Endophthalmitis After Filtering Surgery With Mitomycin

David S. Greenfield, MD; Ivan J. Suñer, MD; Michael P. Miller, MD; Tracy A. Kangas, MD, PhD; Paul F. Palmberg, MD, PhD; Harry W. Flynn, Jr, MD

Objective: To identify the incidence, causative organisms, and clinical outcomes of eyes with bleb-associated endophthalmitis after glaucoma filtering procedures with adjunctive mitomycin.

Methods: Retrospective analysis of 773 consecutive eyes that underwent glaucoma filtering surgery at the Bascom Palmer Eye Institute, Miami, Fla. The course of 609 eyes from 485 patients with a minimum of 3 months of follow-up were reviewed.

Results: Mean follow-up was 16.0±11.5 months (range, 3-48 months). Of the 609 eyes, 13 (2.1%) developed bleb-associated endophthalmitis an average of 18.5±13.2 months after surgery (range, 1-45 months). The incidence of bleb-associated endophthalmitis was significantly greater after inferior trabeculectomy (7.8% per patient-year) than after superior trabeculectomy (1.3% per patient-year) by Kaplan-Meier estimates ($P=.02$, log rank test). The cumulative incidence was 13% for inferior limbal blebs and 1.6% for superior limbal blebs. Nine (69.2%) of the 13 eyes were culture positive. *Streptococcus sanguis* and *Haemophilus influenzae* (6/13 [46.2%]) were the most frequent causative organisms. The mean increase in intraocular pressure after endophthalmitis treatment was 1.2 mm Hg, with a mean decrease in visual acuity of 1.42 logMAR units. Eight (61.5%) of the 13 eyes had a final acuity of 20/400 or better.

Conclusions: The incidence of bleb-associated endophthalmitis after guarded filtering surgery performed with adjunctive mitomycin is higher than the reported rate in eyes undergoing filtering surgery without the use of antifibrotic agents (0.2%-1.5%). Inferior limbal trabeculectomy carries the highest risk of infection. Eyes with mitomycin blebs maintained excellent filtration capacity. However, after treatment of the infection, the visual outcomes were generally poor.

Arch Ophthalmol. 1996;114:943-949

THE USE OF mitomycin, an antibiotic derived from the broth of *Streptomyces caespitosis,* was first described as intraoperative adjunctive chemotherapy in glaucoma filtering surgery was first reported by Chen[1] in 1983 and later by Palmer[2] in 1991. As a bifunctional alkylating agent that acts at all stages of the cell cycle, mitomycin has been shown to inhibit fibroblast proliferation by preventing DNA synthesis.[3] Several studies have reported that a single intraoperative application of mitomycin results in a greater overall intraocular pressure reduction than does postoperative fluorouracil in patients at high risk for failure of glaucoma filtering surgery.[4,5] Mitomycin not only inhibits fibroblast proliferation, but also alters the conjunctival vascular endothelium and may alter the ciliary body epithelium.[6] Histological specimens have demonstrated that mitomycin produces filtering blebs that have thinner epithelium and more atrophic stroma and are more avascular.[7]

With improved surgical success rates, less corneal toxic effects, decreased reliance on postoperative medications, and the need for only a single intraoperative application, mitomycin use has become increasingly popular in eyes with poor surgical prognoses as well as in eyes undergoing primary filtration surgery.[8] Despite the enhanced reduction in intraocular pressure after glaucoma filtering surgery with mitomycin, there has been a concomitantly higher incidence of certain complications, such as hypotony maculopathy.[9,10] Thin-walled, avascular blebs in hypotonous eyes are believed to be more susceptible to infection than

See Patients and Methods on next page

From the Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami (Fla) School of Medicine. Dr Greenfield is now with The New York (NY) Eye and Ear Infirmary. *The authors have no proprietary interest in any of the materials presented in this report.*

Downloaded from www.archophthalmol.com on February 26, 2011

PATIENTS AND METHODS

We reviewed the records of all patients undergoing mitomycin filtering procedures that were performed or supervised by 1 surgeon (P.F.P.) between April 1, 1991, and October 1, 1994. Of 773 procedures, 60 cases were excluded because they were followed up by the resident service or represented reoperations on eyes already included in this series. Of the remaining 713 eyes, 104 (14.6%) with less than 3 months of follow-up were excluded. None of the excluded patients had developed endophthalmitis as of their last examination. In total, 609 eyes from 485 patients met the criteria for this study.

Surgery was performed by a standardized technique throughout the study period. Surgical procedures included either superior or inferior limbal-based trabeculectomy, fornix-based combined trabeculectomy and seton implantation, or fornix-based trabeculectomy combined with phacoemulsification or extracapsular cataract extraction (as previously described).[19]

Guarded filtration procedures were performed after administration of regional anesthesia and povidone-iodine preparation. Limbus-based conjunctival incisions were performed by means of a superior approach 10 mm posterior to the surgical limbus. An inferior trabeculectomy was used in patients with extensive superior conjunctival cicatrization. A polypropylene-ligated seton was implanted at the time of filtering surgery in eyes at high risk for trabeculectomy failure due to severe conjunctival cicatrization or inflammation.

