

Fine Needle Diathermy Occlusion of Corneal Vessels

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PURPOSE. To develop a novel technique, fine needle diathermy (FND), for the occlusion of corneal vessels and to evaluate its safety and efficacy in a series of patients.

METHODS. Fourteen patients were treated with FND to occlude corneal vessels. Patients were categorized into four groups: group 1 ($n = 4$), high risk patients with stromal vascularization before keratoplasty; group 2 ($n = 2$), patients with progressive lipid keratopathy; group 3 ($n = 4$), post keratoplasty patients with active rejection episodes associated with vessels; and group 4 ($n = 4$), patients with disciform vascularized scars with recurrent inflammation. The success of the treatment in terms of vessel occlusion and the clinical outcome were monitored.

RESULTS. All patients in group 1 had successful corneal transplantation, and the grafts remained clear without graft rejection. Patients in group 2 with lipid keratopathy had 100% obliteration of vessels with stabilization of corneal scar. All four patients in group 3 had complete regression of vessels with reversal of graft rejection. Patients with vascularized disciform scar had resolution of the inflammation without recurrence. Average follow-up was 10.3 months (minimum, 6 months; maximum, 24 months). No serious complications were observed with FND.

CONCLUSIONS. FND is a useful and inexpensive technique that can serve as an adjunct or alternative to laser occlusion for the treatment of established corneal vessels. It is fairly safe and effective, although complications such as intrastromal bleeding and crystalline deposits can occur and at times it may have to be repeated once or twice to achieve the desired result. (*Invest Ophthalmol Vis Sci.* 2000;41:2148-2153)

The avascularity of the cornea is one of its unique features. Absence of vessels helps to maintain the cornea in a transparent state and also confers a degree of immune privilege to the cornea.^{1,2} However, blood vessels are important for the host to mount a healing response against injury and infection. Corneal neovascularization occurs as a sequel to corneal insult resulting from infectious, allergic, toxic, anoxic, and immune causes whereupon it serves to facilitate the healing process or acts as a warning sign of corneal distress.^{3,4} Once established, these vessels help to transport humoral and cellular elements of immunologic defense and "raw material" required for repair and regeneration. They also help to carry administered antibiotics and other drugs to the site of infection and at the same time eliminate toxic substances.

The disadvantage of the corneal neovascular response is that once the healing process is completed, the vessels often persist with circulating blood. This may interfere with corneal transparency by leakage of lipids or by recurrent inflammation. A sequel of corneal vascularization is the establishment of lymphatics, which are normally absent in the cornea. Lymphatics augment the afferent arc of the immune response, favoring sensitization to corneal and other antigens. Corneal vascularization also disrupts the "immune privilege" status of the cor-

nea and jeopardizes the survival of a corneal graft, which is often required in such situations to restore vision. It is an established and recognized risk factor for corneal graft rejection and failure.^{5,6}

Various modalities of treatment have been used to directly or indirectly occlude corneal vessels, including steroids, radiation, cystine, cryotherapy, sulfuric acid, dextran, and conjunctival recession.⁶⁻⁹ The argon laser¹⁰⁻¹⁵ and the 577-nm yellow dye lasers^{16,17} have also been used to obliterate corneal vascularization, treating vascularization in lipid keratopathy and graft rejection. Pregraft treatment of corneal vascularization has been found to improve the chances of graft survival after keratoplasty.¹⁸ Current evidence suggests that the yellow dye laser (577 nm) is the most effective therapeutic modality to treat corneal vessels.^{16,17} However, the lack of availability and the expense of this equipment in most centers makes the treatment inaccessible to most ophthalmologists.

We have developed an alternative, simple, and inexpensive method of occluding corneal vessels called fine needle diathermy (FND). Our main aim was to assess and report the efficacy and safety of this method of vessel occlusion. Whether the objectives of vessel occlusion (e.g., clearance of lipid keratopathy or prolonged graft survival) were achieved or not will be described to some extent and constitute the secondary aim of this report.

METHODS

Assessment of Corneal Vascularization

Fourteen patients with corneal vascularization were selected and prospectively followed at the Queens Medical Center, University Hospital, Nottingham, from June 1995 to April 1998.

