

Anterior Stromal Puncture for the Treatment of Recurrent Corneal Erosion Syndrome: Patient Clinical Features and Outcomes

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- **PURPOSE:** To evaluate the clinical features and outcomes of patients with recurrent corneal erosion syndrome who underwent anterior stromal puncture.
- **STUDY DESIGN:** Retrospective, nonrandomized, consecutive case series.
- **METHODS:** Database search of patients from 2003-2013 who underwent anterior stromal puncture was conducted at a tertiary care hospital cornea clinic. Charts of 30 patients (35 eyes) were reviewed. Outcome measures included demographics, laterality, history of corneal trauma, prior ocular history, frequency and duration of symptoms, failed treatments, signs on examination, degree of symptom resolution, additional treatments needed, and complications.
- **RESULTS:** Mean patient age at presentation was 37 (\pm 11.5 SD) years, 60% were male. A total of 83.3% of patients had unilateral and 16.7% had bilateral involvement. In all, 62.9% of eyes had prior history of corneal trauma and 2.9% had prior laser-assisted in situ keratomileusis. Ninety-seven percent of eyes had symptoms of pain upon awakening refractory to conservative treatment. In 97% of eyes, there were findings of microcysts, fingerprint lines, loose epithelium, and/or faint scars. Mean follow-up was 14 months (range: 3-120 months). At final follow-up, 62.9% of eyes were symptom free and 37.1% experienced milder episodes. Seventeen percent required additional treatment: 16.6% superficial keratectomy, 66% repeat anterior stromal puncture, and 16.7% phototherapeutic keratectomy. No complications were observed.
- **CONCLUSION:** Anterior stromal puncture using a short (5/8 inch) 25 gauge bent needle is a simple, safe, and cost-effective procedure for symptomatic relief in patients with recurrent corneal erosion syndrome refractive to conservative measures. Repeat treatment may be performed prior to additional surgical intervention. (Am J Ophthalmol 2014;157:273–279. © 2014 by Elsevier Inc. All rights reserved.)

RECURRENT CORNEAL EROSION SYNDROME IS A disease characterized by repeated episodes of dislodgment of corneal epithelium from the underlying basement membrane because of loosened adhesion between the 2 layers.^{1–3} The first report was published in 1872 by Hansen,⁴ where he termed the condition “intermittent neuralgic vesicular keratitis.”

Recurrent corneal erosion syndrome may be either primary or secondary, depending on whether the defect in the epithelial basement membrane is intrinsic or acquired. Abnormalities of epithelial adhesion resulting in recurrent erosions can be associated with previous traumatic abrasions, with anterior corneal dystrophies (eg, map-dot fingerprint dystrophy, Reis-Bucklers, epithelial basement membrane dystrophy [EBMD]), or with degenerations (eg, anterior basement membrane degeneration). In the case of previous trauma, superficial injury to the cornea may cause damage to the epithelial basement membrane.

Patients suffering from recurrent corneal erosion syndrome often experience pain, photophobia, tearing, redness, and decreased vision, classically when they are awakened from sleep, because of friction exerted on the corneal epithelium. This painful attack can recur frequently, hence the name of the disease. Erosions occur along a spectrum; in some cases there is extensive loss of corneal epithelium accompanied by severe symptoms that may take several days to resolve.⁵ In other cases there is a small area of epithelial loss; this type of erosion occurs more frequently but is milder and of shorter duration.

There are many reported medical and surgical treatment modalities available for recurrent corneal erosion syndrome. Nonsurgical treatments include topical lubricating drops, gels, hypertonic saline and ointments, inhibitors of matrix metalloproteinase-9 such as doxycycline,⁶ corticosteroids,⁷ and autologous serum drops.⁷ Surgical intervention includes superficial keratectomy with or without a diamond burr,⁸ phototherapeutic keratectomy (PTK),⁹ and anterior stromal puncture with or without neodymium-doped yttrium-aluminum-garnet (Nd:YAG) laser.^{7,10}

In 1986, McLean and associates were the first to report on using the technique of anterior stromal puncture for patients with recurrent corneal erosion syndrome.¹¹ The purpose of our study was to investigate the long-term clinical outcomes in a large series of patients with recurrent corneal erosion

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syndrome refractive to medical management who underwent anterior stromal puncture and to describe their clinical features. Reasons for treatment failure were also evaluated.