Meticulous hemostasis was achieved with light bipolar cautery. A one-half thickness, rectangular 2.5×1.0-mm scleral miniflap was outlined at the surgical limbus. In all cases, mitomycin (0.5 mg/mL) was applied by means of a saturated surgical spear (Weck-Cel, Weck Ophthalmics, Jacksonville, Fla) placed on the sclera for 5 minutes, after which copious irrigation was performed with balanced salt solution. A clear corneal paracentesis track was made 90° from the filtration site. As previously reported, a corneal safety valve incision was created as prophylaxis against postoperative hypotony by making a 1.0-mm clear corneal tunnel anterior to the base of the scleral flap.[20] With the use of a 0.75-mm Kelly Descemet punch (Storz Ophthalmics, St Louis, Mo), an internal block of clear corneal tissue was removed. A peripheral iridectomy was performed and the scleral flap was reapposed with 2 to 3 interrupted 10-0 monofilament nylon sutures. Limbus-based conjunctival incisions were closed with a running 10-0 nylon suture on a CU-5 (Ethicon Inc, Somerville, NJ) needle. Fornix-based conjuntival incisions were closed with three 10-0 nylon mattress sutures. Additional balanced salt solution was placed into the anterior chamber to reform the filtering bleb and to monitor for leaks. No subconjunctival antibiotics were administered, and the eyes were patched after receiving topical neomycin, polymyxin B sulfate, and 0.1% dexamethasone ointment.

Postoperative medications included 1.0% prednisolone acetate drops every hour while the patient was awake, 1.0% atropine sulfate drops twice daily in phakic eyes, and dexamethasone ointment at night. The prednisolone acetate was tapered during a 3-month period. Argon laser suture lysis was performed selectively for elevated intraocular pressure. Bleb needling procedures were performed to elevate the scleral flap in patients with elevated intraocular pressure secondary to episcleral fibrosis, Tenon cyst formation, or internal ostium obstruction. All patients received a detailed description of endophthalmitis symptoms and were warned to return immediately if they occurred.

A diagnosis of bleb-associated endophthalmitis was made on the basis of the clinical features of diffuse bulbar conjunctival hyperemia, fibrinopurulent inflammatory precipitate within the filtering bleb, and marked intraocular inflammation. Patients with minimal anterior chamber reaction and without vitritis were not considered to have endophthalmitis.

Patients were admitted and intraocular fluids were obtained in all eyes via anterior chamber tap, vitreous biopsy, or pars plana vitrectomy. Intraocular fluids from the anterior chamber and vitreous were separately inoculated directly onto fresh aerobic and anaerobic blood agar, chocolate agar, Sabouraud agar, and thioglycolate broth. Vitrectomy specimens were passed through a 0.45-μm filter, that was sectioned, and placed on media as above. Alternatively, 10 to 20 mL of vitrectomy specimen was inoculated into blood culture bottles. All media except the Sabouraud agar were incubated at 37°C. Sabouraud agar was incubated at room temperature (25°C). Drops were placed on slides and processed with Gram and Giemsa stains. In 3 patients, additional eyelid and conjunctival filtering bleb cultures were obtained with a broth-moistened swab to inoculate the culture media directly. All eyes received intravitreal, periocular, parenteral, and topical antibiotics. Intravitreal, periocular, and topical corticosteroids were variably used.

Microbiology logs were examined to confirm the source and final culture results. Microbiologic information could not be obtained for 1 patient (patient 3), who developed endophthalmitis while traveling in a small city in Israel. Cultures were considered positive when (1) there was semiconfluent growth (11-20 colonies per plate) on 1 solid medium at the inoculation site, (2) there was moderate growth (1-10 colonies per plate) on 2 or more media at the inoculation site, (3) there was moderate growth on 1 solid medium and the thioglycolate and/or the smears were positive, (4) there was moderate growth of *Haemophilus influenzae*, or (5) there was growth in 1 liquid medium (thioglycolate) and the smears were positive. Identification and sensitivity evaluation was done by standard microbiological protocols.

Charts were reviewed with special attention to predisposing factors, history before diagnosis, treatment received before, during, and after endophthalmitis, and ocular examination before, during, and after endophthalmitis. Attempts were made to determine the clinical presentation and outcome of patients treated for bleb-associated endophthalmitis at institutions outside of the Bascom Palmer Eye Institute, Miami, Fla. The Student *t* test was used to analyze the demographic data, and Kaplan-Meier survival analysis was used to estimate the incidence of bleb-associated endophthalmitis per patient-year.

thicker blebs.[11] This was evidenced by the higher rate of bleb-associated endophthalmitis in patients after full-thickness procedures[12,13] and after guarded filtration procedures with fluorouracil[14-18] compared with trabeculectomy without antifibrotic agents. There have been anecdotal reports of patients who have been treated for the the development of bleb-associated endophthalmitis after filtering surgery with mitomycin.[5] The purpose

