

# Successful Prevention of Bacterial Endophthalmitis in Eyes with the Boston Keratoprosthesis

Marlene L. Durand, MD\* and Claes H. Dohlman, MD, PhD†

**Purpose:** To determine the influence of topical vancomycin prophylaxis on the incidence of bacterial endophthalmitis in eyes with a Boston Keratoprosthesis (KPro).

**Methods:** A retrospective chart review was performed for 255 eyes of 231 patients who received a KPro between March 1990 and December 2006. Preoperative diagnoses were burn, ocular cicatricial pemphigoid (OCP), Stevens-Johnson Syndrome (SJS), and graft failure/other. Patients used topical antibiotic prophylaxis for the duration of the KPro: polymyxin-trimethoprim or a quinolone in the 1990s, or a quinolone with or without vancomycin beginning in late 1999. For each KPro eye, the follow-up interval was divided into months on or off vancomycin (vancomycin versus no-vancomycin group). The incidence of endophthalmitis was calculated with Kaplan-Meier survival curves.

**Results:** The 255 eyes were followed for 673.6 patient-years (mean, 2.64 years; range, 1 week to 13 years). There were 18 cases of bacterial endophthalmitis; 17 occurred at least 6 weeks post-operatively (range, 1.5 to 46 months). Gram-positive cocci caused over 80% of cases. Only 1 case, due to an atypical mycobacterium, occurred in a patient using vancomycin.

The incidence of bacterial endophthalmitis was lower in the vancomycin group than in the no-vancomycin group: 0.35% versus 4.13% per patient-year ( $P = 0.001$ ). It was also lower in SJS eyes using vancomycin versus no vancomycin: 1.76% versus 18.39% per patient-year ( $P = 0.009$ ). In eyes with preoperative diagnoses of burn, OCP, or graft failure/other, the incidence in the vancomycin group was zero.

**Conclusion:** Topical vancomycin plus a quinolone is effective in preventing bacterial endophthalmitis in KPro eyes.

**Key Words:** vancomycin, keratoprosthesis, endophthalmitis, antibiotic prophylaxis

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From the \*Infectious Disease Unit, Massachusetts Eye and Ear Infirmary and Massachusetts General Hospital; and †Department of Ophthalmology, Massachusetts Eye and Ear Infirmary and Harvard Medical School, Boston, Massachusetts.

Reprints: Dr. Marlene L. Durand, MD, Infectious Disease Unit, Jackson 504, Massachusetts General Hospital, Fruit Street, Boston, MA 02114 (e-mail: mdurand@partners.org).

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## INTRODUCTION

The greatest vision-threatening risk facing any type of keratoprosthesis (KPro) is bacterial endophthalmitis. The device bridges the nonsterile ocular surface with the sterile anterior chamber, subjecting the eye to the risk of rapid invasion of pathogenic organisms through the space between the tissue and plastic material. Acute bacterial endophthalmitis may occur months or years after KPro placement, similar in this respect to bleb-related endophthalmitis.<sup>1</sup> To prevent this complication, all patients with the Boston KPro placed since 1990 have received prophylactic antibiotic eyedrops daily and indefinitely. During the 1990s, the regimen used was polymyxin-trimethoprim, ciprofloxacin, or ofloxacin. A review of our experience of that decade revealed that this regimen was inadequate for some eyes, particularly those with cicatrizing (autoimmune) diseases such as Stevens-Johnson Syndrome (SJS) or ocular cicatricial pemphigoid (OCP).<sup>2</sup> Because gram-positive bacteria, such as staphylococci and streptococci, caused all cases of endophthalmitis in those patients, topical vancomycin was subsequently added to the prophylactic regimen for many KPro eyes, and for nearly all eyes with autoimmune diseases.

To determine the effect of a topical vancomycin-containing prophylactic regimen on the incidence of bacterial endophthalmitis in KPro eyes, we reviewed our experience over the past 17 years.