PATIENTS AND METHODS

THIS RETROSPECTIVE OBSERVATIONAL CASE SERIES WAS Research Ethics Board approved by the Toronto Western Hospital, University Health Network Institutional Review Board (IRB # 13-5976-BE). This study was conducted in compliance with the tenets of the Declaration of Helsinki.

Database search was conducted at a tertiary care hospital cornea clinic (Toronto Western Hospital, University Health Network, Toronto, Canada). Retrospective chart review was conducted for 30 patients (35 eyes) examined from January 2003 to August 2013 that underwent anterior stromal puncture for symptoms and signs of recurrent corneal erosion syndrome. Indication for intervention was symptoms of recurrent corneal erosion refractory to medical treatment. No patients were excluded from the analysis. Outcome measures included patient demographics, laterality, history of superficial corneal trauma, prior ocular history, frequency and duration of presenting symptoms, prior failed treatments, presenting signs on slit-lamp examination, degree of symptom resolution, additional treatments required after anterior stromal puncture, and intraoperative and postoperative complications.

- **SURGICAL TECHNIQUE:** Anterior stromal puncture was performed with the patient sitting at the slit lamp. A few drops of topical anesthetic eye drops (eg, Proparacaine) were administered to the affected eye. The tip of a short (5/8 inch) 25 gauge needle, attached to a 1-mL syringe, was bent near the needle hub using the plastic needle cover, taking care not to dull the needle tip. A lid speculum was sometimes inserted depending on patient cooperation but was often unnecessary. The surgeon then held the syringe and would aim the needle tip 90 degrees to the corneal surface (Figure 1) to gently indent the affected epithelium, creating micropunctures over the area that felt loose on contact. The vertical nature of needle entry created more consistent, small micropunctures as opposed to horizontal, wide scratches with tangential entry that would create a larger and potentially more visually significant scar. Sufficient pressure was needed such that resistance could be felt against the stroma at approximately 5%-10% stromal depth. The epithelium often felt poorly adherent to the Bowman layer on indentation in a focal area, but on occasion the complete corneal surface was abnormal, indicating that the patient likely had EBMD, a bilateral problem (Figure 2), rather than posttraumatic recurrent corneal erosion syndrome (Figure 3). Punctures were made less than 1 mm apart. Performing the procedure with fluorescein staining and under cobalt blue light

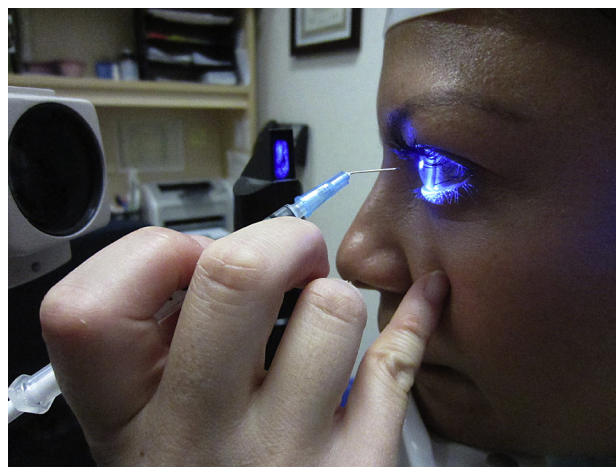


FIGURE 1. Anterior stromal puncture for recurrent corneal erosion syndrome: at the slit lamp, a bent short (5/8 inch) 25 gauge needle attached to a 1-cc syringe is angled 90 degrees to the cornea.

allowed the surgeon to determine that adequate treatment was complete as bubbles could be visualized (Figure 4). One could distinguish between subepithelial bubbles, which tended to be round, and the desired intrastromal air bubbles, which were more triangular, indicating that the needle tip had sufficiently “tickled” the stromal surface to allow for better epithelial adherence.

