



## REFRACTIVE SURGERY

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### At Issue: preferred regimen for curing haze after PRK

**Q:** At Issue posed the following question to a panel of experts: "What is your preferred regimen for curing haze after PRK?"

#### **A:** Corticosteroids prescribed, reduced up to 6 months

**Noel A. Alpins, MD, FACS:** In my practice, the incidence of corneal haze has dramatically decreased since laser in situ keratomileusis (LASIK) has become the principal mode of treatment. The corneal haze evident after higher correction surface ablation treatment does not occur significantly when treatments are confined to 3 D of myopia or less. Reduction in the incidence and severity of haze for higher corrections is achievable by reducing tissue temperature with the application of ice packs to the eye before and after photorefractive keratectomy (PRK) treatment and the application during the procedure of chilled balanced salt solution.

I use an MPMZ algorithm for PRK and LASIK that has no more than 3 D per zone or 2 D per pass with a 3-second pause between passes to allow drying and cooling. The use of bandage contact lenses to accelerate the epithelial healing process avoids the haze secondary to delayed re-epithelialization. The application of mild/moderate strength corticosteroids such as fluorometholone (FML; Allergan) for 4 weeks postoperatively and titrating their withdrawal against the superficial stromal appearance aids reduction in the deposit at the superficial stromal level.

The treatment of established haze is principally directed at patient counseling to provide enough time for its spontaneous resolution over a period of 12 to 36 months. Where re-treatment is required, due to the commonly associated regression, this can be undertaken with the LASIK technique to avoid the induction of a greater amount of haze and regression. I use this in preference to transepithelial re-treatment or plano phototherapeutic keratectomy (PTK) for haze removal, as recurrence is evident with all re-treatment modalities. I have not employed treatment using mitomycin C to reduce keratocyte production after surgery.

Corticosteroids are indicated four times daily, with a reduction to two times daily over a 3- to 4-month period for established haze or after re-treatment to aid its resolution, maintain correction and improve best corrected visual acuity. It can sometimes be necessary to continue to reduce dosages up to 6 months. But, together with this, patience, time and optical correction of the remaining refractive error, particularly at night, are the most consistent means of symptom control during resolution.

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#### **A:** Make use of mitomycin C

**Richard J. Duffey, MD:** In a practice dominated by LASIK laser vision correction, I have seen a limited amount of haze or subepithelial fibrosis associated with PRK surgery. However, it does occur in a limited number of patients in our practice, and I still see referrals from elsewhere for treatment.

Past treatment modalities have included prolonged use of topical steroids, PTK and lamellar keratoplasty, all with significant side effects and limitations. A better mode of treatment involves the use of mitomycin C in a similar fashion to that used in recurrent pterygia treatment. The following has been my approach to the treatment of subepithelial haze associated with PRK:

- Place two drops of topical proparacaine, one drop of ofloxacin and one drop of nonsteroidal when the patient has been placed on the minor operating room table.
- Do your typical lid prep with Betadine (povidone-iodine; Alcon) swabs with no Betadine being placed directly in the cul-de-sac.
- The lid speculum is placed and a 6- to 7-mm (depending on size of subepithelial fibrosis) epithelial débridement is done with a Greishaber blade.
- The subepithelial anterior stromal haze will be visible to this point and much can be removed with the same Greishaber blade. Smooth the surface with a battery-operated, diamond-dusted burr. It is very important to remove as much scar tissue as possible, as the mitomycin C will simply inhibit new scar formation and does very little to pre-existing scarring.

- An 8-mm corneal sponge (the same used as a corneal shield during cataract surgery) is soaked with 0.02% mitomycin C and placed on the corneal surface for 2 to 3 minutes depending upon the original amount of haze (longer for more haze and shorter for less haze).
- Upon removal of the sponge, the cornea, conjunctiva and cul-de-sacs are copiously irrigated with balanced salt solution.
- A bandage contact lens is placed, followed by antibiotic/steroid and nonsteroidal drops.

The bandage contact lens is removed after epithelialization is complete, typically between 3 to 7 days. The antibiotic/steroid is tapered from four times per day over a 4-week period. If increased haze is noted during the postoperative healing process, additional topical steroids can be used in a tapering fashion over a 1- to 3-month period.