## PATIENTS AND METHODS

The study was approved by the Human Studies Committee of the Massachusetts Eye and Ear Infirmary. Charts were reviewed of all patients who were followed between 1990 and July 1, 2007, and who received a Boston KPro at Massachusetts Eye & Ear Infirmary between March 1, 1990, and December 1, 2006. Surgery was performed in all patients by one of the authors (CHD). The two types of KPros used are shown in Fig. 1. During this time, 235 patients received KPros but 4 were excluded from this analysis: 2 were lost to follow-up soon after surgery and 2 lost vision soon after surgery (intraocular hemorrhage in one, severe choroidal detachment in the other). Of the remaining 231 patients, 19 received a KPro in both eyes at different times, 4 patients received both types of KPros (Type 1 or Type 2) at different times in the same eye, and 1 patient received a repeat KPro of the same type in the same eye but with an 8-year hiatus between losing the first KPro and placement of the second. These 24 eyes were counted separately. Eyes that required an exchange KPro (for example, to repair a leak around a KPro)



FIGURE 1. KPro types 1 and 2.

were counted only once, with start date as date of the primary KPro. Therefore, this study included 255 eyes in 231 patients.

Ninety-six eyes received a primary KPro between March 1, 1990, and Dec. 31, 1999, and 159 eyes received a primary KPro between January 2000 and December 2006. The patients had a variety of ocular diagnoses, which fell into 4 main categories: ocular cicatricial pemphigoid (OCP), Stevens-Johnson syndrome (SJS), chemical or thermal burns (burn), and graft failure/other (Table 1). This last category included noncicatrizating ocular conditions, such as dystrophies, aniridia, trauma, herpetic keratitis, and degenerations, that led to repeated corneal graft failure.

### Keratoprosthesis

A Type 1 or Type 2 Boston KPro was used in all patients (Fig. 1). Type 1 is used in eyes that can maintain a hydrated ocular surface and have relatively normal lid function. Type 2 has a stem extending anteriorly through a surgically closed lid and is used in those with end-stage dry eye conditions. A Type 1 KPro was placed in 201 eyes and a Type 2 in 54 eyes. Since January 2000, most KPros implanted (over 85%) have been Type 1. For surgical techniques and postoperative regimens, see elsewhere.<sup>3</sup> Since mid-1999, most patients with a Type 1 KPro have used a therapeutic soft contact lens (Kontur Kontakt Lens, Richmond, CA), usually either of 16.0 mm diameter/9.8 mm base curve or 18.0 mm diameter/7.0 mm base curve. This

TABLE 1. Preoperative Diagnosis in 255 KPro Eyes and Duration of Follow-up

	Number of Eyes	Cumulative Follow-up (years)
Burn	38	131.4
OCP	47	140.5
SJS	30	78.6
GF/Other	140	323.1
Total	255	673.6

Note. Burn, chemical or thermal burn; OCP, ocular cicatricial pemphigoid; SJS, Stevens-Johnson Syndrome; GF/Other, graft failure/other.

lens is kept in place continuously for weeks to months and is replaced only when it is lost or dislocated or shows evidence of debris. The lens helps maintain ocular surface hydration.<sup>4</sup>

### Antibiotic Prophylaxis

Topical antibiotic solutions have been used in all eyes since 1990 as prophylaxis against endophthalmitis. These are usually administered 3 times daily, beginning immediately after KPro surgery, and after a week the frequency is reduced to once or twice daily, to be continued indefinitely. For Type 1 KPro eyes, eyedrops are instilled in the lower fornix in the usual fashion. In Type 2 KPro eyes, antibiotics are applied around the KPro nub. Antibiotic drops are used rather than ointments because ointments would grease up the optical surface and are hard to clean off. A single commercially available antibiotic was used as the prophylactic regimen in all patients from 1990 until late 1999. In the early 1990s, this was usually polymyxin-trimethoprim. A topical quinolone became the primary agent by the late 1990s. This was initially ciprofloxacin 0.3% or ofloxacin 0.3%, but in recent years it has been moxifloxacin 0.5% or gatifloxacin 0.3%. The type of antibiotic was not rotated over time. Beginning in November 1999, topical vancomycin was added as a second agent to the quinolone regimen for many eyes, especially those with autoimmune eye diseases. Vancomycin drops were made up by the pharmacy at a concentration of 1.4% (14 mg/mL) and were kept refrigerated by the patient during use and discarded after 1 week. After April 2005, topical vancomycin included benzalkonium chloride 0.005%, which patients used at room temperature. This solution has been shown to have chemical stability for up to 60 days.<sup>5</sup> Most eyes (74%) implanted with a KPro for the first time during 2000–2006 received a topical regimen that included vancomycin for all (60%) or part (14%) of their follow-up time.