Immediately following the procedure, patients were given a drop of topical antibiotics and a bandage contact lens (BCL) was placed over the cornea. The patient was then discharged home with instructions to use a combination of antibiotic and steroid drop (eg, tobramycin 0.3%/dexamethasone 0.1%; Tobradex; Alcon, Fort Worth, Texas, USA) 4 times daily until follow-up at 1 week and then tapered over 1 month. The bandage contact lens was left in situ for at least an additional 6 weeks to allow for the epithelium and basement membrane to heal, and for reestablishment of tight adhesions of regenerated epithelium to Bowman layer.¹² The BCL was replaced at the 1-week follow-up visit if it had debris on it. The patient's second follow-up visit was usually 5 weeks later, at which time the BCL was removed. The patients were instructed to continue lubrication drops 4 times daily or more as needed (in that case, preservative-free drops) and to use ointment at night (either Muro128 or Lacrilube). Our patients reported high adherence to this treatment regimen, especially the ones that remained symptomatic after the first anterior stromal puncture procedure.

RESULTS

SIXTY PERCENT OF PATIENTS (18/30) WERE MEN, 40% (12/30) women. The mean age of patients was 37 (\pm 11.5 SD)

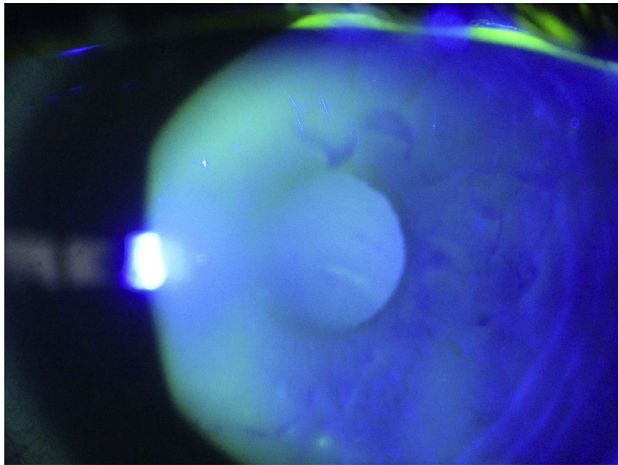
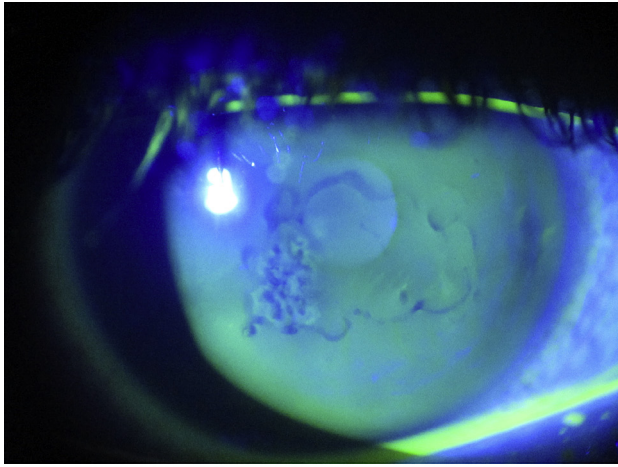


FIGURE 2. Anterior stromal puncture for recurrent corneal erosion syndrome: eyes with epithelial basement membrane dystrophy under cobalt blue light. (Top) Right eye shows a negative fluorescein staining pattern of fingerprint lines in the central cornea. This eye began to have symptoms only after trauma from a mascara brush scratch. (Bottom) Similar slit-lamp findings are present in the mid-peripheral left asymptomatic cornea.

years. A total of 83.3% of the patients (25/30) had unilateral involvement and 16.7% (5/30) had bilateral involvement. Of 35 eyes, 62.9% (22/35) had a prior history of trauma, 2.9% (1/35) had prior laser-assisted in situ keratomileusis (LASIK), 2.9% (1/35) had a known history of EBMD, and 31.4% (11/35) had symptoms consistent with recurrent erosion but had no prior ocular history of surgery, trauma, or other ocular comorbidities; these eyes were given a diagnosis of presumed EBMD. Ninety-seven percent of the eyes (34/35) had pain on awakening in the morning; 40% (14/35) had dry eye symptoms. In 97.1% of eyes (34/35) on slit-lamp examination, there were positive findings of microcysts, fingerprint lines, loose epithelium, and/or faint scars. One eye did not have positive findings on slit-lamp examination; however, this patient did experience recurrent episodes of pain on awakening in this eye and had epithelial basement membrane dystro-