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Informed consent was obtained from all patients before their inclusion in the study. The research followed the tenets of the Declaration of Helsinki, and the protocol was approved by the local Ethics Committee of the Queens Medical Center.

Details were taken on the cause and duration of corneal vascularization and whether any prior treatment was given. In each patient, the extent of corneal vascularization was recorded with respect to the number of quadrants involved, the depth of vessels, and whether they were active or quiescent. History regarding previous treatment of corneal vascularization with argon laser, systemic steroids, and immunosuppression was also noted.

Pre- and posttreatment anterior segment color photographs were taken to compare and study the effectiveness of the procedure.

Measurement of the extent of corneal vascularization was performed using a semiquantitative method by counting the number of "red lines" (blood-filled vessels both superficial and deep in the cornea) in each quadrant. The result was expressed as the total number of red lines per quadrant of corneal vascularization.

Description of the Technique of FND

Amethocaine 1% eye drops were used to induce topical anesthesia (in children general anesthesia was used). Using an operating microscope set at a low intensity of illumination (to reduce blepharospasm and reflex Bell's phenomenon), a wire lid speculum was inserted to keep the eye open. In more light sensitive individuals, a green filter (TG 475 nm wavelength) was introduced in the light path. Using the microscope, the depth of vessels was assessed and the number of vessels in each quadrant to be cauterized was noted.

A stainless steel 3/8 circle side cutting, single-armed needle attached to a 10-0 monofilament black nylon suture was used with a microsurgical needle holder (dimensions: 0.15 mm cross-sectional diameter, 6.19 mm overall length; catalog No. 8065-208001; Alcon Surgical, Hemel Hempstead, UK). The needle was inserted close to the limbus, parallel to and at same depth as the blood vessel(s) to be occluded. With relatively larger vessels it was possible to insert the tip of the needle into the lumen of the blood vessel(s). This was not normally associated with bleeding unless the needle was inadvertently withdrawn before application of the diathermy probe. A unipolar diathermy unit (Valley Laboratory UK, Pfizer Hospital Products) was set to its lowest setting (0.5-1 mA). (Any unipolar diathermy unit with the capability of low power setting could be used.) An appropriate electrode was strapped around the foot of the patient and connected to the equipment. In the coagulating mode, the diathermy probe was brought into contact with the corneal needle, and contact was maintained until mild blanching of the corneal stroma occurred (usually a second or less; Fig. 1). Each feeder vessel was treated individually. For vessels spread along the graft-host junction and for very deep vessels arising from an iris adhesion, the needle was passed in a circumferential manner. Most of the vessels were treated in one session, but occasionally it was necessary to repeat the procedure at a later date to occlude secondary (collateral) vessels, which developed after the first session. The objective was always to treat the afferent vessels before occluding the efferents. Where the afferent and efferent vessels were close together, it was possible to treat both of them simultaneously by a single pass of the needle.