Downloaded from www.archophthalmol.com on February 26, 2011

Table 1. Demographic Data*

Data	Endophthalmitis	All Cases
Age, y		
Mean±SD	73.0±9.5	71.2±15.2
Range	53-85	0.7-94
Sex		
Male	7 (53.8)	280 (46.0)
Female	6 (46.2)	329 (54.0)
Race		
Hispanic	6 (46.2)	298 (48.9)
White	7 (53.8)	252 (41.4)
Black	0 (0)	59 (9.7)
Eye		
Right	7 (53.8)	299 (49.1)
Left	6 (46.2)	310 (50.9)
Follow-up, mo		
Mean±SD	18.5±13.2	16.0±11.5
Range	1-45	3-48
Diagnosis		
POAG	10 (76.9)	359 (59.0)
CACG	2 (15.4)	86 (14.1)
MMG	0 (0)	47 (7.7)
Other	1 (7.7)	117 (19.2)
Surgery†		
Trabeculectomy	9 (69.2)	289 (47.4)
Superior	4	251‡
Inferior	5	38
Trabeculectomy, CE	4 (30.8)	287 (47.1)
Phacoemulsification	2	124
ECCE	2	163
Trabeculectomy, seton implantation	0 (0)	33 (5.4)

*Unless otherwise indicated, data are represented as No. (%) of patients. POAG, indicates open-angle glaucoma; CACG, chronic angle-closure glaucoma; MMG, mixed-mechanism glaucoma; CE, cataract extraction; and ECCE, extracapsular cataract extraction.

†Percentages have been rounded.

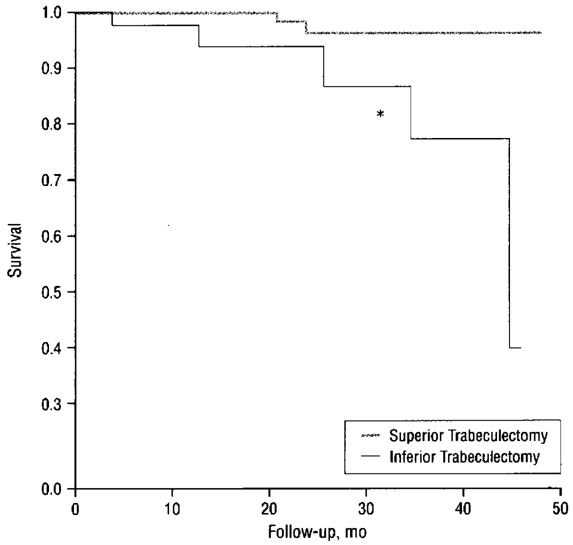
‡137 (54.6%) of 251 cases represent primary trabeculectomy.

of this investigation was to determine the incidence, causative organisms, and clinical outcomes of eyes with bleb-associated endophthalmitis after glaucoma filtering procedures with adjunctive mitomycin.

RESULTS

A total of 609 eyes from 485 patients with at least 3 months of follow-up were selected for review. Glaucoma diagnoses included primary open-angle glaucoma in 359 eyes (58.9%), chronic angle-closure glaucoma in 86 (14.1%), mixed-mechanism glaucoma in 47 (7.7%), pseudoexfoliation glaucoma in 38 (6.2%), neovascular glaucoma in 18 (3.0%), uveitic glaucoma in 14 (3.0%), pigmentary glaucoma in 12 (2.0%), angle-recession glaucoma in 11 (1.8%), juvenile open-angle glaucoma in 8 (1.3%), congenital glaucoma in 6 (1.0%), Axenfeld-Reiger syndrome in 3 (0.5%), normal-tension glaucoma in 3 (0.5%), iridocorneal endothelial syndrome in 2 (0.3%), and aniridia in 2 (0.3%). The demographic and surgical data are summarized in **Table 1**.

Overall, 13 (2.1%) of the 609 eyes developed bleb-associated endophthalmitis an average of 18.5±13.2 months after surgery (range, 1-45 months). No cases of



Follow-up, mo	0	10	20	30	40
No. of eyes at risk					
Superior	251	150	69	29	11
Inferior	38	30	17	10	7

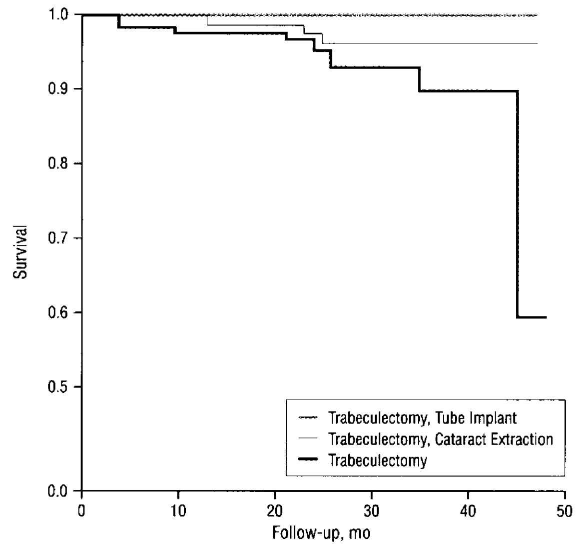
Figure 1. *Kaplan-Meier estimation of patient survival without the development of bleb-associated endophthalmitis after trabeculectomy with mitomycin. Asterisk indicates* P=*.02, log rank test.*

acute postoperative endophthalmitis occurred. Six patients underwent pars plana vitrectomy, and 7 patients had anterior chamber and vitreous taps performed. Additional intravitreal antibiotic injections were required in 5 patients. Two patients eventually required evisceration after inadequate response to primary intravitreal antibiotic therapy.