I have had a very high degree of success with removal of subepithelial haze with attendant improvement in visual acuity, and often a resolution of the induced myopic refractive error, which had developed in the patient due to the haze formation. Removal of the subepithelial haze often causes a hyperopic shift; therefore, I recommend no additional refractive laser treatment at the time of the mitomycin C application. If additional refractive ablation is required, I would recommend that it not be done for 3 to 6 months following the mitomycin C debridement, and that LASIK be considered as an alternative treatment so as to induce less or no further subepithelial fibrosis.

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### **A: Debulk haze with a transepithelial ablation**

**Daniel S. Durrie, MD:** One of the advantages of being involved with the early clinical trials on PRK is that I was able to see the normal healing course of the original patients. Patients done starting back in 1989 were in the clinical trials, and we were not allowed to intervene in the normal healing process. Because of this, we learned that all haze disappears unless it is aggravated by further intervention. Even some of the worst we saw with the early model of the Summit (Waltham, Mass.) and Visx (Santa Clara, Calif.) lasers faded with time. What I have seen since approval of the lasers in the United States in 1995 are cases where a fairly normal healing haze was converted into a severe haze and even corneal scars by early intervention. This is one of the things we see with procedure changes from clinical trials to the real world — patients and doctors were not willing to just let the haze process develop without some type of intervention. Attempts to scrape haze or to repeat ablation usually worsened the haze in the long run rather than helped it.

Now we are faced with a group of patients who have had multiple interventions and have had significant grade 3+ to 4+ haze, which causes decreased visual acuity and the need for further treatment. It is important to remember that unless the stroma has been scarred by intervention, the “healing haze” always sits on top of the stroma and is not embedded into it. Therefore, my treatment of choice is usually debulking the haze with a transepithelial ablation, trying to remove 75% to 80% of the haze. My goal through this transepithelial ablation is to try to not hit the corneal stroma, but only hit the haze. Therefore, I use visual clues to try to decide how much laser ablation is necessary. I program into the excimer laser under PTK mode 150 pulses, turn the room lights down and watch the autofluorescence of the epithelium and haze to make sure that the epithelium is not penetrated. The blue fluorescence turns to a black or absence fluorescence when the corneal stroma is ablated. Therefore, it usually is somewhere between 130 and 150 pulses where the haze has been partially removed. Then I follow patients with FML four times per day for a month and rarely have to put them on stronger steroids. The residual haze usually resolves on its own over 3 to 6 months and, using this technique, I have not had to use antimetabolites.

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### **A: Use a stepladder treatment approach**

**Peter S. Hersh, MD, FACS:** For a patient suffering haze after PRK, I use a stepladder approach to treatment. First, in cases where haze is decreasing best spectacle corrected visual acuity or has caused regression, I start prednisolone acetate 1% drops every 2 hours and start to taper at 1 week. I prefer frequent dosing of a high potency steroid based on laboratory work we did several years ago suggesting that such a dosage was necessary to decrease collagen output by keratocytes. If this regime is successful in clearing haze and stopping regression, steroids are then slowly tapered (four times daily for 1 week, twice daily for 1 week, once daily for 1 week and then discontinued).

Second, in patients with haze recalcitrant to medical therapy, or recurrent haze, I suggest laser re-treatment. When re-treating such patients, I prefer a transepithelial approach to avoid any mechanical trauma to the corneal surface. After laser epithelial removal, I then will treat the residual refractive error using PRK. Since I have found that re-treatments frequently can lead to overcorrection, the laser is generally programmed for approximately 75% of the residual refractive error. The patient is examined after the laser treatment and if a substantial haze remains, then additional pulses using a PTK technique are cautiously applied to reduce residual haze. After treatment, a bandage soft contact lens is applied and prednisone acetate 1% is used every 2 hours and tapered over several weeks.

