Delayed-onset Endophthalmitis Associated with Conjunctival Filtering Blebs

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Objective: The purpose of the study is to evaluate the causative organisms, treatment methods, and visual acuity outcomes of patients treated for delayed-onset endophthalmitis associated with conjunctival filtering blebs.

Methods: The medical records of 32 patients with conjunctival filtering bleb-associated endophthalmitis treated at the Bascom Palmer Eye Institute between 1989 and 1995 were reviewed retrospectively. Bleb-associated endophthalmitis was diagnosed at 1 month or more after surgery in all patients. Patients with bleb infections only but without signs of intraocular infection were excluded from this series.

Results: Previous antimetabolite therapy was used in 20 patients, including mitomycin C in 14 and 5-fluorouracil in 6. Streptococcal species were the most frequently cultured organisms occurring in 15 (47%) of 32 eyes. Of the 32 patients, 30 received intraocular antibiotics. The initial treatment included a pars plana vitrectomy in 18 patients and a vitreous tap without vitrectomy in 12 patients. Two of three patients who presented with no light perception vision were treated by evisceration. Overall, 15 (47%) of 32 patients achieved a final visual acuity of 20/400 or better. Of those patients with Streptococcal species cultured from the eye, 6 (40%) of 15 had a visual acuity of 20/400 or better compared to 9 (52%) of 17 in patients with non-Streptococcal species.

Conclusions: Delayed-onset endophthalmitis associated with conjunctival filtering blebs is a current and future concern, especially with increasing use of mitomycin C. The Streptococcal species are a common causative organism. Despite current treatment of these patients, the visual acuity outcomes generally are worse than in patients with acute-onset endophthalmitis after cataract surgery.

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The incidence of postoperative endophthalmitis associated with glaucoma filtering surgery with or without antimetabolites has been reported to range from 0.061% to 13.2%.[1,2] Delayed-onset endophthalmitis associated with conjunctival filtering blebs is caused by a different spectrum of organisms than those in acute-onset, postcataract surgery endophthalmitis.[3–6]

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In the past decade, new techniques such as the use of antimetabolites, such as mitomycin C and 5-fluorouracil (5-FU), have been used to facilitate bleb survival. The use of antifibrotic agents has become increasingly popular in eyes at high risk for failure of glaucoma filtering surgery. Several studies have reported that a single intraoperative application of mitomycin C provides greater intraocular pressure reduction than does postoperative 5-FU.[7,8] Histologic specimens have shown that the application of mitomycin C leads to the development of thinner and more avascular blebs that may be at greater risk of endophthalmitis on long-term follow-up.[9] Greenfield et al[2] reported that the incidence of bleb-associated endophthalmitis after filtering surgery with mitomycin C is higher than in eyes undergoing filtering surgery without the use of antifibrotic agents.

Table 1. Clinical Data of Patients with Delayed-onset Endophthalmitis Associated with Conjunctival Filtering Blebs