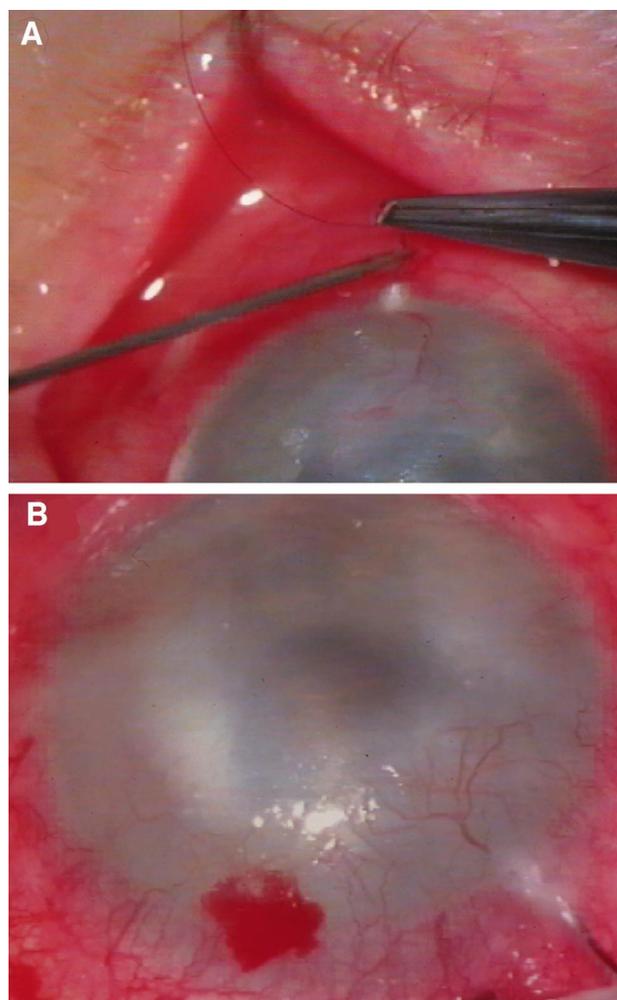


FIGURE 1. (A) A 3/8 circle, side-cutting, single-armed needle used to occlude the vessel and the electric current applied to the needle. (B) Immediate blanching of the vessel and adjacent stroma, associated with corneal intrastromal hemorrhage.

After the procedure, patients were treated with chloramphenicol 0.5% and dexamethasone 0.1% eye drops for 1 week. Patients with a history of herpes simplex keratitis were given additional prophylactic topical 3% acyclovir eye ointment.

Patients were followed-up at 2 weeks posttreatment and then every 2 months for 6 months. At each follow-up visit, patency and recanalization of vessels, visual acuity, intraocular pressure, and any other complications were noted. Patency of vessels was assessed using slit-lamp biomicroscope examination by observing the flow of red blood cells through corneal vessels.

Patient Groups

Patients were divided into four categories. Group 1 ($n = 4$) consisted of pre-penetrating keratoplasty (PK) patients with two or more quadrant vascularization. Three of these patients had previous graft failure with vascularization, and one had corneal scarring after herpes simplex keratitis. Group 2 ($n = 2$) had patients with progressive lipid keratopathy associated with deep stromal vessels in a single quadrant. Group 3 ($n = 4$) was made up of patients with post keratoplasty rejection episodes