### Bacterial Endophthalmitis

Acute bacterial endophthalmitis was suspected in patients with sudden onset of eye pain, decreased vision, and intraocular inflammation. The one case of indolent bacterial endophthalmitis (due to mycobacteria) was suspected because of progressive decrease in vision and persistent intraocular inflammation. Suspected cases were considered confirmed and included in this analysis if cultures of aqueous, vitreous, or both yielded bacteria.

### Cultures

In eyes with suspected endophthalmitis, samples of aqueous, vitreous, or both were obtained. These samples were cultured for bacteria and fungi by inoculation on blood agar, chocolate agar, thioglycolate broth, and Sabouraud dextrose agar.

### Statistics

To determine the long-term effect of vancomycin in preventing bacterial endophthalmitis, we included only the 254 eyes with at least 1 week of follow-up. We therefore excluded the 1 case of endophthalmitis that occurred on postoperative day 3. Of note, this patient was not on vancomycin; inclusion would have increased the apparent benefit of vancomycin prophylaxis.

We calculated the incidence of bacterial endophthalmitis by exposure to vancomycin as the number of eyes that developed bacterial endophthalmitis after KPro placement, divided by the sum of the accumulated months of follow-up for all KPro eyes. The start date of follow-up was the date of initial KPro placement, and the end date was the last date the patient was seen (on or before July 1, 2007). In patients who developed bacterial endophthalmitis, had the KPro removed, or lost all vision in the KPro eye, the end date was the date of these events. Topical vancomycin was used for the entire follow-up interval in some eyes, whereas in other eyes vancomycin was used for none or only part of the follow-up interval. For each KPro eye, follow-up time was allocated into exposed (time on vancomycin) or unexposed (not on vancomycin) categories, to the nearest month. The time-related cumulative incidence of endophthalmitis in each category was evaluated by means of Kaplan-Meier survival curves. Results are expressed in percent per patient-year (number of cases of endophthalmitis per 100 patient-years).

## RESULTS

We followed 255 eyes for a total of 673.6 years, for a mean follow-up time of 2.64 years (range, 1 week to 13 years). The preoperative diagnostic categories (burn, OCP, SJS, and graft failure/other) are listed in Table 1. Autoimmune preoperative diagnoses of OCP and SJS, previously associated

with a high risk of developing endophthalmitis,<sup>2</sup> accounted for 30% of cases and 33% of the follow-up time.

There were 18 cases of bacterial endophthalmitis, for an overall incidence of 0.027 cases per patient-year (Table 2). Fifteen cases (83%) were due to gram-positive cocci: 10 were due to various streptococci (Group B, viridans streptococci, *S. pneumoniae*), 2 were due to *Staphylococcus aureus*, and 3 to *S. epidermidis*. Two cases were due to gram-negative bacteria (*Pseudomonas* species and *Serratia marcescens*). The *Pseudomonas* case occurred 2 years after the patient had returned to his home in Saudi Arabia. The *Serratia* case occurred in an eye with a severe burn and developed acutely on postoperative day 3: a nosocomial source was suspected but not found. One case was due to an atypical mycobacterium, *Mycobacterium abscessus*.