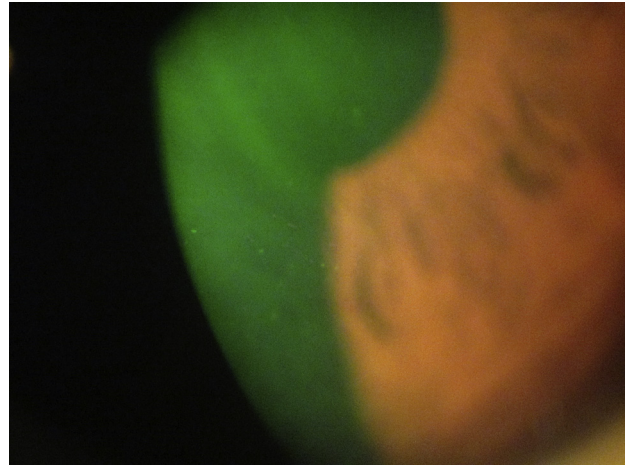


FIGURE 3. Anterior stromal puncture for recurrent corneal erosion syndrome: an eye with posttraumatic recurrent corneal erosion syndrome. Note the epithelial microcysts on the cornea in a patient with a history of prior trauma from a fingernail injury. The fellow eye was asymptomatic with no slit-lamp abnormalities.

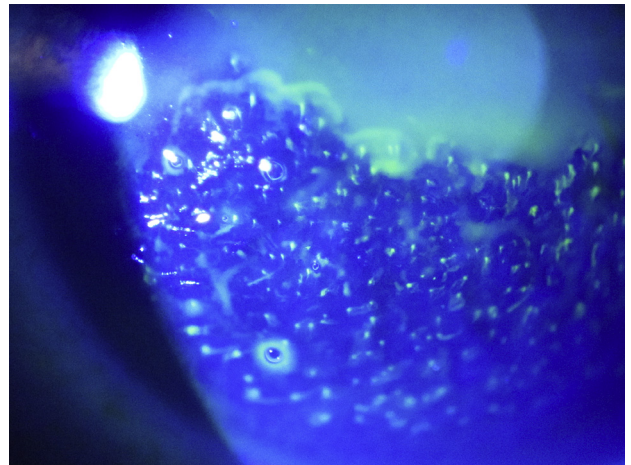


FIGURE 4. Anterior stromal puncture for recurrent corneal erosion syndrome: cornea immediately after treatment. Note the bubbles visible using fluorescein staining, which form at the locations where the epithelium has been punctured and basement membrane stimulated.

phy findings in his fellow eye, and therefore he underwent anterior stromal puncture treatment in the symptomatic eye. All eyes were treated with anterior stromal puncture. The mean follow-up was 14 months (range of 3-120 months). Thirty-three percent of patients (10/30) had a minimum of 6 months follow-up and 23.3% (7/30) were followed for more than 12 months. Median duration of follow-up was 3 months.

A total of 62.9% of eyes (22/35) were completely symptom free; 37.1% (13/35) suffered recurrent erosion episodes

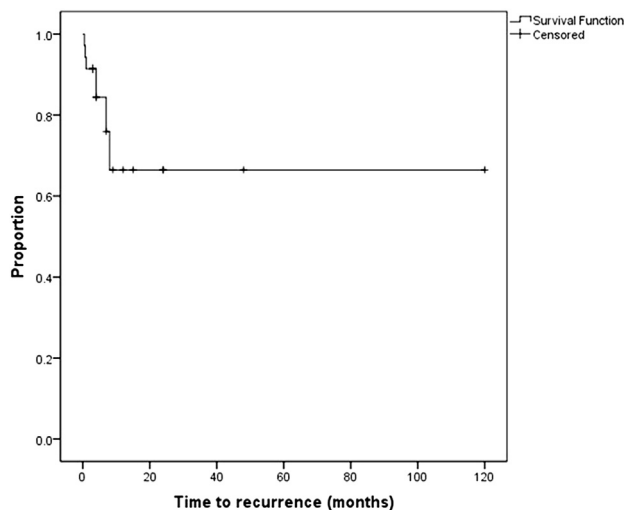


FIGURE 5. Anterior stromal puncture for recurrent corneal erosion syndrome: Kaplan-Meier survival curve demonstrating the time to recurrence of recurrent corneal erosion symptoms after treatment.

