

## PTERYGIUM SURGERY WITH MITOMYCIN AND TARSORRHAPHY

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### ABSTRACT

*Purpose:* To determine if a pterygium surgical procedure consisting of minimal conjunctival removal, excision of the hypertrophic subconjunctival fibrovascular tissue, application of mitomycin 0.25 mg/mL for 1 minute combined with temporary nasal tarsorrhaphy, and use of postoperative dexamethasone/antibiotic drops achieves the following: safely simplifies pterygium removal, controls the early side effects of mitomycin, reduces the rate of recurrence, and lessens the need for conjunctival transplantation.

*Methods:* Twenty eyes in 19 patients underwent the procedure with use of mitomycin; 15 eyes had primary and 5 had recurrent pterygia. These were compared with a previous group of 28 eyes in 26 patients that underwent pterygium/tarsorrhaphy surgery without use of mitomycin; 20 eyes had primary and 8 had recurrent pterygia. Postoperatively, all eyes in both groups were treated with dexamethasone/antibiotic drops.

*Results:* In the mitomycin group, with an average follow-up of 12.1 months, 19 eyes healed uneventfully; there have been no recurrences. The nonmitomycin group, with an average follow-up of 42.6 months, has had nine recurrences (32%); four required a second procedure. Recurrence was significantly lower in the mitomycin group ( $P = .006$ ). Conjunctival healing, as reflected in the time from surgery until tarsorrhaphy opening, was significantly delayed in the mitomycin group, 36.7 versus 17 days ( $P = .001$ ). The delay in conjunctival healing may explain the complications associated with the use of mitomycin in pterygium surgery.

*Conclusion:* Minimal conjunctival removal, extensive fibrovascular tissue excision, 1-minute application of mitomycin 0.25 mg/mL, temporary nasal tarsorrhaphy, and frequent application of dexamethasone/antibiotic drops postoperatively provided a safe and successful approach to pterygium management in this series.

*Trans Am Ophthalmol Soc 2005;103:108-115*

### INTRODUCTION

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A pterygium is a fibrovascular growth of the conjunctiva over the ocular surface extending onto the cornea. Most pterygia extend over the nasal sclera onto the cornea and may eventually obstruct vision, necessitating surgical removal.

Surgery for pterygium was first reported in 1000 BC.<sup>1-3</sup> Throughout the three-millennium history, complications, recurrence, and worsening of the pterygium following surgery have vexed the procedure.<sup>1-6</sup> Mitomycin, isolated from *Streptomyces caespitosus*, is an antibiotic with antineoplastic properties that blocks DNA synthesis.<sup>7</sup> It was introduced as an adjunct to pterygium surgery in 1963.<sup>8</sup> Although the recurrence rate was reduced by use of mitomycin, reports of side effects associated with its use (eg, pyogenic granuloma, dellen of the sclera, perforation of the eye, glaucoma, cataract, corneal edema) have remained obstacles to its usefulness.<sup>9-16</sup> These complications may also occur following surgery without mitomycin as a consequence of nonhealing of the cornea and scleral surface (eg, incomplete pterygium removal resulting in pyogenic granuloma, corneoscleral dellen, dellen with subsequent perforation) (Figures 1, 2, and 3).

The objective of this study is to determine if a new surgical procedure achieves the following: improves the safety and simplicity of pterygium removal, prevents most postoperative complications, reduces the recurrence rate, and lessens the need for conjunctival transplantation.<sup>17</sup>

### METHODS

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#### Surgical Technique

The technique involves combining minimal removal of the conjunctiva with extensive excision of the hypertrophic subconjunctival fibrovascular tissue and topical application of mitomycin, 0.25 mg/mL, for 1 minute followed by copious irrigation with balanced salt solution. Next, the conjunctiva is reattached to the leading edge of the medial rectus muscle with 9-0 Vicryl, and a temporary nasal tarsorrhaphy is performed (Figures 4A, 4B, and 4C). Postoperatively, topical dexamethasone/antibiotic is used for an average of six times daily the first week and tapered by one drop per week, over a 6-week period. The tarsorrhaphy is opened when the cornea, conjunctiva, and scleral surface have healed adequately. A previous group underwent the same procedure except without the application of mitomycin.

From the University of Tennessee Health Science Center, Memphis, Tennessee (Dr Wood, Dr Williams), and Associated Ophthalmic Specialists, Inc, Germantown, Tennessee (Dr Wood, Ms Williams, Ms Hamilton).

\*Presenter.

