ: Results of neodymium:YAG laser transscleral cyclophotocoagulation for postkeratoplasty glaucoma. *J Glauc* 1993;2:241-245.
18. The Fluorouracil Filtering Surgery Study Group: Fluorouracil filtering surgery study one-year follow-up. *Am J Ophthalmol* 1989;108:625-635.
19. Skuta GL, Beeson CC, Higginbotham EJ, et al: Intraoperative mitomycin versus postoperative 5-fluorouracil in high-risk glaucoma filtering surgery. *Ophthalmology* 1992; 99:438-444.

DISCUSSION

DR MICHAEL A. KASS. Shields and Shields present an interesting review of 500 patients who underwent neodymium (Nd):YAG cyclophotocoagulation to one eye. At final examination 94% of the patients had decreased intraocular pressure, with a mean reduction of 24 mm Hg. The authors judged that 87% of the patients had sufficient reductions of intraocular pressure to protect their optic nerves. It should be noted that 107 of the 500 patients (21%) required two or more laser procedures to reach this level of pressure control.

The authors reported low incidences of postoperative pain, inflammation, and intraocular pressure elevations. They concluded that Nd:YAG cyclophotocoagulation was better tolerated in the immediate postoperative period than cyclocryotherapy. However, 39% of the patients lost two or more lines of vision or dropped one low vision category. Among the 32 patients who had visual acuity of 20/30 or better prior to laser treatment, 12 (37.5%) lost two or more lines of vision and 5 (15.6%) lost five to ten lines of vision. The authors concluded that the laser treatment was responsible for the loss of vision in approximately 50% of the cases, with the other 50% caused by other disease processes.

I wish to recognize the great dedication of the senior author to this project. Cyclodestructive procedures have been somewhat out of fashion, and it is noteworthy that Dr Shields has had the commitment and intellectual curiosity to pursue this subject over a number of years.

This report has a number of great strengths. First, this is one of the largest series of cyclodestructive procedures ever published. Second, all of the procedures were performed either by Dr Shields or under his direction. Third, the patients appear to

have had careful follow-up. Fourth, the senior author gradually refined the technique and also introduced a new instrument for the procedure.

There are also a few concerns about this report that are worth mentioning. This is a retrospective series, and as such there is no control group. Since cyclodestructive procedures are usually performed on a heterogeneous group of patients, historical controls are not very useful either. After reading this paper, I find it difficult to determine whether this procedure is actually better than cyclocryotherapy or some other surgical approach, such as a seton procedure or a filtering procedure with mitomycin C. There are a number of published reports on these other approaches that have results and complication rates comparable to what is presented in this report For example, Bellows and Grant (*Am J Ophthalmol* 1978;85:615-621) in 1978 reported on a series of 26 eyes (18 patients) that underwent one or more cyclocryotherapy treatments. Twenty-four of 26 eyes (92%) had intraocular pressures ≤19 mm Hg with a 7- to 95-month follow-up. Complications developed in 7 of the 18 patients, but most of these were minor, only two patients developed cystoid macular edema, and only two patients had significant reductions in vision. The authors concluded that Nd:YAG cyclophotocoagulation produced fewer complications in the early postoperative period than cyclocryotherapy. I have the same clinical impression, but unfortunately this study does not provide scientific evidence one way or the other.

The authors hae made a number of detailed observations, but I believe the data analysis would have been improved by including some type of multivariate model so the effects of diagnosis, age, race, preoperative level of intraocular pressure, and previous number of intraocular operations could be included. The pair-wise analysis of the data utilized by the authors provides interesting hypotheses to test but does not control for other variables.

I mentioned previously that the authors discussed a level of intraocular pressure that protects the optic nerve. This level of pressure is going to be quite variable from patient to patient and is usually impossible to determine except in retrospect after a long period of follow-up. I think it would have been better to report the reduction of intraocular pressure and the level of intraocular pressure and let the reader draw his or her own conclusions. I think it would also have been useful to include some report of medications used before and after laser treatment to determine whether some of the patients were able to reduce their dependence on medication.

As a personal aside, I generally do not like the categories of glaucoma in aphakia or pseudophakia that are used in this paper. In fact, 285 of the 500 patients (57%) fit into one of these two categories. These categories are very heterogeneous groups that may include anything from preexisting open-angle glaucoma to chronic angle closure associated with persistent iridocyclitis. As such, the diagnostic categories of glaucoma in aphakia and pseudophakia include patients who have very different prognoses and who are likely to have different responses to surgery.

Finally, 13 of the patients in this study were categorized as "no light perception" prior to laser treatment. Others were listed as "light perception." One has to question this approach, as there have been a few reports of sympathetic ophthalmia associated with Nd:YAG cyclodestruction (*Ophthalmic Surg* 1989;20:544-546;

1990;21:736-737; *Ophthalmology* 1992;99:1818-1822). The linkage between sympathetic ophthalmic and Nd:YAG cyclophotocoagulation is certainly not clear, but I wonder whether some of the patients in this series might have benefited from an enucleation or additional medical management.