Patients with endophthalmitis presented with acute ocular symptoms; none had evidence of infection outside the eye. All but one presented 6 weeks or more after surgery (range, 6 weeks to 46 months). Nearly all patients presented with abrupt loss of vision and severe intraocular inflammation; many also had pain. The case due to atypical mycobacteria was a patient with SJS who presented with acute painless decrease in vision but with minimal intraocular inflammation. Endophthalmitis was not suspected until vitrectomy 4 weeks later, when intraocular stains and cultures were positive for *M. abscessus*. This patient had developed a chronic lid infection due to this atypical mycobacterium around the Type 2 stem

**TABLE 2.** Bacterial Endophthalmitis in KPro Eyes, 1990–2006

Case	Category (Preoperative Diagnosis)	KPro Type	Surg. year	Infection (Months Postop)	Vancomycin, Current Use	Bacteria	Final Vision
1	OCP	2	1990	9	no	<i>S. aureus</i>	NLP
2	SJS	1	1994	13.5	no	<i>S. pneumoniae</i>	NLP
3	SJS	1	1995	14.5	no	<i>S. pneumoniae</i>	NLP
4	Burn	2	1996	38	no	<i>S. aureus</i>	HM
5	Burn	1	1996	46	no	<i>S. pneumoniae</i>	LP
6	OCP	2	1996	2.5	no	viridans streptococci	NLP
7	OCP	1	1996	36	no	viridans streptococci	20/200
8	OCP	1	1997	28.5	no	viridans streptococci	NLP
9*	SJS	1	1999	1.5	no	Group B <i>Streptococcus</i>	LP
10	SJS	2	1999	6	no	<i>S. epidermidis</i>	LP
11†	GF/other	1	1999	26	no	<i>Pseudomonas</i> sps.	N/A
12	GF/other	1	1999	1.5	no	<i>S. epidermidis</i>	20/50
13	GF/other	1	2000	4	no	<i>S. epidermidis</i>	20/40
14	GF/other	1	2000	36	no	<i>S. pneumoniae</i>	NLP
15‡	SJS	2	2001	33.5	yes	<i>M. abscessus</i>	LP
16§	GF/other	1	2002	5.5	no	viridans streptococci	NLP
17¶	Burn	1	2004	3 days	no	<i>Serratia</i>	NLP
18†	GF/other	1	2005	4	no	streptococci	N/A

Note. OCP, ocular cicatricial pemphigoid; SJS, Stevens-Johnson Syndrome; Burn, chemical or thermal burn; GF/other, graft failure/other; *S. aureus*, *Staphylococcus aureus*; *S. epidermidis*, *Staphylococcus epidermidis*; *S. pneumoniae*, *Streptococcus pneumoniae*; *M. abscessus*, *Mycobacterium abscessus*. LP, light perception; NLP, no light perception.

\*Patient 9 stopped prophylactic eyedrops (ciprofloxacin) 3 days before onset of endophthalmitis.

†Patient 11 developed endophthalmitis due to “a rare variant of *Pseudomonas*” after return home to the Middle East. Patient 18 developed streptococcal endophthalmitis after return home to the southern U.S. Final visual acuity not available (N/A).

‡Eye 15 is the right eye and eye 10 is the left eye of the same patient. This patient was on vancomycin and quinolone prophylaxis at the time of the second episode, which presented subacutely (see text).

§Patient 16 continued ofloxacin gtt but stopped vanco eyedrops 4 days before onset of endophthalmitis.

¶Note that onset of endophthalmitis for patient 17 is given in days, rather than months.

several months earlier and had responded to topical and systemic antibiotics.

Treatment of bacterial endophthalmitis included vitreous aspirate or vitrectomy plus intraocular injection of antibiotics in all but the earliest 3 cases (cases 1–3). In those cases, intravitreal antibiotics were not given (case 1) or given more than 24 hours after presentation. In the remaining cases, vitrectomy or vitreous aspirate plus intravitreal and systemic antibiotics were given as soon as endophthalmitis was suspected.