**Bold** type indicates **AAO** member.

## Data Analysis

A two-tailed Fisher's exact test was used to assess independence of the two groups. This nonparametric test is commonly used to analyze binomial distributions in which the observed frequency is less than 5 in more than 25% of the categories. Fisher's was used to calculate the exact probability that the observed differences between the mitomycin- and nonmitomycin-treated groups were due to chance. The strength of the relationship between treatment and recurrence was estimated by using a Cramer's V test statistic. An independent samples *t* test was used to compare the mean tarsorrhaphy length between the two groups.

## RESULTS

Twenty eyes in 19 patients, 15 primary and five recurrent cases, have undergone the procedure with mitomycin (Table 1). The group consisted of 15 men and four women ranging in age from 26 to 74 years, with an average age of 53.8 years at the time of surgery. Twenty-eight eyes in 26 patients, 20 primary and eight recurrent cases, underwent the same surgery except without mitomycin (Tables 2 and 3). In this group, there were 19 men and seven women ranging in age from 31 to 78 years, with an average age of 56.1 years at the time of surgery.

The initial results in the mitomycin group (average follow-up, 12.1 months; range, 2 to 29 months) show no recurrences and no severe complications (Figure 5A). One patient developed early fibrovascular proliferation after he discontinued his drops and the tarsorrhaphy opened; the eye healed without incident following repair of the tarsorrhaphy and resumption of the dexamethasone/antibiotic drops. His other eye underwent pterygium surgery with mitomycin and without incident.

In the group without mitomycin treatment (average follow-up, 42.6 months; range, 5 to 143 months), all eyes healed without early complications. Nine of the 28 eyes had recurrence of the pterygium. The average time to recurrence for the five that stabilized was 6.2 months (Figure 5B). The four eyes requiring a second procedure (ie, conjunctival transplant) had the recurrence in an average of 5 months, and the second operation was performed an average of 8.8 months after the first.

Recurrence of the pterygium was significantly lower among patients who were treated with mitomycin than in patients who were not treated with mitomycin ( $P = .006$ ). None of the patients in the mitomycin group have had a recurrence. In contrast, nine (32%) of the eyes that did not receive mitomycin have had a recurrence. The Cramer's V was .41 ( $P < .05$ ), suggesting a strong relationship between treatment and recurrence.

The number of days that all patients in both groups had the tarsorrhaphy was compared by using an independent samples *t* test. Patients receiving mitomycin had the tarsorrhaphy significantly longer (average, 36.7 days) than did untreated patients (average, 17 days) ( $P = .001$ ). The mean difference between the two groups was almost 20 days. The 95% confidence interval for this comparison ranged from about 7.5 to 31.9 days.

**TABLE 1. DEMOGRAPHIC DATA FOR PTERYGIUM SURGERY PATIENTS TREATED WITH MITOMYCIN AND NASAL TARSORRHAPHY: NO RECURRENCES**

PATIENT	SEX	AGE (YEARS)	EYE	PRESENTED AS	TARS (DAYS)*	LENGTH OF FOLLOW-UP (MONTHS)
1a	M	47	OS	Primary	23	2
1b†	M	46	OD	Primary	36	9
2	M	62	OS	Recurrent	30	3
3	M	70	OD	Primary	64	3
4	M	67	OS	Primary	9	3
5	M	56	OD	Recurrent	88	3
6	F	49	OD	Primary	44	4
7	F	57	OS	Primary	23	4
8	M	56	OS	Primary	23	4
9	M	63	OD	Primary	27	6
10	M	46	OS	Primary	28	7
11	M	67	OD	Recurrent	22	9

**TABLE 1 (CONTINUED). DEMOGRAPHIC DATA FOR PTERYGIUM SURGERY PATIENTS TREATED WITH MITOMYCIN AND NASAL TARSORRHAPHY: NO RECURRENCES**

<b>PATIENT</b>	<b>SEX</b>	<b>AGE (YEARS)</b>	<b>EYE</b>	<b>PRESENTED AS</b>	<b>TARS (DAYS)*</b>	<b>LENGTH OF FOLLOW-UP (MONTHS)</b>
12	M	42	OD	Primary	48	18
13	M	55	OS	Primary	39	20
14	M	46	OD	Recurrent	37	21
15	F	26	OS	Primary	9	22
16	M	41	OS	Primary	NA	24
17	M	74	OD	Primary	NA	25
18	M	50	OD	Primary	18	26
19	F	55	OS	Recurrent	93	29

NA = not available; Tars = tarsorrhaphy.