Nine (3.1%) of 289 eyes developed bleb-associated endophthalmitis after trabeculectomy alone. Bleb-associated endophthalmitis developed in 5 (13.2%) of 38 eyes after inferior trabeculectomy and 4 (1.6%) of 251 eyes after superior trabeculectomy. Kaplan-Meier estimates (**Figure 1**) showed that the incidence of bleb-associated endophthalmitis was significantly greater after inferior trabeculectomy (7.8% per patient-year) than after superior trabeculectomy (1.3% per patient-year) (P=.02, log rank test). The overall incidence of infection after trabeculectomy was 2.5% per patient-year.

No patients (0 of 33 eyes) developed bleb-associated endophthalmitis after combined trabeculectomy and seton implantation. Four (1.4%) of 287 eyes developed bleb-associated endophthalmitis after combined trabeculectomy with cataract extraction and intraocular lens implantation; 2 (1.6%) of 124 eyes after phacoemulsification with intraocular lens implantation; and 2 (1.2%) of 163 eyes after extracapsular cataract extraction with intraocular lens implantation. Kaplan-Meier estimates (**Figure 2**) showed the overall incidence of bleb-associated endophthalmitis after combined trabeculectomy with cataract extraction to be 1.0% per patient-year. The differences in the incidence of infection between these 3 surgical cohorts were statistically insignificant.

Downloaded from www.archophthalmol.com on February 26, 2011



Follow-up, mo	0	10	20	30	40
No. of eyes at risk					
Trabeculectomy, tube implant	33	19	13	12	6
Trabeculectomy, cataract extraction	287	199	99	43	10
Trabeculectomy	289	179	86	38	18

Figure 2. *Kaplan-Meier estimation of patient survival without the development of bleb-associated endophthalmitis after trabeculectomy with mitomycin, combined trabeculectomy–cataract extraction, or combined trabeculectomy–seton implantation.* $P=.20$, *log rank test.*

Microbiologic culture results (**Table 2**) were available in 12 of 13 patients. Vitreous culture results of the 1 patient who developed endophthalmitis in Israel could not be obtained. Nine (69.2%) of 13 patients demonstrated culture-positive endophthalmitis. Organisms recovered from the vitreous specimens included *Streptococcus sanguis* (a member of the viridans species) in 3 patients (23.1%), *H influenzae* in 3 patients (23.1%), *Enterococcus faecalis* in 1 patient (7.7%), *Pseudomonas aeruginosa* in 1 patient (7.7%), and *Staphylococcus epidermidis* in 1 patient (7.7%). Three patients had extraocular (eyelids and conjunctiva) in addition to intraocular (anterior chamber and vitreous cavity) cultures performed. There was no correlation between the external and intraocular culture results for these 3 patients.

Seidel testing at the time of diagnosis of endophthalmitis demonstrated bleb leaks in only 1 (7.7%) of 13 individuals. This patient (patient 12) had a persistent bleb leak of 3 weeks' duration after argon laser suture lysis. However, antecedent interventional procedures were performed in 2 patients who presented with bleb-associated endophthalmitis within 7 days after a bleb-needling procedure (patient 2) and argon laser suture lysis (patient 4). In addition, at the time of vitreous tap, patient 5 was found to have a cataract wound dehiscence 5 days after blunt ocular trauma. Noteworthy is that he had moderate posterior blepharitis and was receiving minocycline therapy at the time of diagnosis. Additional predisposing factors for infection were identified in 1 patient (patient 8) who had bilateral mucopurulent bacterial conjunctivitis at the time of diagnosis (no conjunctival cultures were performed).

Snellen visual acuity data were recorded for all patients before diagnosis, at the time of diagnosis, and after treatment of bleb-associated endophthalmitis. LogMAR conversions of Snellen acuity (Table 2) were calculated for statistical correlations.[21,22] Final visual outcome was correlated with neither the causative organism nor the duration of symptoms before treatment. The mean decrease in logMAR acuity after treatment of bleb-associated endophthalmitis was 1.15 ± 1.27 (range, 0.0-3.52).

The mean intraocular pressure before the development of bleb-associated endophthalmitis was 11.6 ± 4.1 mm Hg (range, 3-20 mm Hg). After recovery from bleb-associated endophthalmitis, the mean intraocular pressure was 13.0 ± 6.8 mm Hg (range, 5-26 mm Hg), and 7 (53.9%) of 13 patients had controlled intraocular pressure without medication. Four (33.3%) of 12 patients who had intraocular pressure of 12 mm Hg or less before endophthalmitis required topical antihypertensive therapy after infection to control intraocular pressure of 20 mm Hg or more. One of these patients required a Krupin seton implantation 6 months after infection (patient 7). Two patients (patients 5 and 13) eventually required evisceration.