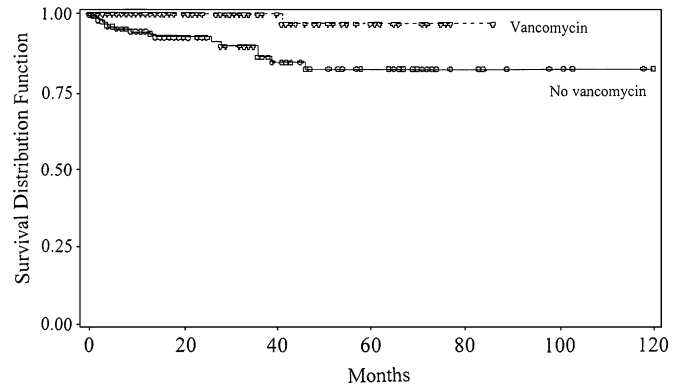
The visual outcome was poor in most cases, most likely reflecting the virulence of the causative organisms. The only two patients who regained excellent vision (cases 12, 13) had *S. epidermidis* as the pathogen, an organism associated with the best outcomes in other types of endophthalmitis.<sup>6</sup>

Only one case of bacterial endophthalmitis occurred in a patient using topical vancomycin, whereas 17 cases occurred in patients not on vancomycin at the time of symptom onset. All but one were using another topical prophylactic antibiotic, usually a quinolone, when endophthalmitis developed. One patient (case 9) had been on ciprofloxacin prophylaxis but stopped this and developed Group B streptococcal endophthalmitis 3 days later. Another patient (case 16) had been using both vancomycin and ofloxacin eyedrops but stopped vancomycin and developed viridans streptococcal (*Streptococcus mitis*) endophthalmitis 4 days later.

Two cases of endophthalmitis occurred in one patient. This patient with SJS had a KPro placed in one eye in 1999 but developed *S. epidermidis* endophthalmitis 6 months later despite quinolone prophylaxis. When a Type 2 KPro was placed in the other eye in 2001, she was maintained on topical vancomycin plus a quinolone. Two and one-half years later, she developed a subacute *M. abscessus* endophthalmitis in this eye following a chronic lid infection, as noted above.

Outcomes in 254 eyes that were followed for at least 1 week postoperatively were further analyzed by vancomycin use (vancomycin versus no-vancomycin groups), as noted in the Methods section. The one case of endophthalmitis that occurred on postoperative day 3 was excluded from this analysis. The Kaplan-Meier analysis for the incidence of bacterial endophthalmitis in the vancomycin versus no-vancomycin groups is given in Fig. 2. The incidence was significantly lower in the vancomycin group than in the no-vancomycin group: 0.35% versus 4.13% per patient-year ( $P = 0.001$ ) (Fig. 3).

These 254 patients were also evaluated by preoperative diagnosis, and the Kaplan-Meier graph for these categories is given in Fig. 4. There was no significant difference in the incidence of endophthalmitis among the burn, OCP, and graft failure/other categories ( $P > 0.05$  between categories). Each was significantly lower than the incidence in SJS eyes, however. We also looked at the incidence of endophthalmitis by vancomycin use within each category, but this comparison could be made for only the SJS category because there were no cases of endophthalmitis in the non-SJS categories using vancomycin. In the SJS category, comparison of Kaplan-Meier curves revealed that the endophthalmitis incidence in the vancomycin group was significantly less than in the no-vancomycin group: 1.76 versus 18.39 cases per patient-year ( $P = 0.009$ ) (Table 3). This beneficial effect of vancomycin in