Patient No.	Age (yrs)/Sex	Eye	Previous Surgery	Months Between Surgery and Diagnosis of Endophthalmitis	Bleb Site	Bleb Leak	Antimetabolites		
							5-FU	*Mitomycin C*	*None*
1	81/F	L	Scheie procedure	9	Superior	+	−	−	+
2	46/F	R	Trabeculectomy	9	Superior	−	−	−	+
3	76/F	L	Trabeculectomy/penetrating keratoplasty	14	Superior	−	−	−	+
4	60/F	L	CE/IOL with inadvertent bleb	48	Superior	−	−	−	+
5	77/F	R	CE/IOL with inadvertent bleb	6	Superior	+	−	−	+
6	84/F	R	Trabeculectomy	36	Superior	+	−	−	+
7	58/F	R	Trabeculectomy	1	Superior	+	−	+	−
8	19/M	L	Trabeculectomy	7	Superior	−	+	−	−
9	56/F	L	Trabeculectomy	15	Superior	−	−	+	−
10	84/F	L	ECCE/IOL with inadvertent bleb	84	Superior	−	−	−	+
11	54/M	R	Trabeculectomy	6	Superior	−	−	−	+
12	82/M	L	Trabeculectomy	60	Superior	−	−	−	+
13	68/M	R	ECCE/IOL/trabeculectomy	108	Superior	+	−	−	+
14	76/F	R	Trabeculectomy	2	Superior	+	−	+	−
15	69/F	R	ICCE/trabeculectomy	96	Superior	−	−	−	+
16	64/F	L	Trabeculectomy	4	Superior	−	−	+	−
17	76/F	R	Trabeculectomy	1.5	Superior	−	−	+	−
18	53/F	L	ECCE/IOL/trabeculectomy	20	Superior	−	−	+	−
19	84/M	L	Phaco/IOL/trabeculectomy	6	Superior	−	−	+	−
20	76/F	R	Trabeculectomy	1	Superior	+	−	+	−
21	65/F	R	Trabeculectomy	2	Superior	−	−	+	−
22	65/F	L	Trabeculectomy	1	Inferior	+	+	−	−
23	87/F	L	Trabeculectomy	1.5	Inferior	−	−	+	−
24	75/F	R	Trabeculectomy	20	Inferior	−	+	−	−
25	77/M	L	Trabeculectomy	8	Inferior	−	+	−	−
26	69/F	L	Trabeculectomy	43	Inferior	−	−	+	−
27	55/M	R	Trabeculectomy	27	Inferior	−	+	−	−
28	71/F	L	Trabeculectomy	44	Inferior	−	−	+	−
29	56/F	L	Trabeculectomy	58	Inferior	+	−	−	+
30	84/M	L	Trabeculectomy	40	Inferior	−	−	+	−
31	79/M	L	Trabeculectomy	26	Inferior	−	−	+	−
32	59/M	L	Trabeculectomy	29	Superior	+	+	−	−

L = left; R = right; CE = cataract extraction; IOL = intraocular lens; ECCE = extracapsular cataract extraction; ICCE = intracapsular cataract extraction; 5-FU = 5-fluorouracil.

To study risk factors, causative organisms, methods of treatment, and visual acuity outcomes, we reviewed the medical records of all patients coded with a diagnosis of bleb-associated endophthalmitis treated at our hospital over the past 6 years.

Patients and Methods

Before examining the medical records for the purpose of this study, the planned investigation was approved by the University of Miami, School of Medicine, Subcommittee for the Protection of Human Subjects in Research. The medical records of these patients were reviewed retrospectively.

Between 1989 and 1995, 32 patients presented to the Bascom Palmer Eye Institute, Anne Bates Leach Eye Hospital, with delayed-onset endophthalmitis associated with conjunctival filtering blebs. Delayed-onset, bleb-associated endophthalmitis was diagnosed 1 month or more after intraocular surgery. Acute-onset (within 1 month of glaucoma filtering surgery) patients with endophthalmitis were excluded from the current series. Patients with bleb infections only but without signs of intraocular infection also were excluded from this series.

The clinical history, including the type of surgery performed, the use of antimetabolites, and the interval from surgery to endophthalmitis, was reviewed. Other clinical factors, such as the location and appearance of the bleb, the lens status, and the presence of anterior and posterior segment inflammation, culture results, antibiotic treatment, and complications of treatment