\*Number of days before opening.

†Tarsorrhaphy prematurely opened and drops were discontinued by patient, resulting in fibrovascular proliferation on the sclera; resolved with tarsorrhaphy reclosure and resumption of dexamethasone drops.

**TABLE 2. DEMOGRAPHIC DATA FOR PTERYGIUM SURGERY PATIENTS TREATED WITHOUT MITOMYCIN AND WITH TARSORRHAPHY: NO RECURRENCES**

<b>PATIENT</b>	<b>SEX</b>	<b>AGE (YEARS)</b>	<b>EYE</b>	<b>PRESENTED AS</b>	<b>TARS (DAYS)*</b>	<b>LENGTH OF FOLLOW-UP (MONTHS)</b>
20	M	78	OD	Primary	NA	6
21	M	67	OS	Primary	37	6
22	F	37	OD	Primary	9	6
23	M	54	OS	Primary	20	7
24	F	71	OD	Primary	16	11
25	M	54	OS	Primary	16	12
26	F	31	OS	Recurrent	16	13
27	M	61	OD	Primary	19	16
28	F	65	OS	Primary	9	17
29	M	59	OD	Primary	16	17
30	F	64	OS	Primary	16	34
31	M	47	OS	Recurrent	18	59
32	M	77	OD	Primary	18	61
33	M	50	OS	Primary	24	76
34	M	69	OS	Primary	11	79
35	M	49	OD	Recurrent	10	83
36a	M	40	OD	Recurrent	18	79
36b	M	36	OS	Recurrent	18	129
37	M	50	OS	Recurrent	13	143

NA = Not available; Tars = tarsorrhaphy.

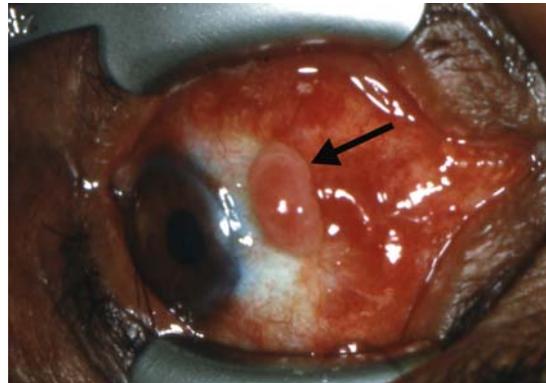
\*Number of days before opening.

**TABLE 3. PTERYGIUM SURGERY PATIENTS TREATED WITHOUT MITOMYCIN AND WITH TARSORRHAPHY: RECURRENCES**

PATIENT	SEX	AGE (YEARS)	EYE	PRESENTED AS	TARS (DAYS)*	RESULT OF RECURRENCE	TIME TO RECURRENCE (MONTHS)	TIME TO CONJUNCTIVAL TRANSPLANT (MONTHS)	LENGTH OF FOLLOW-UP (MONTHS)
38	M	71	OS	Primary	NA	Stabilized	5		10
39	F	38	OD	Primary	12	Stabilized	6		29
40	M	41	OD	Primary	NA	Stabilized	3		34
41a	F	73	OS	Primary	9	Stabilized	8		83
41b	F	73	OD	Primary	9	Stabilized	9		88
42	M	57	OD	Recurrent	23	Conjunctival transplant	2	2	5
43	M	38	OS	Primary	42	Conjunctival transplant	5	12	20
44	M	56	OD	Recurrent	16	Conjunctival transplant	7	8	29
45	M	64	OS	Primary	11	Conjunctival transplant	6	13	41

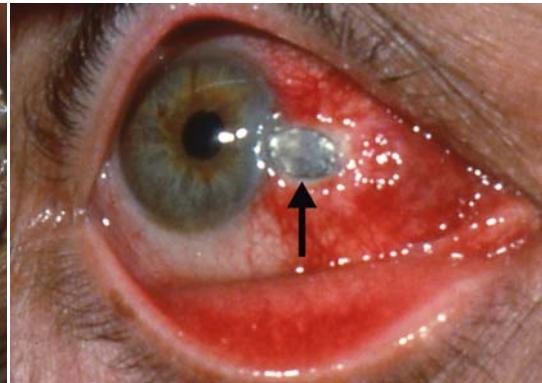
NA = not available; Tars = tarsorrhaphy.