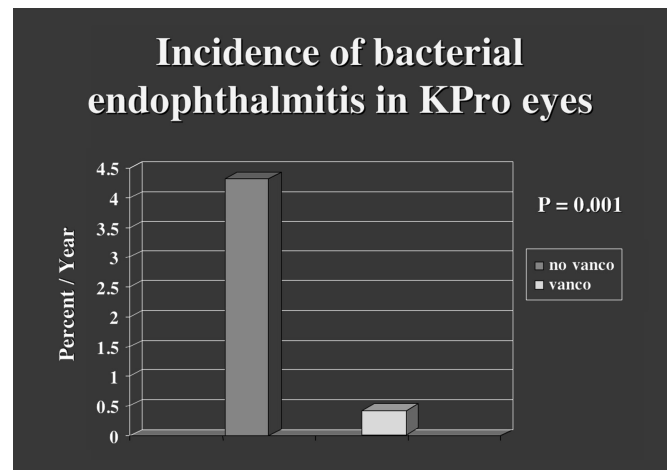


**FIGURE 2.** Kaplan-Meier graph of the incidence of bacterial endophthalmitis in the vancomycin versus no-vancomycin group, in 254 KPro eyes with at least 1 week follow-up. Endophthalmitis occurred significantly less often in the vancomycin group than in the no-vancomycin group ( $P = 0.001$ ).

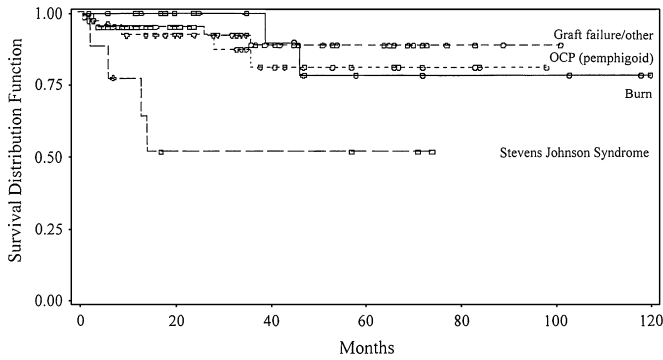
SJS eyes was seen despite the fact that cumulative follow-up time was longer in the vancomycin group than in the no-vancomycin group for this high-risk category (682 patient-months vs. 261 patient-months), allowing more time for observation of adverse events.

## DISCUSSION

In our review of the past 17 years of experience in 255 KPro eyes, we found that bacterial endophthalmitis almost always occurred abruptly, months to years postoperatively, and had devastating consequences. Virulent organisms such as



**FIGURE 3.** Bar graph showing the incidence of bacterial endophthalmitis, in the no-vancomycin group versus the vancomycin group: 4.13% versus 0.35% per patient-year of follow up, respectively. The no-vancomycin group used a single non-vancomycin antibiotic, such as a quinolone, while the vancomycin group used vancomycin plus a second antibiotic, such as a quinolone. The only case of bacterial endophthalmitis that occurred in a KPro eye on vancomycin was due to an atypical mycobacterium, and this case had an indolent presentation.



**FIGURE 4.** Kaplan-Meier graphs for bacterial endophthalmitis in 254 KPro eyes with at least 1 week follow-up, by pre-operative ocular diagnosis: Graft failure/other, ocular cicatricial pemphigoid (OCP), chemical or thermal burn (Burn), or Stevens-Johnson syndrome (SJS). Please note that this includes both the vancomycin group and the no-vancomycin group.

*S. pneumoniae* and other streptococci caused the majority of endophthalmitis cases, and over 80% of infected KPro eyes lost useful vision even though most received prompt treatment. The need for chronic topical antibiotic prophylaxis to prevent this complication in KPro eyes seems clear. Indeed, one patient in this study developed vision-destroying endophthalmitis 3 days after stopping her chronic topical antibiotics.

The optimal prophylactic regimen, especially for eyes with autoimmune conditions, appears to require an agent that has excellent gram-positive coverage. Vancomycin provides this. The addition of topical vancomycin to the standard prophylactic regimen, now a quinolone, has dramatically decreased the incidence of bacterial endophthalmitis in Boston KPro eyes. In 254 eyes with at least 1 week of follow-up (cumulative follow-up, 673.6 years), the incidence of bacterial endophthalmitis was 0.35% per patient-year in the group using a topical vancomycin-containing regimen. This was nearly 12 times lower than in eyes using the standard antibiotic prophylaxis without vancomycin ( $P = 0.001$ ).