Table 2. Initial Ocular Examination at Time of Endophthalmitis Diagnosis

Patient No.	Purulent Bleb	Anterior Chamber	Lens Status	View to Fundus
1	+	Hypopyon	Phakic	Red reflex
2	+	Marked cells	Phakic	No view
3	+	Hypopyon	Phakic	Red reflex
4	+	Hypopyon	IOL	No view
5	+	Hypopyon	IOL	Red reflex
6	−	Hypopyon	IOL	No view
7	+	Marked cells	Phakic	Hazy view
8	−	Hypopyon	IOL	No view
9	+	Hypopyon	Phakic	Hazy view
10	+	Hypopyon	IOL	No view
11	−	Hypopyon	IOL	Hazy view
12	+	Hypopyon	Phakic	No view
13	−	Hypopyon	IOL	No view
14	−	Hypopyon	IOL	No view
15	−	Hypopyon	Aphakic	No view
16	−	Hypopyon	Phakic	Hazy view
17	+	Hypopyon	Phakic	Red reflex
18	+	Hypopyon	IOL	Hazy view
19	+	Hypopyon	IOL	Hazy view
20	−	Hypopyon	Phakic	Hazy view
21	−	Hypopyon	IOL	Hazy view
22	−	Marked cells	IOL	No view
23	+	Marked cells	IOL	Red reflex
24	+	Hypopyon	IOL	Hazy view
25	+	Hypopyon	IOL	Red reflex
26	−	Hypopyon	IOL	No view
27	+	Hypopyon	IOL	No view
28	−	Hypopyon	IOL	Hazy view
29	+	Hypopyon	Aphakic	Hazy view
30	+	Hypopyon	IOL	No view
31	+	Hypopyon	IOL	No view
32	−	Hypopyon	Aphakic	No view

IOL = intraocular lens.

were recorded. Because no prospective protocol was followed, the methods of treatment were selected by the individual treating physician. The final visual acuity outcomes and post-treatment complications were recorded.

All culture results were obtained using the standard microbiologic procedures and specific culture criteria reported previously from the Bascom Palmer Eye Institute.[10] Standard microbiologic procedures include plating anterior chamber specimens on chocolate agar, 5% sheep blood agar, anaerobic blood agar, and thioglycolate broth. Smaller vitreous specimens are processed similar to anterior chamber specimens. Vitreous samples greater than 10 ml are either filtered, sectioned, and plated similar to anterior chamber specimens or placed in blood culture bottles. The criteria for a positive culture included one of the following: growth of the same organism in two or more culture media or semiconfluent growth on one or more solid media at the inoculation site.

Results

Ten (31%) of 32 patients were men and 22 patients (69%) were women (Table 1). Thirteen right eyes and 19 left eyes were in the current series. The average age at the time of presentation was 68 years, with a range of 19 to 87 years. The average time from surgery to endophthalmitis was 26 months, with a range of 1 to 108 months.

Twenty-three (72%) of 32 of the patients had a history of trabeculectomy. Of these 23 patients, 6 had received adjunctive 5-FU and 14 had received adjunctive mitomycin C. Eight of the 14 patients with mitomycin C were described previously (Tables 1–5, patients 16–21, 30, and 31) in a report on the incidence of filtering bleb-associated endophthalmitis by one surgeon.[2] Since mitomycin C was first used in April 1991, endophthalmitis associated with adjunctive mitomycin C occurred more frequently in the past 2 years of the current study (Fig 1). A total of 12 patients had received no antimetabolite therapy, including 3 patients who had undergone trabeculectomy. Two other patients had inadvertent conjunctival filtering blebs after cataract surgery. Five patients had undergone a combined cataract surgery and trabeculectomy. One patient had undergone a Scheie procedure, and one had undergone combined trabeculectomy and penetrating keratoplasty.

Initial ocular examination findings were recorded (Table 1). Inferior limbal blebs were noted in 10 (31%) of 32 patients, and superior blebs were reported in 22 (69%) of 32. A visible bleb leak or positive Seidel test was recorded in 10 (31%) of 32 patients. The bleb was defined as "purulent" when purulent material was viewed inside the bleb on slit-lamp examination; this purulence was present in 19 (59%) of 32 patients (Table 2). A hypopyon was recorded in 28 (88%) of 32 patients, and 21 (66%) of 32 patients had opacification of the vitreous that obscured fundus details. Three (9%) of the 32 patients were aphakic, 20 (63%) of 32 were pseudophakic, and 9 (28%) of 32 were phakic.