\*Number of days before opening



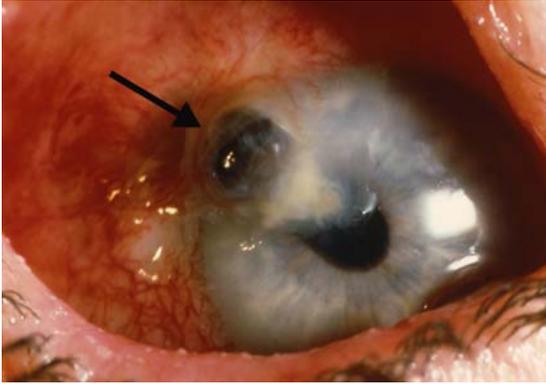
**FIGURE 1**

Postoperative pterygium with pyogenic granuloma (arrow) due to incomplete removal of subconjunctival fibrovascular tissue, edema, and chronic nonhealing. Mitomycin was not used in this eye.



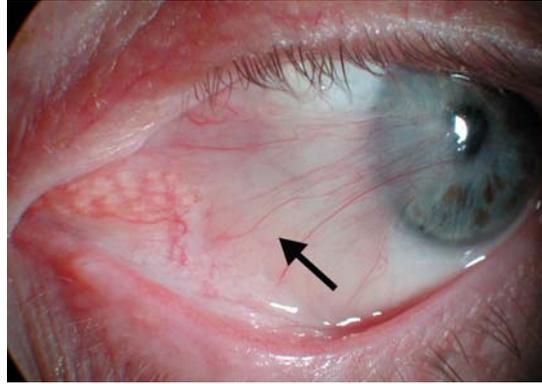
**FIGURE 2**

Postoperative pterygium with corneoscleral dellen (arrow) due to incomplete removal of subconjunctival fibrovascular tissue and surrounding edema. Mitomycin was not used in this eye. (Photo courtesy of Dr Randolph Black, Albuquerque, New Mexico.)



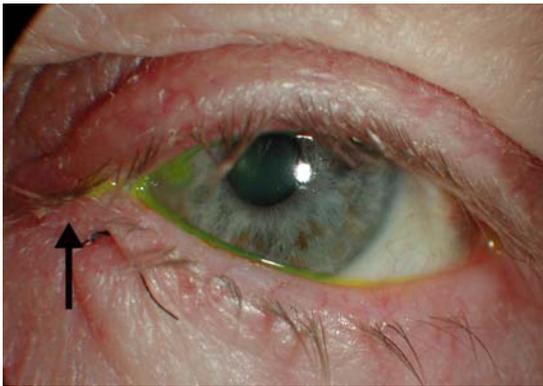
**FIGURE 3**

Postoperative pterygium with chronic nonhealing resulting in limbal and corneal dellen and subsequent perforation (arrow) with iris prolapse. Mitomycin was not used in this eye.



**FIGURE 4A**

Preoperative recurrent pterygium; note healthy-appearing conjunctiva covering subconjunctival hypertrophic fibrovascular tissue (arrow). This eye underwent minimal excision of the leading edge of the pterygium, extensive excision of the subconjunctival hypertrophic fibrovascular tissue, 1-minute application of mitomycin 0.25 mg/mL followed by irrigation with balanced salt solution, suturing the conjunctiva in front of the head of the medial rectus, and nasal tarsorrhaphy for 30 days.



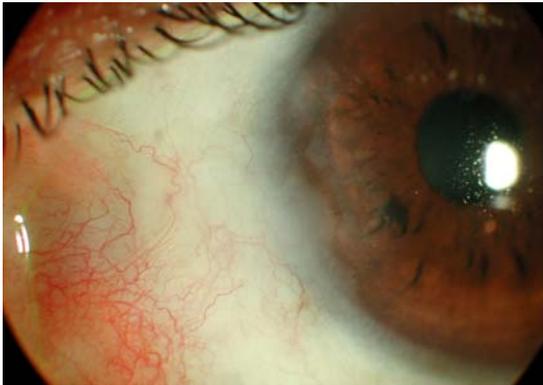
**FIGURE 4B**

Eye in Figure 4A 1 week after pterygium surgery with temporary nasal tarsorrhaphy (arrow) secured by running 6-0 nylon suture. Note how operative site is covered, and patient can still use eye.