The ongoing potential for infection in KPro eyes is similar to that in eyes with filtering blebs placed for glaucoma control. In many respects, KPro-related endophthalmitis resembles bleb-related endophthalmitis. In both, the

pathogenesis is most likely related to acquisition of virulent organisms on the ocular surface that then cross an altered barrier between the ocular surface and the aqueous. In both, the pathogens are usually virulent bacteria, the onset of endophthalmitis is months to years after surgery rather than in the immediate postoperative period, cases present acutely and worsen rapidly, and visual outcome is poor. The incidence of bacterial endophthalmitis in our study of KPro eyes is also similar to findings in published studies of the incidence in bleb-related endophthalmitis.<sup>7,8</sup> Our incidence of 0.35% per patient-year in KPro eyes on topical vancomycin plus a quinolone, and 2.7% per patient-year overall, compares favorably with the 1.3% per patient-year incidence found in eyes with filtering blebs.<sup>7,8</sup>

Our study included many patients (30% of eyes) with SJS and OCP, conditions previously demonstrated to have an increased risk of developing KPro-related complications, including endophthalmitis.<sup>2,9</sup> In the present study, using Kaplan-Meier survival analyses, we found that only SJS eyes had a higher risk of bacterial endophthalmitis compared with other preoperative diagnoses (burn, OCP, graft failure/other). However, 4 of the 5 endophthalmitis cases in SJS eyes occurred in the 1990s before we included vancomycin as part of the prophylactic regimen for all SJS eyes. In SJS eyes using a vancomycin-containing regimen, the incidence of endophthalmitis was 1.76% per year, more than 10 times lower than the incidence in the pre-vancomycin era ( $P = 0.009$ ). This low incidence was not due to inadequate cumulative follow-up in SJS eyes on vancomycin versus no-vancomycin. Indeed, the cumulative follow-up for SJS eyes on vancomycin was 56.8 years, versus 21.8 years in the no-vancomycin group.

Although vancomycin appears to be the dominant factor in the decreased incidence of endophthalmitis in KPro eyes in recent years, additional factors should still be considered. The standard use of soft contact lenses for around-the-clock wear in Type 1 KPro eyes was introduced mid-1999, and these lenses have been found to protect the corneal tissue against excessive dehydration and tissue melt.<sup>4</sup> Tissue melt may predispose to endophthalmitis. None of the Type 1 eyes that developed endophthalmitis prior to 1999 and only half of those after 1999 were using a soft contact lens at the time of symptom onset. Similarly, we reintroduced holes in the KPro backplate at about the same time; these holes facilitate nutrition from the aqueous for the overlying corneal graft carrier, decreasing tissue melt around the Kpro.<sup>10</sup> It is hard to conceive, however, that these factors would have a major impact on the outcome of this study, especially considering the significant difference between the vancomycin and no-vancomycin groups.

The price of chronic broad-spectrum antibiotic prophylaxis is selection of resistant organisms. There were no cases of endophthalmitis due to vancomycin-resistant enterococci or vancomycin-tolerant staphylococci in the present study, although we did not perform bacterial surveillance cultures of the ocular surface to look for these organisms in the colonizing flora of uninfected KPro eyes. There was one case of endophthalmitis due to an atypical mycobacterium in this study, and that infection may have reflected selection pressure from broad-spectrum antibiotics. We also saw a slight increase

**TABLE 3.** Incidence of Bacterial Endophthalmitis in 254 KPro Eyes With at Least 1 Week of Follow-up (no Vancomycin Group Versus Vancomycin Group). Rate Is Number of Cases Per 100 Patient-years (% Per Patient-year)

Category	No vancomycin	Vancomycin	
Burn	2.41	0.00	
OCP	4.39	0.00	
SJS	18.39	1.76	$P = 0.009$
GF/Other	3.14	0.00	
Total	4.13	0.35	$P = 0.001$

Note. Burn, chemical or thermal burn; OCP, ocular cicatricial pemphigoid; SJS, Stevens-Johnson Syndrome; GF/other, graft failure/other.