I thank the authors for the opportunity to review this manuscript, and I again wish to recognize the senior author's commitment and intellectual curiosity in pursuing this project.

DR WALTER STARK. I would like to congratulate Drs Shields and Shields on the presentation of one of the largest groups of very complicated cases, similar to ones we see in our keratoplasty service. Dr Shields, unless I heard you incorrectly, in the presentation you indicated that you were treating in the pars plana. Do you have histology to demonstrate or document that you are destroying the ciliary body or ciliary processes in the treatment of glaucoma. And number two, I was impressed with the lack of pain in this large group of patients. Sher and Lindstrom and associates were the first to publish, as far as I know, on the use of prostaglandin inhibitors in the prevention of pain, which can be quite severe, after the Excimer laser. I would ask, have you tried any topical prostaglandin inhibitors in these patients? It may be a good group to conduct a randomized trial for the reduction of pain after treatment.

DR HUGH TAYLOR. I would also like to compliment Dr Shields on a very important study on a very difficult group of patients to treat. I would like to draw to his attention some work done by a member of my department, Dr Brooks and colleagues, who about 3 years ago did a small prospective control trial comparing transscleral YAG cyclophototherapy with cyclocryotherapy. I believe the results have been presented at ARVO, but in brief they treated approximately 40 patients, randomized to either the YAG or cyclocryotherapy. The initial postoperative reaction was less in the YAG treated patients, although the long-term outcome was more favorable in those people treated with cyclocryotherapy. This was a small study and I think it certainly made everyone aware that we need further clinical investigation.

DR M. BRUCE SHIELDS. As always I am very grateful to all the discussants, especially Dr Kass for his kind words and also the very honest and constructive suggestions. I can't disagree with anything he says. There are a lot of drawbacks to a study of this type. The first thing that Dr Kass mentioned was the lack of controls and this is very true. This was a truly uncontrolled study and there is clearly a need for controlled studies. In point of fact, we are just about to embark on our next clinical trial in which we all randomize patients into the treatment I just described or into a similar treatment with a diode laser. The latter has several significantly different aspects to the YAG laser and will give us the opportunity to compare, in a more controlled fashion, the two modalities. Ultimately, we really do need to have trials where we can compare these cyclodestructive procedures with other modalities such as implant drainage devices. So I can only agree with the need for that.

With regard to the definition of success. That always is a problem and Dr Kass may well be right to just present the data and let each reader draw their own conclusion as to whether that is a success or not. The problem is that it becomes so cumbersome. You have to provide a variety of different pressure levels to show the reader what in fact you wound up with. But I think that is a good point. I also think it is a good point about classifications. It is certainly true that glaucoma in aphakia is not a diagnosis and in fact Dr Grant stressed that point with us fellows. In fact, that is why he told us never to use the term aphakia glaucoma, because that sounded like one disease. When we study glaucoma in aphakia we are in fact referring to a rather heterogeneous group as Dr Kass points out. That was one of the reasons why we shied away from trying to get into too much statistical analyses of these data. Because there are so many variables. With such a heterogeneous group, we thought it might be best just to let you know what we found for what it is worth.

A very good question about the low vision patients. We did include a significant number with light perception and even a few with no light perception. Many of those were in the early stages of the study before Wilensky's group reported their findings of sympathetic ophthalmia. As most of you know, there have been cases reported in which this procedure was done in NLP eyes and sympathetic ophthalmia did occur. I think it is significant that we did not appreciate, at least, any cases of sympathetic ophthalmia in our patients. However, we have become much more cognizant of that and the number of patients with LP and NLP that we recommend for this procedure has been greatly reduced. We now look for other ways of treating pain other than with this modality. I should also point out that we are now shying away from those patients with good vision and are utilizing this treatment in the patient, usually with a range of 20/200 to hand motion vision.

Dr Stark made two very good points. Dr Stark I may have misspoken. I didn't mean to say pars plana, if I did say that. I meant to say pars plicata, because that is in fact what we think of as the target tissue and that is what we think we are treating when we apply the laser a particular distance from the limbus. Your question about the topical prostaglandin synthetase inhibitors is a good one. We actually have, in the last year, begun to use Acular. However, this was not for the pain but because of a study which suggested that it might reduce the incidence of macular edema with inflammation. So for those eyes in which we feel there may be some central vision, we have been using that, although our experience is not sufficient to make comments at this point.

Dr Taylor referred to the very excellent paper by Brooks and associates which does compare cyclophotocoagulation and cyclocryotherapy. To my knowledge this is the only paper in which this has been done in a true head on prospective study and, as Dr Taylor pointed out, the one thing that was of interest here was the similar pressure reduction, and you will notice I didn't claim that the cyclophotocoagulation is better with regard to pressure reduction. I think, if anything, the two are comparable as best we can tell from the one study by Brooks and from antidotal comparisons of different studies. What causes me to hold to my statement that cyclophotocoagulation is better than cyclocryotherapy is that we are reducing the side effects in the early postoperative period, albeit not with controlled studies, and I think we are

coming up with an operation that will control the pressure in these desperate patients, hopefully, with less visual loss.