COMMENT

Bleb-associated endophthalmitis is a devastating complication of glaucoma filtering surgery. The incidence rate of bleb-associated endophthalmitis has been difficult to establish. While many investigators have described the cumulative incidence of infection in a given population, few of these figures reflect the true incidence per patient-year of follow-up. Moreover, few reports have studied large cohorts of patients with uniformity in surgical technique, well-defined culture criteria to support the diagnosis of endophthalmitis, and well-defined periods of follow-up. Assuming an incidence of approximately 1%, Wand and associates[23] estimated that about 5000 new cases of bleb-associated endophthalmitis occur annually in the United States. To appreciate more clearly the potential gravity of this complication in the era of adjunctive antifibrotic agents, we analyzed the rate of infection after filtering surgery with mitomycin in a large series by 1 surgeon.

A review of the literature (**Table 3**) illustrates the variability in the reported rate of bleb-associated endophthalmitis.[12-18,24-28] It is unclear whether this variability reflects differences in the surgical procedure performed, hence the nature of the filtering bleb achieved, or rather variability among the sample size and the length of follow-up. For guarded filtering procedures, the cumulative rate of bleb-associated endophthalmitis with adjuvant fluorouracil has ranged from 1.0% to 9.4%. We found the cumulative rate of bleb-associated endophthalmitis after trabeculectomy with mitomycin to be 2.1%. Clearly, the rate of infection after trabeculectomy with adjunctive antifibrotic agents of any kind (ranging from 1.0%-3.8%)[14-18] exceeds the reported rate of infection for trabeculectomy without antifibrotic use (ranging from 0.2%-1.5%).[26-29] Moreover, the rate of endophthalmitis in patients who received antifibrotic therapy seems to be

Downloaded from www.archophthalmol.com on February 26, 2011

Table 2. Visual Outcomes Following Infection*

Patient No.	Pre-BAE Visual Acuity†	Post-BAE Visual Acuity†	Δ in Vision (LogMAR)	Organism	Symptom Duration, d
1	0.10 (20/25)	3.0 (HM)	2.9	*Haemophilus influenzae*	3
2	0.10 (20/25)	0.48 (20/60)	0.38	*Pseudomonas aeruginosa*	ND
3	1.0 (20/200)	1.0 (20/200)	0.0	ND	ND
4	0.30 (20/40)	1.0 (20/200)	0.7	*H influenzae*	2
5	2.3 (2/200)	5.0 (NLP)	2.7	*Enterococcus faecalis*	5
6	0.10 (20/25)	0.30 (20/40)	0.2	*Staphylococcus epidermidis*	1
7	0.0 (20/20)	0.40 (20/50)	0.4	*Streptococcus sanguis*	ND
8	0.48 (20/60)	4.0 (LP)	3.52	*S sanguis*	2
9	0.18 (20/30)	0.18 (20/30)	0.0	NG	1
10	0.18 (20/30)	1.0 (20/200)	0.82	*S sanguis*	2
11	0.30 (20/40)	2.3 (2/200)	2.0	NG	1
12	0.18 (20/30)	0.30 (20/40)	0.12	NG	4
13	0.30 (20/40)	5.0 (NLP)	4.70	*H influenzae*	4

*BAE indicates bleb-associated endophthalmitis; HM, hand motions; NLP, no light perception; LP, light perception; ND, no data; and NG, no growth.
†Data are depicted as LogMAR acuity (Snellen acuity).

Table 3. Incidence of Bleb-Associated Endophthalmitis

Procedure	Reference (Year)	Incidence, %/ No. of Patients
Elliot's (corneoscleral) trephination	Sugar and Zekman[24] (1958)	8.3/46
	Tabbara[25] (1976)	9.6/121
Iridencleisis	Hattenhauer and Lipsich[12] (1971)	3.4/86
	Tabbara[25] (1976)	3.4/86
Scheie's procedure	Hattenhauer and Lipsich[12] (1971)	1.5/302
	Tabbara[25] (1976)	1.2/157
Posterior lip sclerectomy	Hattenhauer and Lipsich[12] (1971)	1.6/182
	Lamping (1986)	3.3/120
Trabeculectomy	Katz et al[26] (1985)	0.2/1100
	Mills[27] (1981)	0.5/435
	Wilson[28] (1977)	0.3/309
	Freedman[29] (1978)	1.5/133
Fluorouracil trabeculectomy	Ticho and Ophir[14] (1993)	3.8/105
	FFSS[15] (1993)*	1.0/100
	Rockwood et al[16] (1987)	1.9/155
	Wolner et al[18] (1991)†	3.0/133
	Wolner et al[18] (1991)‡	9.4/96
Mitomycin C trabeculectomy	Present study (1996)†	1.3/251
	Present study (1996)‡	7.8/38
Mitomycin C trabeculectomy, cataract extraction	Present study (1996)	1.0/287
Mitomycin C trabeculectomy, seton implantation	Present study (1996)	0/33

*FFSS indicates Fluorouracil Filtering Surgery Study Group.
†Superior trabeculectomy.
‡Inferior trabeculectomy.

similar to the rate of infection in patients after full-thickness procedures (range, 1.6%-3.3%).[12,13] Among all patients who received adjunctive mitomycin, we found statistically insignificant differences in the incidence of endophthalmitis among patients who had trabeculectomy compared with those who had trabeculectomy combined with simultaneous cataract extraction or seton implantation. However, a trend was observed with a higher overall rate of infection after trabeculectomy alone (3.1%) compared with combined trabeculectomy, cataract extraction, and intraocular lens implantation (1.4%). This finding may lend credence to those who argue that the thinner cystic conjunctival filtering blebs achieved with these procedures are responsible for the increased rate of endophthalmitis, rather than the nature of the surgical procedure performed. This is supported by the fact that the rate of infection is less after combined procedures, which often produce thicker-appearing blebs, than after trabeculectomy alone.