in fungal infections in KPro eyes using topical vancomycin plus a quinolone, as reported previously, even though there was no change in the rate of fungal colonization as determined by surveillance cultures.<sup>11</sup> The long-term use of topical corticosteroids and use of continuous-wear therapeutic contact lenses were additional risk factors for fungal keratitis and endophthalmitis in that study. In contrast with bacterial endophthalmitis cases, most cases of fungal infection show signs of early colonization of the contact lens or infection of the cornea days before endophthalmitis onset, so there is time to prevent deeper infection. In addition, the visual outcome in cases of fungal infection in KPro eyes has been very good in most,<sup>11</sup> in contrast with the very poor visual outcome of bacterial endophthalmitis cases.

Perhaps the most surprising result of this study is that so few eyes with KPros develop endophthalmitis. The cornea is only 0.5 mm thick, and the KPro spans this. In many KPro eyes, the lens has been removed and the eye is single-chambered. In these eyes, bacteria that reach the aqueous could also reach the retina. Common ocular surface bacteria, like staphylococci, are only 1 micron in diameter. The interface between the plastic KPro stem and the corneal stroma is unlikely to be tighter than this, so bacteria may contaminate the aqueous on a regular basis in KPro eyes. Despite this, the rate of endophthalmitis in our study was very low.

For the immediate future, perhaps attention should be given to adding vancomycin to the antibiotic regimen (usually a quinolone) of all KPro patients and vaccinating all patients against *S. pneumoniae*. Longer-term efforts might focus on engineering changes to tighten the interface between the corneal stroma and KPro surfaces, a trial of new vancomycin-like antibiotics (e.g. daptomycin, linezolid) if topical toxicity studies are favorable, and the development of slow-release antibiotic-impregnated KPro devices or contact lenses. Any

measure that improves the safety and longevity of KPro wear could have a major vision-restoring impact worldwide.

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#### REFERENCES

1. Kangas TA, Greenfield DS, Flynn HW, et al. Delayed-onset endophthalmitis associated with conjunctival filtering blebs. *Ophthalmology*. 1997;104:746–752.
2. Nouri M, Terada H, Alfonso EC, et al. Endophthalmitis after keratoprosthesis: incidence, bacterial causes, and risk factors. *Arch Ophthalmology*. 2001;119:484–489.
3. Dohlman CH, Harissi-Dagher M, Khan BF, et al. Introduction to the use of the Boston Keratoprosthesis. *Exp Rev Ophthalmol*. 2006;1:41–48.
4. Dohlman CH, Dudenhoefer E, Khan BF, et al. Protection of the ocular surface after keratoprosthesis surgery: the role of soft contact lenses. *CLAO J*. 2002;28:72–74.
5. McLellan C, Ngo V, Pasedis S, et al. Testing the long-term stability of vancomycin ophthalmic solution. *Int J Pharm Compounding*. 2008;12:456–459.
6. The Endophthalmitis Study Group. Microbiologic factors and visual outcome in the Endophthalmitis Vitrectomy Study. *Am J Ophthalmology*. 1996;122:830–846.
7. Debry PW, Perkins TW, Heatley G, et al. Incidence of late-onset bleb-related complications following trabeculectomy with mitomycin. *Arch Ophthalmol*. 2002;120:297–300.
8. Muchley ED, Lehrer RA. Late-onset blebitis and endophthalmitis: incidence and outcomes with mitomycin C. *Optom Vis Sci*. 2004;81:499–504.
9. Yaghouti F, Nouri M, Abad JC, et al. Keratoprosthesis: preoperative prognostic categories. *Cornea*. 2001;20:19–23.
10. Harissi-Dagher M, Khan BF, Schaumberg DA, et al. Importance of nutrition to corneal grafts when used as a carrier of the Boston keratoprosthesis. *Cornea*. 2007;26:564–568.
11. Barnes SD, Dohlman, CH, Durand ML. Fungal colonization and infection in the Boston Keratoprosthesis. *Cornea*. 2007;26:9–15.