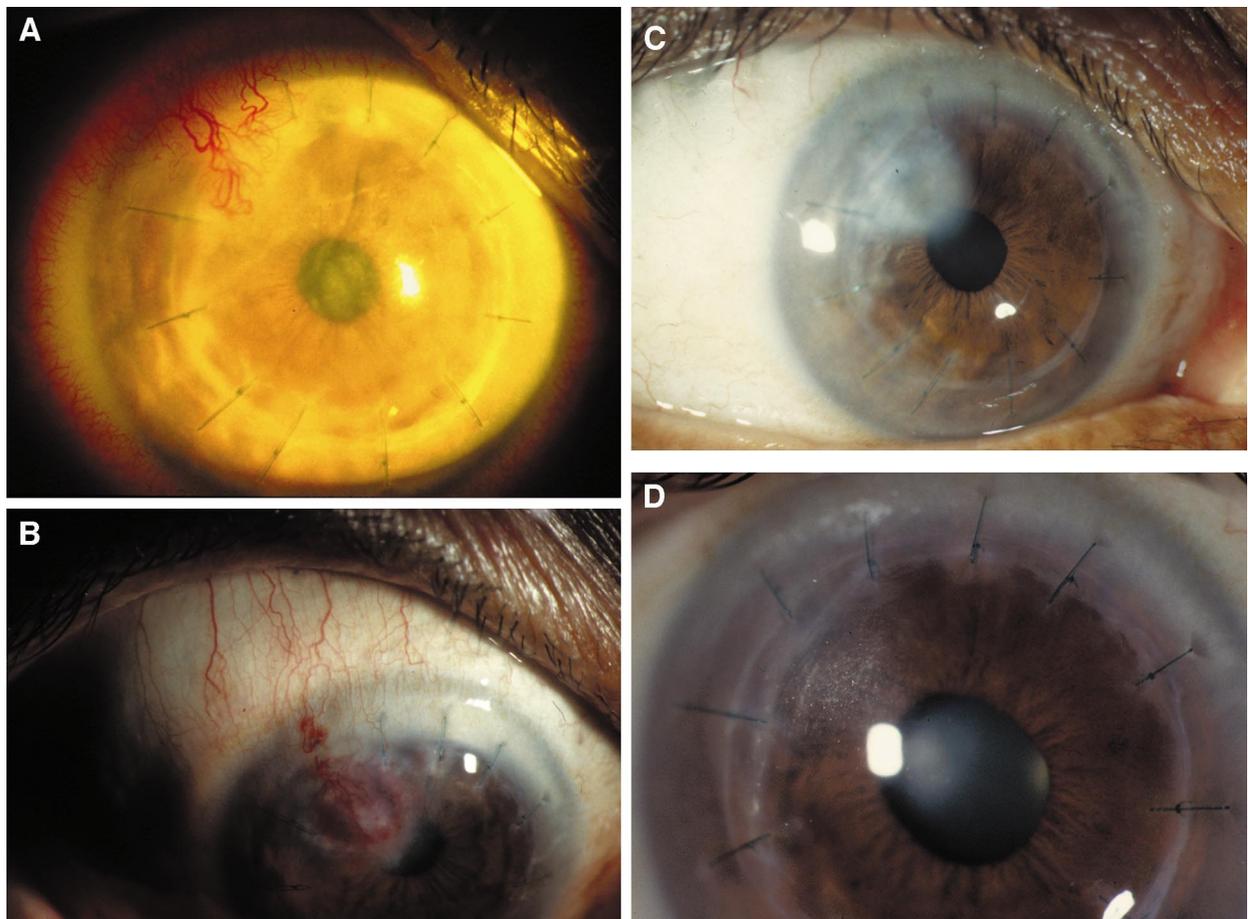


FIGURE 2. (A) New vessels extending to the donor cornea associated with a rejection reaction and localized corneal edema. (B) Corneal intrastromal hemorrhage seen soon after FND. This resolved leaving a localized scar (C), but the rejection episode was aborted. The scar cleared with residual crystalline deposits (D), which eventually disappeared.

associated with vessels that extended up to or beyond the graft host junction. FND was performed after the failure of conventional medical management with steroids. Three of these pa-

tients already had unsuccessful treatment with argon laser occlusion of vessels before FND was used. Group 4 ($n = 4$) consisted of patients with herpes simplex interstitial or disci-

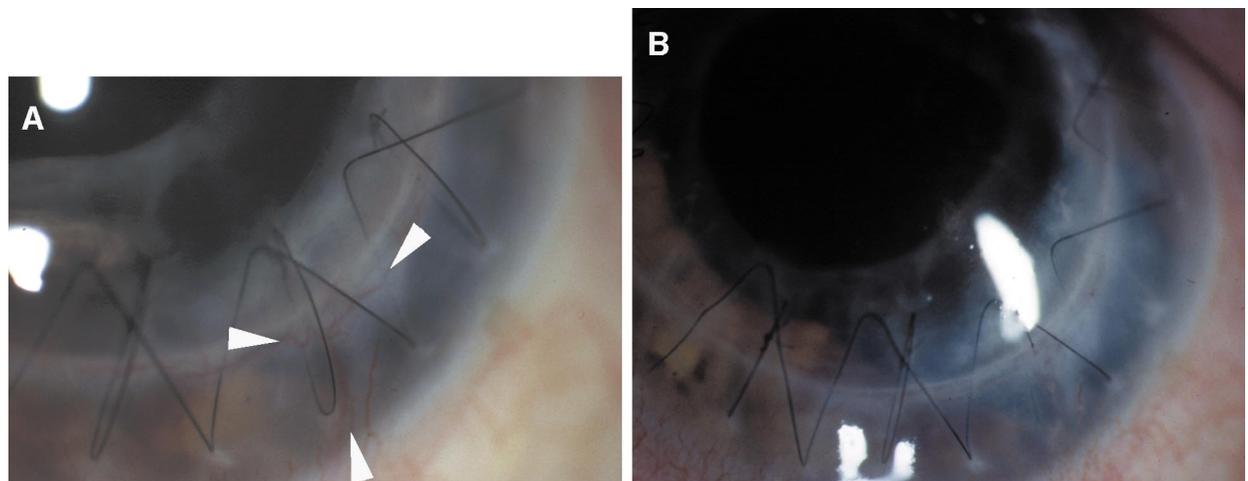


FIGURE 3. (A) New vessels arborizing in host-graft junction (arrowheads) associated with a rejection reaction. (B) Appearance of the same cornea, after FND with resolution of rejection. The corneal vessels remain closed. In this patient, the closure of the vessel preceded the resolution of the rejection reaction.

form keratitis vascularized scars with recurrent inflammation manifest clinically as stromal edema, cloudiness, and keratic precipitates.