In 1991, Wolner et al[18] reported that the incidence of bleb-associated endophthalmitis in patients after inferior trabeculectomy with fluorouracil was significantly greater (4.2% per patient-year) than in procedures performed superiorly (1.7% per patient-year). The results of our investigation in patients after trabeculectomy with mitomycin support this conclusion. In the cur-

Downloaded from www.archophthalmol.com on February 26, 2011

Figure 3. *Slit-lamp photograph of a patient with bleb-associated endophthalmitis demonstrating inferior filtering bleb exposure secondary to poor lower eyelid coverage.*

rent series, an alarmingly high (13% [5/38 cases]) cumulative incidence of infection was identified in patients after inferior trabeculectomy compared with (1.6% [4/251 cases]) for superior trabeculectomy. These figures are a minimum estimate, since it is possible that patients have developed infection without our notification. The Kaplan-Meier estimates based on follow-up available to us were 7.8% per patient-year for filtration surgery at the inferior limbus and 1.3% per patient-year for superior filtration surgery. The Kaplan-Meier estimates may likely represent an overestimation, since many patients returned to the care of the referring physician after 3 to 6 postoperative months, and late follow-up was more likely to be obtained on those patients who had complications.

The reasons for this increased rate of inferior bleb infection are mutifactorial. Inferior filtering blebs are frequently exposed and poorly covered by the lower eyelid (**Figure 3**). This may result in a more friable epithelium, secondary to the effects of repeated trauma as the lower eyelid rubs the bleb with each blink. Moreover, these blebs are chronically exposed to the bacterial flora that reside in both the tear pool and the eyelid margin. Additionally, photographic evidence has demonstrated tear film migration into the anterior chamber through a leaking inferior filtering bleb in a patient treated in Panama for an intraocular infection.[30] Thus, the mechanically abrasive action of the lower eyelid could create and maintain an opening in the conjunctiva and transmit resident bacteria into the anterior chamber with each blink.

Mandelbaum and colleagues[31,32] postulated that the organisms responsible for bleb-associated endophthalmitis usually reside transiently on the ocular surface before infection. Of their patients, 72% had different organisms isolated from the ocular surface than from inside the eye. The results of our investigation support that finding. No correlation was found between the intraocular and extraocular culture results in the 3 patients in whom we obtained external in addition to internal cultures. Moreover, our results support the conclusion of Mandelbaum et al that the most frequent pathogens in bleb infections are viridans-type *Streptococcus* and *H influenzae*, representing nearly 50% of all cases.

Table 4. Eyes at Risk for Infection*

Risk Factor	Reference (Year)	No. (%) of Patients in Present Study
Antimetabolite use	Wolner et al[18] (1991)	13 (100)
Inferior location	Wolner et al[18] (1991)	5 (38.5)
Conjunctivitis	Tabbara[25] (1976)	1 (7.7)
Bleb manipulation	Bellows and McCulley[35] (1981)	4 (30.8)
Seidel positivity	Wolner et al[18] (1991)	1 (7.7)
Age <60 y	Wolner et al[18] (1991)	1 (7.7)
Male sex	Wolner et al[18] (1991)	6 (46.2)
Contact lens use	Bellows and McCulley[35] (1981)	0 (0.0)
Hypotony	Chandler and Grant[11] (1965)	1 (7.7)
Thin blebs	Chandler and Grant[11] (1965)	Unable to judge
Blepharitis	Bellows and McCulley[35] (1981)	1 (7.7)
URI	Mandelbaum and Forster[32] (1987)	1 (7.7)
NLDO	Tabbara[25] (1976)	0 (0.0)

**URI indicates upper respiratory infection; NLDO, nasolacrimal duct obstruction.*

No statistically significant correlation was identified between the final visual outcome and either the duration of symptoms before presentation or the organism responsible for endophthalmitis. Patient 2, who had *P aeruginosa* endophthalmitis, recovered a visual acuity of 20/20 that was eventually reduced to 20/60 by an epiretinal membrane. Fong and Pesavento[33] described a patient with subacute *P aeruginosa* endophthalmitis after cataract extraction who recovered a visual acuity of 20/80. On the basis of the results of this investigation, the overall mean decrease in logMAR visual acuity after bleb-associated endophthalmitis was 1.42. As reported by Brown et al,[34] bleb infection without vitreous involvement (blebitis) appears to have a much better visual prognosis than fulminant endophthalmitis.