Finally, in cases of haze that recur after the two treatments discussed, I will again perform re-treatment, but this time using mitomycin 0.02%. In such a case, the transepithelial approach is similarly used. A mitomycin pledget is used (I use a 4.5-mm trephine to cut a circular piece of filter paper). It is positioned directly over the area of haze and applied for 2 minutes. Care is taken to avoid excess mitomycin leaking over the remainder of the cornea. After removal of the pledget, the surface of the cornea is vigorously irrigated with

balanced salt solution. PRK laser treatment then is given to treat approximately 75% of the refractive error and subsequent PTK is used for residual haze as necessary. At the end of the procedure, a bandage soft contact lens is placed and prednisone acetate 1% is applied every 2 hours for 1 week and tapered thereafter. Using this technique, I have not yet seen haze recur. However, overcorrection can be a problem and can be avoided by being conservative in laser application. Indeed, some investigators have advocated mechanical stripping of any plaque-like haze with the subsequent use of mitomycin, without laser ablation. They suggest that simply removing the fibrous plaque mechanically will reduce the refractive error and mitomycin will prevent recurrence.

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## **A: Myopic PRK followed immediately by PTK**

**Donald G. Johnson, FRCS(C):** It is important to point out that this technique is performed with the Visx Star S2 laser using international card software version 3.10.

This method is successful in "almost" all cases. Utilize the epithelium treatment in the pull down menu. A 4 D, 6.5-mm myopic PRK is performed on the untouched epithelium following immediately into 6.5-mm PTK. This is performed in a dark room with the microscope light (using ring light only) low enough to visualize the natural epithelial and haze fluorescence. This allows accurate visualization of the breakthrough point of the "epithelium and haze" onto normal stroma

It will always give a central smooth removal. Removing a diameter of 4 mm to 5 mm is sufficient to include all the important haze. It is not necessary to see fluorescence disappearance out to 6.5 mm. In the rare case where there is still a mild layer of haze centrally, a couple of repeated 0.5 D, 4-mm PRKs can be done until breakthrough does occur. These are done in the Contoured Ablation Pattern method in the pull down menu with the Ablation Profile Adjustment turned off.

Over 10 years and 45,000 cases (in some of the earlier cases, this technique produced significant haze problems), there have been only four eyes that have had the haze return significantly. I have recently re-treated these eyes by removing the haze with the same technique and applying mitomycin C immediately.

Naturally, the best treatment for haze is prevention. With our present primary treatment, even a grade 1 haze has less than a 0.5% incidence.

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## **A: Corticosteroids and lubricating drops**

**Olivia N. Serdarevic, MD:** In all patients referred to me with haze after PRK, I first always check for keratitis sicca, meibomitis and exposure keratopathy, which can precipitate and/or aggravate haze in PRK and even LASIK patients, and treat the underlying condition causing any corneal desiccation before continuing with my general regimen for treatment of haze after PRK.

My preferred regimen consists of aggressive topical administration of corticosteroids and lubricating drops. I use prednisolone acetate 1% drops (Pred Forte; Allergan) administered six times per day for about 2 weeks and then tapered over a month, and hydroxypropyl methylcellulose 0.3% lubricating drops (GenTeal; CIBA Vision) administered 5 minutes after the corticosteroid drops. If the haze decreases and best corrected visual acuity improves but more corticosteroid therapy is required, I continue with fluorometholone 0.1% drops (FML).

If corticosteroid therapy combined with lubrication is inadequate and haze and undercorrection with decreased visual acuity persist, I treat with a combination of PTK and PRK with postoperative mitomycin topical application. One of the first to suggest this therapy was Till Ancheutz, MD, of Gaggenau, Germany, who demonstrated in experimental studies in animals decreased fibroblast proliferation on confocal microscopic examination after treatment with mitomycin. Dr. Ancheutz and then Percy Amoils, MD, of Johannesburg, South Africa, demonstrated the clinical efficacy of mitomycin in reducing new collagen production and haze after re-treatments.

When using this treatment approach, I first perform PTK to remove about 10 to 20  $\mu\text{m}$  of tissue to smooth the surface, then PRK for correction of the regression and end with more PTK to remove about 10  $\mu\text{m}$  to further smooth the surface. After the cornea is re-epithelialized completely at about 4 days postoperatively, I commence treatment with mitomycin 0.02% twice per day for about 3 weeks. To prevent corneal wound healing problems, I never treat with mitomycin before re-epithelialization to prevent wound healing problems.

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