A total of 14 patients, ranging from 10 to 84 years of age (average age, 52.14 years), were treated. The youngest was a 10-year-old girl. There were nine females and five males. Four patients had new vessels in four quadrants, two in three quadrants, three in two quadrants, and the remaining five in one quadrant. Nine patients had active new vessels at the time of the treatment (Figs. 2 and 3), and in five patients the vessels were associated with a quiescent stage of the primary condition. Six patients had prior treatment with argon laser and four had systemic steroid treatment. Follow-up period varied from a minimum 6 months to a maximum of 24 months (see Table 1).

RESULTS

All four patients in group 1 underwent successful PK. Three had post PK treatment with oral FK506, an immunosuppressant agent (Tacrolimus, Prograf, Fujisawa Ltd. Japan), a macrolide antibiotic with potent immunosuppressive activity, isolated from the soil fungus *Streptomyces tsukubaensis*). Not a single episode of rejection was observed in any of these patients until the last follow-up (minimum 9 months post PK).

All vessels in patients of group 2 were successfully closed immediately and remained shut throughout the period of follow-up. The progression of lipid keratopathy was arrested, but deposited lipids showed only marginal clearance at the time of last follow-up visit (24 months). In the four patients in group 3, with rejection reactions persisting for 1 to 2 weeks, unresponsive to topical and subconjunctival steroids and to attempted closure with argon laser (3 patients), the rejection resolved within 2 to 3 days after occlusion of vessels by FND. Steroid drops were continued after FND occlusion of the vessels (Figs. 2 and 3).

Patients in group 4 were also maintained continuously on low-dose topical steroid medication (prednisolone acetate, 0.5%, once a day or once every other day) after FND. In all 4 patients, the inflammation began to resolve within 1 week, and the frequency of inflammatory episodes was reduced. In one

patient with herpes simplex viral interstitial keratitis (with secondary glaucoma, controlled by trabeculectomy), although the episodes of flare-up were reduced, a small (<1 mm) well-circumscribed, circular area of thinning with ectasia developed in the area of HSV keratitis scar after FND.

Four patients (two in group 1, one in group 2, and one in group 4) required repeat FND once, and one patient (group 4) required repeat FND twice, after 1 to 2 weeks, due to recanalization of the vessels occluded or opening of collaterals, after the first treatment session. The two patients in group 1 had deep vessels in two and three quadrants, respectively. The patients in group 3 had recurrent graft rejections associated with deep stromal vessels in two quadrants approaching the host graft junction. Despite treatment with argon laser and steroids, the vessels were still active. The rejection resolved with regression of vessels after FND.

Of the 14 patients treated, occlusion of all vessels treated was observed in 8 patients (57.1%); in 4 patients (28.5%) 75% of treated vessels were occluded, and in 2 patients (14.2%) only 50% of the treated vessels were occluded. Four of the latter 6 patients required repeat treatment.

Corneal intrastromal hemorrhages were observed in three patients, which cleared without any sequelae in two patients and in one left a fine crystalline deposit that itself did eventually clear (Figs. 2B, 2C, 2D).

DISCUSSION

The advantages and disadvantages of corneal vascularization have long been recognized. The need to treat corneal opacification, recurrent immune-mediated inflammation, and reduced vision associated with corneal vessels has always been felt, and various methods to occlude vessels have been developed and used over the years.