Table 4 summarizes the patient and bleb characteristics that have been reported as risk factors in the development of endophthalmitis.[11,18,25,32,35,36] We did not identify a higher rate of endophthalmitis among males or patients younger than 60 years, as reported by Wolner et al.[18] Many studies have indicated that a leaking filtering bleb may be a risk factor for infection.[12,13,18,31] It is difficult to analyze statistically the relative risk of infection in patients with bleb leaks, since the overall number of patients with leaking blebs who do not develop endophthalmitis is currently unknown. In the present series, known iatrogenic or accidental bleb trauma preceded the development of infection in 4 (31%) of 13 patients. In all but 1 patient, however, Seidel testing at the time of diagnosis was negative. We suspect that eyes that develop endophthalmitis shortly after bleb needling or laser suture lysis actually were associated with a conjunctival buttonhole, but that the blebs appeared Seidel negative due to being plugged by mucopurulent debris. We observed a strand of mucopurulent material attached to the conjunctive over a laser suture lysis site in 1 case.

While the visual acuity outcomes remain poor af-

Downloaded from www.archophthalmol.com on February 26, 2011

ter treatment, this report demonstrates that mitomycin blebs maintain excellent filtration capacity after infection. The appropriate management (eg, surgical closure) of those functional mitomycin blebs that persist after endophthalmitis currently remains unknown.

In agreement with a recent report by Wand et al,[23] we believe that the routine, long-term use of prophylactic antibiotics is of questionable value in the prevention of bleb-associated endophthalmitis, and our patients were not receiving them. However, many of our patients were using maintenance prednisolone acetate solutions that contain 0.01% benzalkonium chloride, a preservative found in most topical agents, which has been shown to exhibit intrinsic bacteriostatic properties.[37]

In conclusion, the incidence of endophthalmitis in the current series after glaucoma filtering surgery with mitomycin appears to exceed the reported rate of bleb-associated endophthalmitis without antifibrotic use. In addition, a trend was observed with a higher incidence of endophthalmitis among patients who had trabeculectomy alone compared with trabeculectomy combined with simultaneous cataract extraction and intraocular lens implantation. The highest risk of infection exists in patients with inferior limbal filtering blebs. On the basis of the high incidence of endophthalmitis associated with inferior filtering blebs in this series and that of Wolner et al,[18] we now recommend filtration with a superiorly placed seton rather than an inferior filtering bleb when the superior conjunctiva shows extensive vascularization and/or scarring.

Since the time that this report was accepted for publication, 2 additional studies have been published which further support our conclusions regarding the high risk of endophthalmitis in filtering blebs located at the inferior limbus.[38,39]

Accepted for publication February 19, 1996.

This study was supported in part by a grant from the Kaster Family Trust, the Stabler Companies, the Mary Mikesell Mapp, and Research to Prevent Blindness Inc, New York, NY. Dr Greenfield is a 1994-1996 Heed Ophthalmic Foundation Fellow.

Presented as a poster exhibit at the Annual Meeting of the Association for Research in Vision and Ophthalmology, Fort Lauderdale, Fla, May 14, 1995.

We gratefully acknowledge Darlene Miller, MA, for her assistance with the microbiological data and Jean Newland for her assistance with the data collection.

Reprints: David S. Greenfield, MD, The New York Eye and Ear Infirmary, 310 E 14th St, New York, NY 10003.