after anterior stromal puncture, but these episodes were reported to be milder. The patients in this group reported recurrent episodes of corneal erosion starting from a few days after the procedure (2 patients) to 6 months after the procedure (Figure 5). Seventy-one percent of eyes (25/35) had signs of EBMD following the treatment. Seventeen percent of eyes (6/35) required additional treatment; from this group of 6 eyes that had an additional treatment, 1 eye had superficial keratectomy, 4 eyes had repeat anterior stromal puncture, and 1 eye had PTK. No adverse reactions such as haze or infections were observed during the follow-up period. None of the patients developed any dense central scarring that was visually significant.

Clinical features of the 6 eyes from 5 patients that had additional interventions after a single anterior stromal puncture treatment are listed in the Table. Two of the 5 patients that underwent repeat anterior stromal puncture had bilateral involvement. The fellow eye had milder symptoms that responded to medical treatment, excluding Patient 2, who had both eyes treated. Four of the 6 eyes that had repeat anterior stromal puncture had a history of trauma; 1 eye had a history of soft contact lens wear. Four of the 5 patients that had additional anterior stromal puncture treatment had resolution of their symptoms. One patient failed repeat anterior stromal puncture treatment because of persistent loose epithelium and thus elected for superficial keratectomy. He remained symptomatic at the time of this manuscript preparation and is contemplating PTK. The repeat treatments were performed between 2 weeks after anterior stromal puncture procedure and 11 months following the procedure.

Eighty-three percent of patients (25/30) had a successful treatment of anterior stromal puncture and did not require further surgical procedures. Sixty-four percent of these

patients (16/25) had a history of trauma, 4% (1/25) had LASIK 1 year prior to anterior stromal puncture, 8% (2/25) had EBMD, and 24% (6/25) had no history of trauma, EBMD, or refractive surgery. Only 12% (3/25) had bilateral involvement; 2 patients had EBMD and 1 patient had bilateral corneal trauma.

Postoperatively, 71.4% of eyes that were treated (25/35) had faint non-visually significant corneal scars on slit-lamp examination, 9% (3/35) had EBMD signs and no scarring, 9% (3/35) had clear corneas, and 11% (4/35) had loose epithelium. These 4 eyes needed further treatment.

DISCUSSION

RECURRENT CORNEAL EROSION SYNDROME IS A RELATIVELY common ophthalmic syndrome, seen by both corneal specialists and general ophthalmologists. Patients suffering from recurrent corneal erosion syndrome often experience recurrent episodes of pain, photophobia, tearing, redness, and decreased vision, which often are debilitating. There are many different prophylactic and treatment options available for recurrent corneal erosion syndrome; however, there is no agreement as to what is the best management. Many of the patients respond to topical lubricating drops, gels, and ointments, which serve to prevent recurrent erosions by keeping the eye lubricated during rapid eye movement and prior to eye opening in the morning upon awakening. Hyperosmotic agents are used as well to minimize epithelial edema. Patching during an acute attack with lubricants or an antibiotic ointment helps to resolve the attack in the majority of patients. Inhibitors of matrix metalloproteinase-9 such as topical corticosteroids, doxycycline, and autologous serum drops have also been reported for the medical treatment of recurrent corneal erosion syndrome.^{6,7,13} Therapeutic bandage contact lenses provide symptomatic relief and encourage healing of the epithelium. It may be tried after medical modalities of treatment have failed. Overnight use of scleral contact lenses has been reported to be effective in recurrent corneal erosion syndrome attributable to ocular surface disorders.¹⁴

There are several surgical management options for recurrent corneal erosion syndrome, including diamond burr polishing of Bowman layer and PTK. A retrospective, nonrandomized comparative trial of 42 eyes in 39 patients that compared PTK with diamond burr polishing in the treatment of recurrent corneal erosion syndrome secondary to anterior basement membrane dystrophy⁹ found that there was no statistically significant difference between the diamond burr and PTK groups in terms of symptom improvement, recurrence of erosions, haze, or visual acuity. The study concluded that diamond burr treatment, being a simpler, less expensive office procedure, seemed to have advantages over PTK in the treatment of recurrent corneal erosions.