After the diagnosis of endophthalmitis was made, 30 patients were treated with intravitreal antibiotics after intraocular cultures were taken (Table 3). Eighteen (56%)

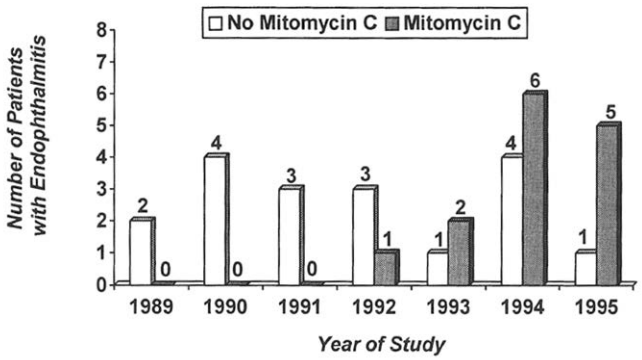

Figure 1. The number of patients in the current study with bleb-related endophthalmitis per year (with and without the use of mitomycin C).

Table 3. Initial Management

Patient No.	Pars Plana Vitrectomy	Vitreous Tap Without PPV	A/C Tap	Intravitreal Antibiotics	Intravitreal Steroids
1	−	+	+	+	−
2	+	−	+	+	+
3	−	+	+	+	−
4	+	−	+	+	+
5	+	−	−	+	+
6	+	−	+	+	+
7	−	+	+	+	+
8	+	−	−	+	−
9	+	−	−	+	+
10	+	−	+	+	+
11	−	+	−	+	+
12	−	+	+	+	−
13	+	−	+	+	+
14	−	+	+	+	+
15	+	−	−	+	+
16	+	−	−	+	+
17	+	−	+	+	+
18	+	−	−	+	+
19	−	+	+	+	+
20	−	+	+	+	+
21	+	−	−	+	+
22	+	−	+	+	−
23	−	+	+	+	+
24	−	+	+	+	−
25	+	−	+	+	+
26	−	+	+	+	+
27	+	−	+	+	+
28	+	−	−	+	+
29	+	−	+	+	+
30	−	+	+	+	+
31	−	−	−	−	−
32	−	−	−	−	−

PPV = pars plana vitrectomy; A/C = anterior chamber.

of the 32 patients underwent an initial pars plana vitrectomy, and 12 (38%) of 32 had an initial needle vitreous tap without pars plana vitrectomy. Two patients (Tables 1–5, patients 30 and 31) who presented with a 100% hypopyon and no light perception were eviscerated primarily. One additional patient (Tables 1–5, patient 30) had no light perception vision on initial examination and was treated by an evisceration 4 days after injection of intravitreal antibiotics.

A variety of different combinations of antibiotics were used in this retrospective study. Thirty (94%) of the 32 patients received intraocular antibiotics. Most patients received intravitreal vancomycin 1 mg/0.1 ml, either alone or in combination with ceftazidime 2.25 mg/0.1 ml or amikacin 400 μg/0.1 ml. One patient received intravitreal amikacin 200 μg/0.1 ml alone. Topical and subconjunctival antibiotics were used in most of the patients who were not eviscerated primarily. Intraocular steroids (dexamethasone 0.4 mg/0.1 ml) were used in 24 (75%) of 32 patients.

Intraocular cultures were positive in 31 (97%) of 32 eyes (Table 4). Vitreous cultures were positive in 27 (93%) of the 29 in which they were performed. Aqueous cultures were positive in 14 (64%) of the 22 eyes in which they were performed. The most common organisms, Streptococcal species, were present in 15 (47%) of 32 eyes. *Streptococcus viridans* was the most common Streptococcal species within this group, occurring in 8 of the 15 eyes. The remaining isolates included *Staphylococcus epidermidis* (seven), *Hemophilus influenza* (five), Moraxella species (two), *Enterococcus faecalis*, (two) and *Propionibacterium acnes* (one).

Streptococcal species was cultured from the eye in all six patients who had undergone prior filtering surgery with 5-FU. In contrast, Streptococcal species was isolated from the eye in only 4 (28%) of 14 patients who had undergone similar surgery with mitomycin C. Streptococcal species was cultured in 5 (41%) of 12 patients not receiving adjunctive antimetabolites.