Topical and periocular steroids have been popular, but the risks of cataracts, glaucoma, and superinfection associated with the long-term use of these drugs have been a limiting factor. Nonsteroidal anti-inflammatory drugs and cyclosporin A were found to be largely ineffective in controlling or limiting

TABLE 1. Demographics and Clinical Data

No.	Age	Eye	Diagnosis	Etiology	CNV QD	Depth	Activity	RX			Pre-VA	Post-VA	Follow-Up	% of Vessel Closure
								No.	Laser	Steroid				
1	60	RE	Disciform scar	Herpes simplex	2	S, D, VD	Q	2	N	Y	1/60	1/60	10	100%
2	75	LE	Disciform scar	Bacterial keratitis	3	S, D, VD	Q	2	N	Y	1/60	2/60	9	75%
3	82	RE	Disciform scar	Herpes zoster	4	S, D	Q	1	N	N	2/60	2/60	9	50%
4	65	RE	Disciform scar	Herpes zoster	1	S, D	A	1	N	N	6/9	6/9	12	50%
5	70	LE	Graft rejection	Corneal edema	4	S, VD, D	A	1	Y	N	HM	HM	10	75%
6	84	RE	Graft rejection	Fuchs dystrophy	1	S, D	A	1	N	Y	1/60	6/60	12	75%
7	51	LE	Graft rejection	Keratoconus	2	S, D	A	2	Y	Y	HM	HM	6	100%
8	70	RE	Graft rejection	Corneal scar	1	D, VD	A	1	Y	Y	6/60	6/24	15	100%
9	12	LE	Lipid keratopathy	Herpes zoster	1	S, D	Q	1	N	N	6/60	6/60	12	100%
10	23	RE	Lipid keratopathy	Unknown	1	S, D	Q	1	N	N	6/9	6/9	8	100%
11	39	LE	Pre-PK	Fuchs dystrophy	4	S, D	A	1	Y	N	2/60	3/60	24	100%
12	24	LE	Pre-PK	Keratoconus	4	D	A	3	N	N	6/18	6/18	9	100%
13	65	LE	Pre-PK	Herpes simplex	2	D, VD	A	2	N	N	CF	CF	9	100%
14	10	RE	Pre-PK	Graft rejection	3	D	A	2	N	Y	6/36	6/24	11	75%

Location-depth of vessels in the cornea: S, superficial; D, deep; VD, very deep; CNV QD, corneal neovascularization quadrants; RX No., number of treatments; Pre-VA, pretreatment visual acuity; Post-VA, posttreatment visual steroid; N, No; Y, Yes. Follow-up is in months.

corneal vascularization.¹⁹ Other invasive and noninvasive methods such as radiation,⁷ thio-tepa,⁸ cryotherapy,⁹ and conjunctival recession have been found to have limited clinical value.

Photocoagulation of vessels^{10-17,20} has been shown to be an effective alternative to the above methods. Cherry and Garner^{13,14} first reported the use of argon laser for the treatment of corneal vessels in humans. In their study four patients were treated, two with chemical burns and two with herpes simplex keratitis. There were two failures, one success, and one partial success. Marsh and coworkers^{11,21} treated 41 lipid keratopathy patients with corneal argon laser photocoagulation (CALP) with a minimum follow-up period of 9 months. Twenty-eight of these patients had a decrease in the extent or density of corneal opacity, and 33 patients had improvement or no change in their vision. Nirankari and Baer¹⁸ treated 13 patients with CALP for deep stromal vascularization. They reported good results with regard to reversal of active graft rejection episodes and partial clearing of corneal opacification after CALP.

Baer et al.¹⁵ prospectively treated 25 eyes of 23 patients with CALP using 577 nm yellow dye laser. They reported reversal of graft rejection and a statistically significant reduction in area of vascularization (reduction of 68% in the vascularized area). They also achieved a significant reduction in the vascularized area, from 46.4% to 27.3%, in nine patients treated for lipid keratopathy. In their series laser photocoagulation was not found to be effective in patients with extensive corneal neovascularization.

In our experience, CALP is of limited value because of its inevitable complications of underlying iris atrophy and pupillary ectasia. The risk of inadvertent retinal (or macular) photocoagulation, although small, is of concern. We have found that laser ablation of corneal efferent vessels (analogous to veins) is comparatively easy because they are wider and have a relatively slower flow. Conversely, the afferent vessels (analogous to arteries) are narrower, deeper, and have a rapid pulsatile flow and are more difficult to ablate. Consequently, recanalization of these vessels occurs in a high proportion of cases.