Anterior stromal puncture is a known technique for the treatment of recurrent corneal erosion syndrome. Its

TABLE. Anterior Stromal Puncture for Recurrent Corneal Erosion Syndrome: Clinical Features of Eyes Needing Additional Interventions After Anterior Stromal Puncture

Patient Number	Patient Age at Surgery (y)	Eye Treated	Fellow Eye Symptomatic	Corneal Signs Diffuse or Focal	Additional Intervention(s) After ASP	Past Ocular History	Previous Trauma	Past Medical History	Symptoms Post Treatment
1	15	Left	Yes	Diffuse	PTK, left eye	None (RCES OU)	No	None	3 months f/u: asymptomatic
2	26	Both	Yes	Diffuse	Repeat ASP, OU Prior to repeat ASP had PTK OU	Trauma OU, MGD	Yes	None	5 years f/u: asymptomatic
3	28	Left	No	Focal	Repeat ASP over the same area	Trauma	Yes	None	4 years f/u: asymptomatic
4	52	Right	Yes	Focal	Repeat ASP over the same area	Soft contact lens wear	No	None	7 months f/u: asymptomatic
5	49	Left	No	Diffuse	Tried to repeat ASP, epithelium remained loose, did superficial keratectomy	Trauma	Yes	HTN	Symptomatic, patient considering PTK treatment

ASP = anterior stromal puncture; HTN = hypertension; MGD = meibomian gland dysfunction; PTK = phototherapeutic keratectomy; RCES = Recurrent corneal erosion syndrome.

mechanism of action is to improve epithelial adherence by inducing scar tissue to form between the epithelium and anterior stroma. McLean was the first to describe anterior stromal puncture in 1986.¹¹ His study included 21 eyes in 18 patients. A 20 gauge needle was used to puncture the cornea perpendicularly, through loose epithelium and Bowman layer deep into the anterior half of the stroma. Such deep stromal penetration would cause visible, obvious scars. Approximately 15-25 punctures were positioned 0.5-1 mm apart. Rubinfeld and associates, in their study on 25 patients, suggested using a smaller-sized bent needle (27 gauge or 30 gauge) for anterior stromal puncture.¹⁵ They found that an insertion depth of 0.1 mm was enough to cause fibrocytic reaction.

The technique we used avoids long, large-bore 20 gauge needles, which are difficult to bend for ergonomic ease, and small 30 gauge needles, which can be floppy and more difficult to control, increasing risk for perforation. We have found that a 25 gauge short bent needle is the perfect size for achieving adequate indentation into the epithelium to trigger the anterior stroma to induce a fibrocytic reaction that leaves no obvious stromal scarring. The risk of corneal perforation is also minimized using this technique. Using the 25 gauge bent needle is simple, is cost effective, and has no need for special equipment (ie, excimer laser or a diamond burr). No chemicals are used, such as alcohol for epithelial debridement, and since the epithelium remains relatively intact, without a large epithelial defect, patients heal very quickly and experience less discomfort. None of the patients in our series had complications of corneal scarring, haze, or infection. In case of recurrent episodes of pain following a treatment of anterior stromal puncture, the procedure can be repeated multiple times and it does not preclude the patient undergoing future PTK or other treatments. Another option available is to perform anterior stromal puncture using the Nd:YAG laser.^{10,16} Our technique has the advantage of not needing any additional expensive equipment such as an Nd:YAG laser.