REFERENCES

1. Chen CW. Enhanced intraocular pressure controlling effectiveness of trabeculectomy by local application of mitomycin C. *Trans Asia Pac Acad Ophthalmol.* 1983;9:172-177.
2. Palmer SS. Mitomycin as adjunct chemotherapy with trabeculectomy. *Ophthalmology.* 1991;98:317-321.
3. Jampel HD. Effect of brief exposure to mitomycin C on viability and proliferation of cultured human Tenon's capsule fibroblasts. *Ophthalmology.* 1992;99:1471-1476.
4. Kitazawa Y, Kawase K, Matsushita H, Minobe M. Trabeculectomy with mitomycin: a comparison study with fluorouracil. *Arch Ophthalmol.* 1991;109:1693-1698.
5. Skuta GL, Beeson CC, Higginbotham EJ, et al. Intraoperative mitomycin versus postoperative 5-fluorouracil in high-risk glaucoma filtering surgery. *Ophthalmology.* 1992;99:438-444.
6. Nuyts RMMA, Felten PC, Pels E, et al. Histopathologic effects of mitomycin C after trabeculectomy in human glaucomatous eyes with persistent hypotony. *Am J Ophthalmol.* 1994;118:225-237.
7. Shields MB, Scroggs MW, Sloop CM, Simmon RB. Clinical and histopathologic observations concerning hypotony after trabeculectomy with adjunctive mitomycin C. *Am J Ophthalmol.* 1993;116:673-683.
8. Kupin TH, Juzych MS, Shin DH, et al. Adjunctive mitomycin C in primary trabeculectomy in phakic eyes. *Am J Ophthalmol.* 1995;119:30-39.
9. Zacharia PT, Depperman SR, Schuman JS. Ocular hypotony after trabeculectomy with mitomycin C. *Am J Ophthalmol.* 1993;116:314-326.
10. Nuyts RMMA, Greve EL, Geijssen HC, Langerhorst CT. Treatment of hypotonous maculopathy after trabeculectomy with mitomycin C. *Am J Ophthalmol.* 1994;118:322-331.
11. Chandler PA, Grant WM. *Lectures on Glaucoma.* Philadelphia, Pa: Lea & Febiger; 1965:402.
12. Hattenhauer JM, Lipsich MP. Late endophthalmitis after filtering surgery. *Am J Ophthalmol.* 1971;72:1097-1101.
13. Lamping KA, Bellows AR, Hutchinson BT, Afran SI. Long-term evaluation of initial filtration surgery. *Ophthalmology.* 1986;93:91-101.
14. Ticho U, Ophir A. Late complications after glaucoma filtering surgery with adjunctive 5-fluorouracil. *Am J Ophthalmol.* 1993;115:506-510.
15. The Fluorouracil Filtering Surgery Study Group. Three-year follow-up of the Fluorouracil Filtering Surgery Study Group. *Am J Opthalmol.* 1993;115:82-92.
16. Rockwood EJ, Parrish RK II, Heuer DK, et al. Glaucoma filtering surgery with 5-fluorouracil. *Ophthalmology.* 1987;94:1071-1078.
17. Whiteside-Michel J, Liebmann JM, Ritch R. Initial 5-fluorouracil trabeculectomy in young patients. *Ophthalmology.* 1992;99:7-13.
18. Wolner B, Liebmann JM, Sassani JW, et al. Late bleb-associated endophthalmitis after trabeculectomy with adjunctive 5-fluorouracil. *Ophthalmology.* 1991;98:1053-1060.
19. Joos KM, Bueche MJ, Palmberg PF, et al. One-year follow-up results of combined mitomycin C trabeculectomy and extracapsular cataract extraction. *Ophthalmology.* 1995;102:76-83.
20. Palmberg PF. Prevention and management of complicated hypotony in trabeculectomy with mitomycin. *Highlights Ophthalmol.* 1993;9:66-77.
21. Westheimer G. Scaling of visual acuity measurements. *Arch Ophthalmol.* 1979;97:327-330.
22. Holladay JT, Prager TC. Mean visual acuity. *Am J Ophthalmol.* 1991;111:372-374.
23. Wand M, Quintiliani R, Robinson A. Antibiotic prophylaxis in eyes with filtration blebs: survey of glaucoma specialists, microbiological study, and recommendations. *J Glaucoma.* 1995;4:103-109.
24. Sugar HS, Zekman T. Late infection of filtering conjunctival scars. *Am J Ophthalmol.* 1958;46:155-170.
25. Tabara KF. Late infections following filtering procedures. *Ann Ophthalmol.* 1976;8:1228-1231.
26. Katz LJ, Cantor LB, Spaeth GL. Complications of surgery in glaucoma: early and late bacterial endophthalmitis following glaucoma filtering surgery. *Ophthalmology.* 1985;92:959-963.
27. Mills KB. Trabeculectomy: a retrospective long-term follow-up of 444 cases. *Br J Ophthalmol.* 1981;65:790-795.
28. Wilson P. Trabeculectomy: long term follow-up. *Br J Ophthalmol.* 1977;61:535-538.
29. Freedman J, Gupta M, Bunke A. Endophthalmitis after trabeculectomy. *Arch Ophthalmol.* 1978;96:1017-1018.
30. Gollamudi SR, Hodapp EA, Cubillas A, Culbertson WW. Photographically documented access of tear film to the anterior chamber through a leaky filtering bleb. *Arch Ophthalmol.* 1993;111:394-395.
31. Mandelbaum S, Forster RK, Gelender H, Culbertson W. Late onset endophthalmitis associated with filtering blebs. *Ophthalmology.* 1985;92:964-972.
32. Mandelbaum S, Forster RK. Endophthalmitis associated with filtering blebs. *Int Ophthalmol Clin.* 1987;27:107-111.
33. Fong DS, Pesavento RD. *Pseudomonas* endophthalmitis presenting as subacute endophthalmitis. *Arch Ophthalmol.* 1995;113:265.
34. Brown RH, Yang LH, Walker SD, et al. Treatment of bleb infection after glaucoma surgery. *Arch Ophthalmol.* 1994;112:47-61.
35. Bellows AR, McCulley JP. Endophthalmitis in aphakic patients with unplanned filtering blebs wearing contact lenses. *Ophthalmology.* 1981;88:839-843.
36. Wild FF. Endophthalmitis in a contact lens wearer. *Am J Ophthalmol.* 1962;54:847-848.
37. Palmberg R, Gutierrez YS, Miller D, et al. Potential bacterial contamination of eyedrops used for tonometry. *Am J Ophthalmol.* 1994;117:578-582.
38. Caronia RM, Liebmann JM, Friedman R, Cohen H, Ritch R. Trabeculectomy at the inferior limbus. *Arch Ophthalmol.* 1996;114:387-391.
39. Higginbotham EJ, Stevens RK, Musch DC, et al. Bleb-related enophthalmitis after trabeculectomy with mitomycin C. *Ophthalmology.* 1996;103:650-656.

Downloaded from www.archophthalmol.com on February 26, 2011