The technique of FND can be performed under topical anesthesia, is simple, is inexpensive, and can be performed by any ophthalmic surgeon. It can be applied at any depth to occlude both afferent and efferent vessels with equal efficacy. When afferent and efferent vessels are located close to each other, both can be occluded simultaneously, with a single pass of the needle. This reduces intrastromal bleeding, which is known to occur when the efferent vessel is occluded before the afferent (as can occur with CALP). Although we have used a side-cutting needle, which most corneal surgeons are familiar with, a round vascular needle could be used instead. However, greater difficulty may be encountered in passing a round-body needle into the desired plane of the vessel to be occluded.

In our study, 14 patients with corneal vascularization were prospectively treated with FND. In patients in group 3 (with graft rejection reactions), successful reversal of rejection episodes was achieved. In 3 patients CALP was attempted before FND. After CALP, early apparent control of the rejection episode in all three patients was followed by relapse. This was related to recanalization of some of the vessels and also shunting of blood through collateral vessels. Moreover, two of the three patients had accidental suture lysis as a result of CALP. This is another important complication that has to be antici-

pated while treating patients for this specific indication with laser. The implications of this for grafts with running sutures is significant. The success in the rejection group could be attributed to inhibition of both afferent and efferent limbs of the immune response by obliteration of both groups of vessels.

In group 2, both the patients had complete obliteration of vessels with stabilization of corneal opacity and visual acuity. Because this group had only two patients, no firm conclusions can be drawn, but these results were comparable to Marsh's studies of lipid keratopathy patients.^{11,12,21} The patients in group 1 had less bleeding during trephination, and the grafts remained clear with no rejection episodes until the last follow-up (9 months). However, because these patients were considered high risk, in all four patients a HLA class I matched (two or three alleles) donor was used, and in three patients FK506 was used postoperatively. Therefore, the success of the corneal transplant procedure with regard to absence of rejection episodes cannot be attributed to FND of corneal vessels alone. Both HLA class I matching and use of immunosuppressive agents are important in preventing rejection episodes, and a randomized study controlling for these variables will need to be done to assess the true worth of FND alone in patients with this indication for vessel occlusion.

In the four patients with disciform keratitis (group 4), FND was associated with resolution of active inflammation in three. Although the clinical course of herpes stromal keratitis may wax or wane, corneal clearing shortly followed FND.

We have found that deep vessels (active or quiescent) occupying two or more quadrants or vessels arborizing in host graft junction needed to be treated more than once. In such situations, although the major vessels remained occluded, finer vessels in the vicinity of the occluded vessels, which at the time appeared inconsequential, acted as collaterals and established a new circulation. Persistence of active stromal inflammation will induce further new vessel ingrowth. However, in many instances, active stromal inflammation is potentiated by the presence of vessels. FND of vessels helps to break this vicious cycle and, together with other adjunctive treatment (e.g., steroid drops), can facilitate the resolution of stromal inflammation.

There were few side effects observed with FND. Transient whitening of the cornea was observed in the stroma immediately surrounding the needle, at whatever depth it was placed. This occurred in all patients treated with FND and persisted for 24 to 48 hours, with complete resolution. No inadvertent corneal perforation with the needle occurred in any of the patients.

Two conclusions can be drawn from this study: FND is a safe and effective alternative treatment for occluding corneal vessels and vessel occlusion has some beneficial effect on graft rejection and before PK. However, this needs to be further evaluated by double-blind, randomized, and controlled studies. Vessel occlusion appears to be a useful adjunct to other treatment modalities in the management of graft rejection episodes. The results obtained from the two patients of lipid keratopathy treated in this study suggest that it may be of some value in arresting the progress of this condition, but the regression of deposited lipid is not accelerated by vessel occlusion. The value of FND in preventing or reducing episodes of graft rejection (in high-risk individuals) and episodes of immune-mediated corneal inflammation (in herpes simplex viral keratitis and others) needs to be further assessed.

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