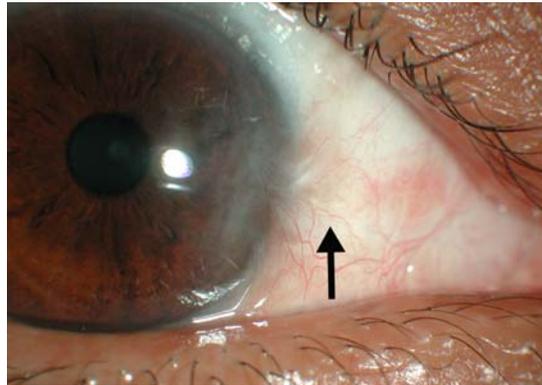
**FIGURE 4C**

Eye in Figure 4A 2 months after pterygium surgery with tarsorrhaphy opened; note healthy conjunctiva adjacent to caruncle.



**FIGURE 5A.**

Left eye 2 years after pterygium surgery with mitomycin. Technique consisted of minimal excision of the leading edge of the pterygium, extensive excision of the subconjunctival hypertrophic fibrovascular tissue, 1-minute application of mitomycin 0.25 mg/mL followed by irrigation with balanced salt solution, suturing the conjunctiva in front of the head of the medial rectus, and nasal tarsorrhaphy. Note the absence of pterygium recurrence and fibrovascular tissue.



**FIGURE 5B.**

Right eye of patient in Figure 5A, 2 years and 10 months after pterygium surgery without mitomycin. Procedure was same as described in 5A but without mitomycin. Note small recurrence and regrowth of fibrovascular tissue (arrow). Postoperatively, this eye remained chronically inflamed and required dexamethasone drops for 20 months. The pterygium stabilized, and a second procedure was not required.

## DISCUSSION

This technique involves combining five separate components to create a new procedure, which has initially provided encouraging results in pterygium management. The safety and simplicity of this technique make it an easily transferable skill to other ophthalmologists.

A review of the essentials of the procedure is as follows: First, minimal conjunctiva is removed, usually just the head of the pterygium. Then, hypertrophic subconjunctival fibrovascular tissue, which can be the progenitor of recurrence and complications, is carefully excised after injecting the tissue with 2% lidocaine with epinephrine. Hemostasis is obtained with the application of topical thrombin or cautery, or both. Mitomycin, 0.25 mg/mL, is applied by means of a small sponge for 1 minute to the exposed sclera and underside of the conjunctiva. This is followed by copious irrigation with balanced salt solution. The conjunctiva is reattached at the head of the medial rectus to reduce conjunctival contracture. A nasal tarsorrhaphy is essential in covering the open cornea and sclera to facilitate healing. The tarsorrhaphy was opened an average of 36.7 days postoperatively in the mitomycin group, as compared with the 17 days in the nonmitomycin group, indicating the prolonged healing time required in the mitomycin group. This delay in healing is most likely responsible for the complications reported with the use of mitomycin in pterygium surgery. Topical corticosteroids reduce neovascularization, inflammation, and edema, which further facilitates the healing process.<sup>18</sup>

Initial results in the mitomycin group (average follow-up, 12.1 months) show no recurrence in 20 eyes. Nineteen eyes have postoperative observation of 3 months or longer, 12 have at least 6 months, and eight have been observed for 1 year or more. This is encouraging because recurrence following mitomycin treatment in pterygium surgery has been reported at 45% within 6 months and 91% within 1 year.<sup>19</sup> All of the recurrences in the nonmitomycin group (average follow-up, 42.6 months; range, 5 to 143 months) were manifest by 9 months postoperatively, with the average recurrence being 5.7 months.

These findings suggest that this technique with mitomycin is a safe and effective approach to pterygium management. Longer follow-up is needed for final evaluation.

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## PEER DISCUSSION

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DR EDWARD J. HOLLAND. There are a variety of surgical techniques that have been described for pterygium. Most recently mitomycin C has been used to prevent recurrence after pterygium excision. In the present study Dr Wood and colleagues utilized pterygium excision with a bare scleral technique and intraoperative mitomycin C (0.25mg per ml for 1 minute). In addition, a temporary nasal tarsorrhaphy was performed and frequent topical steroids were utilized post-operatively. In this study group there were 21 eyes of 20 patients. Sixteen patients had primary pterygium and 15 had recurrent pterygium. This group was compared retrospectively to a group of patients that underwent pterygium excision with a bare scleral technique, tarsorrhaphy, and post-operative steroids. Mitomycin was not utilized in this group of patients. In this comparison group there were 28 eyes and 26 patients. Twenty patients had a primary pterygium and eight had a recurrent pterygium.

The results showed that there were no recurrences in the mitomycin group, although one patient (4.8%) required a repair of the tarsorrhaphy. The range of follow-up in this group was two to 29 months with a mean of 10.9 months. In the non-mitomycin group recurrences were seen in nine of 28 eyes or 32%. Four of 28 eyes needed additional pterygium surgery (14.2%). The mean follow-up time in this group was considerably longer at 42.3 months with a range of 5.5 to 143 months.