Unfortunately, none of the treatments for recurrent corneal erosion syndrome, including anterior stromal puncture, are guaranteed to eliminate symptoms completely. Patients following all treatments need to be supplemented by daytime lubrication with artificial tears and nighttime lubrication with ointment. There are potential risks as well if improper technique is used, including perforation, corneal scarring, changes in refractive power, and topographic irregularities. Rubinfeld and associates in their series of 25 patients had no complications after anterior stromal puncture,¹⁵ similar to our report. Sridhar and associates compared diamond burr polishing of Bowman membrane and PTK; in the PTK group, mild haze was seen in 5 eyes (35.7%). In the diamond burr group, mild haze was seen in 7 eyes (25.9%).⁹

In our series, we found a slight male predominance (60%), and the mean age of patients at the time of diagnosis was 37 (± 11.5 SD) years. Brown and Bron published a case series of 80 patients with recurrent corneal erosion syndrome where

the mean age at the time of presentation was 42 years with a slight male predominance (56%), similar to our findings.¹⁷ Reidy and associates did a retrospective review of 104 patients (68 women, 36 men) with a mean age of 43 years.¹⁸ Other studies found a female predominance.^{19,20} In our series 83.3% of patients (25/30) had unilateral involvement and 16.7% (5/30) had bilateral involvement. Recurrent corneal erosion syndrome may be either primary or secondary, depending on whether the defect in the epithelial basement membrane is intrinsic or acquired; we found that 62.9% (22/35) had a prior history of trauma; our data correlates to other series.^{20,21} In 97% of eyes on examination there were slit-lamp findings of microcysts, fingerprint lines, loose epithelium, and/or faint scars.

The technique of anterior stromal puncture used in our study was effective, with 62.9% of eyes completely symptom-free following a single procedure. A total of 37.1% of eyes had improvement in symptoms, which became milder and less frequent. Only 17% of eyes required additional treatment. On slit-lamp examination after the procedure, 71% of eyes (25/35) had faint non-visually significant corneal scars, indicating that the punctures were sufficiently deep into the anterior stroma for good effect. Reeves and associates in their study presented a higher failure rate of stromal puncture treatment (ie, requiring further treatment) of 23.9%.²² They concluded that one quarter of surgically treated episodes (both stromal puncture and PTK) recurred. The success rate in other series, as calculated by no return of macroerosion of the cornea, ranged from 76%-94%.^{11,15}

Of the eyes that failed a single anterior stromal puncture treatment and needed further treatment, 66% had a previous history of ocular trauma; 1 eye had a history of soft contact lens wear. Three of 6 eyes had treatment over a focal area of the cornea. All but 1 eye had obvious findings of microcysts and fingerprint lines on examination prior to treatment. Four of 6 eyes had symptoms in the fellow eye as well. In our series we found that a similar percentage (64%) of the eyes that did well (ie, no more recurrences or reduced recurrences with milder symptoms after a single anterior stromal puncture treatment) had a history of

trauma as compared to 66% of eyes that failed the treatment. This suggests that trauma is not a predictor of the success of anterior stromal puncture treatment. Twelve percent of patients (3/25) that required just a single treatment had bilateral involvement. This is in contrast to 66.6% of patients who failed a single treatment and had bilateral symptoms. Patients with bilateral EBMD have more diffuse and severe disease, may be considered different from those with unilateral focal superficial trauma, and may benefit from superficial keratectomy instead. Further studies are needed to confirm additional predictors for successful anterior stromal puncture treatment.

Hykin and associates presented a series of 117 patients with a history of recurrent corneal erosion syndrome and concluded that patients with EBMD or a trauma-related focal epithelial basement membrane abnormality were more likely to present with chronic recurrent symptoms than trauma-related cases with no clinically obvious corneal abnormality.²¹ In contrast, Heyworth and associates did a 4-year review for the same cohort of patients and found that those eyes with a traumatic etiology were less likely to suffer chronic recurrent erosion syndrome than those with no trauma and EBMD clinical findings only.²³

Our study has weaknesses inherent to any retrospective study. We did not have sufficient data to determine whether certain corneal findings were more prominent than others, but nevertheless, this is one of the largest series in the literature describing the outcomes after anterior stromal puncture. The technique described is a variation proven to be simple, effective, cost effective, and repeatable. We recommend it as a good first-line surgical intervention that can be done at the slit lamp by any ophthalmologist should a patient with recurrent corneal erosion syndrome symptoms fail medical management alone. The results from this study allow the ophthalmologist to advise patients that a single treatment of anterior stromal puncture should resolve or improve their recurrent corneal erosion syndrome symptoms. The procedure can also be repeated prior to alternate options that require more time, expense, and inconvenience to the patient.

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Biosketch

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