This study is a non-randomized retrospective comparison. Overall, there was a very short follow-up time of 10.9 months in the mitomycin group. The outcomes were certainly very good in the mitomycin group with no recurrences seen. However, the authors did not compare their results to the most accepted treatment of pterygium at this present time, which is excision of pterygium with conjunctival autograft. The authors also did not address the major concern with the use of mitomycin which is the high complication rate that has been reported in other studies.

Complications with topical mitomycin have been well described in the literature including scleral necrosis, perforation, endophthalmitis, endothelial decompensation, limbal stem cell failure, glaucoma, and iritis. In addition, scleral necrosis has been reported beyond ten years after surgery.<sup>1</sup>

Pterygium excision with conjunctival autograft remains the most successful procedure described in the literature. This technique has the lowest recurrence rates and the lowest complication rates of the many techniques for this condition. Bare sclera techniques have a high recurrence rate and should not be utilized. The role of mitomycin, due to its severe potential complications, should be

limited to use in patients with severe multiple recurrences. In addition patients should be warned about the significant risks of this medication.

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DR GEORGE L. SPAETH. You used the word "copious" to describe the irrigation of mitomycin. Japanese glaucoma specialists have described doing glaucoma surgery in Japan, irrigating mitomycin cases with 500 ml of wash water, whereas most of the ophthalmologists in the United States use only 5 or 10 cc of balanced salt solution.<sup>1</sup> Please define your irrigation. Perhaps more importantly, what do you do with the wash water? One investigation has found that nurses who work with mitomycin have a higher incidence of birth defects in their newborns.<sup>2</sup> Mitomycin is very potent and at least some of my glaucoma colleagues just wash it off and it may just reach the floor. Is that fair to the nurses? How do you handle the irrigation fluid?

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DR GEORGE O. WARING III. Describe your tarsorrhaphy. Is it a temporary one wherein you just sew the lids together or do you actually excise part of the lid margin? Is it easier to do the tarsorrhaphy than a conjunctival transplant, which is also quite easy? And which is quicker?

DR ALLAN J. FLACH. Dr Robert Webster of San Francisco did a lot of work with the cyanoacrylate glues and would occasionally use them for tarsorrhaphies with good results. Do you think gluing your tarsorrhaphy might work better in some patients?

DR THOMAS O. WOOD. Following Dr Holland's discussion it seems appropriate to repeat the purpose of our study: safely simplify pterygium removal, control the early side effects of mitomycin, reduce the rate of recurrence, and lessen the need for conjunctival transplantation.

Published complications attributed to mitomycin are carefully referenced. Three cases are presented documenting that these complications were well recognized before the advent of combining mitomycin with pterygium surgery. We concluded that non-healing is the cause of most of the complications associated with mitomycin treatment. This study is directed at stimulating prompt conjunctival healing following surgery, thereby preventing early complications.

Dr Holland's reference to scleral necrosis occurring "beyond ten years after surgery" was reported with high dose mitomycin. In this study, we used low dose mitomycin for only one minute. Although not part of this manuscript, scleral thinning and calcification may occur fifteen years post-terygium surgery without mitomycin

This study, with an average follow up of one year, has had zero mitomycin complications and zero recurrences. Most mitomycin complications occur in the early post-operative period, not ten years later. Additionally, as noted in the manuscript, recurrences following mitomycin treatment were 45% at six months and 91% within the first year following surgery.

Elimination of conjunctival grafting permits surgical options for the future. The past fifteen years has produced approximately 149 articles regarding conjunctival transplantation and 138 referring to mitomycin for the treatment of pterygium. To come to the conclusion that conjunctival transplantation is the best procedure for pterygium surgery, one should have personal experience with our technique, conjunctival transplantation, and knowledge of the 287 publications.

To Dr Spaeth: Concerning the dosage of mitomycin, I suspect that the women having children with birth defects were dealing with systemic mitomycin. I only use a mitomycin soaked, microscopic sponge and irrigate with 10-30 ml of BSS afterwards.. The nurses in our operating room are unbelievably fastidious while handling mitomycin.

To Dr. Waring: The tarsorrhaphy is quick, nasal, and temporary.

To Dr. Flack: I prefer to use a running 6-0 nylon suture; when I use cyanoacrylate glue, it sticks to the wrong tissue.