Overall, 15 (47%) of 32 of patients had a final visual acuity of 20/400 or better (Table 5). Of the Streptococcal group, 6 (40%) of 15 achieved a final visual acuity of 20/

Table 4. Culture Results from Eyes with Delayed-onset Endophthalmitis

Patient No.	Aqueous	Vitreous	Bleb Site
1	*Propionobacterium acnes*	*Propionobacterium acnes*	Not performed
2	*Streptococcus sanguis*	*Streptococcus sanguis*	Not performed
3	Not performed	*Streptococcus pneumoniae*	Not performed
4	*Streptococcus viridans*	Not performed	Not performed
5	Not performed	Moraxella species	Not performed
6	No growth	*Staphylococcus epidermidis*	Not performed
7	*Staphylococcus epidermidis*	Not performed	Not performed
8	Not performed	*Streptococcus mitis*	Not performed
9	Not performed	*Streptococcus viridans*	Not performed
10	No growth	Moraxella species	Not performed
11	Not performed	*Staphylococcus epidermidis*	Not performed
12	No growth	*Streptococcus pneumoniae*	Not performed
13	No growth	*Hemophilus influenzae*	Not performed
14	No growth	*Enterococcus faecalis*	Not performed
15	Not performed	*Hemophilus influenzae*	Not performed
16	Not performed	*Staphylococcus epidermidis*	Not performed
17	*Hemophilus influenzae*	*Hemophilus influenzae*	Not performed
18	No growth	No growth	*Staphylococcus aureus*, *P. aeruginosa*
19	*Hemophilus influenza*	*Hemophilus influenzae*	Not performed
20	*Staphylococcus epidermidis*	No growth	*C. diphtheria*
21	Not performed	*Streptococcus viridans*	Not performed
22	*Streptococcus viridans*	*Streptococcus hominis*	Not performed
23	No growth	*Staphylococcus epidermidis*	Not performed
24	*Streptococcus viridans*	*Streptococcus viridans*	Morganella species
25	*Streptococcus viridans*	*Streptococcus viridans*	Not performed
26	*Staphylococcus epidermidis*	*Staphylococcus epidermidis*, *Streptococcus viridans*	*Staphylococcus epidermidis*
27	*Streptococcus pneumoniae*	*Streptococcus pneumoniae*	*Streptococcus pneumoniae*
28	*S. sanguis*, *S. viridans*	Not performed	Not performed
29	No growth	*Streptococcus sanguis*	Not performed
30	*Enterococcus faecalis*	*Enterococcus faecalis*	Not performed
31	Not performed	*Hemophilus influenzae*	Not performed
32	Not performed	Beta streptococcus, group G	Not performed

400 or better compared to 9 (52%) of 17 in the non-Streptococcal group. Of those patients treated by an initial pars plana vitrectomy, 10 (55%) of 18 had a final visual acuity of 20/400 or better compared to 4 (33%) of 12 in the initial vitreous tap group (relative risk, 1.7). Of the patients who received initial intravitreal steroids, 13 (54%) of 24 achieved 20/400 or better versus 2 (25%) of 8 in patients receiving no initial intravitreal steroids. These differences between compared groups were not statistically significant in this retrospective study. To assess if a treatment difference exists between vitrectomy and non-vitrectomy groups, a sample size of approximately 212 patients would be needed, half randomized to pars plana vitrectomy and half randomized to vitreous tap without pars plana vitrectomy.

Discussion

Localized bleb infection (''blebitis'') without endophthalmitis has been described in eyes after glaucoma surgery.[11] Blebitis generally responds to treatment with topical or subconjunctival antibiotics or both, and intravitreal antibiotics are not required. After the treatment of blebitis, the visual acuity usually remains unchanged.[11] Patients with localized bleb infection were excluded from the current bleb-associated endophthalmitis study. In the current study, all patients had marked intraocular inflammation and, in 88%, a hypopyon was present. In three patients, the severe bleb-associated endophthalmitis led to no light perception visual acuity at the time of our initial examination.

Other series of delayed-onset, bleb-associated endophthalmitis are summarized in Table 6. In a 1985 study of 36 patients with bleb-associated endophthalmitis, 30 (83%) patients had positive intraocular cultures and 17 (57%) of these 30 patients had Streptococcal species cultured from the aqueous or vitreous.[3] Overall, 11 (31%) of 36 patients achieved a final visual acuity of 20/400 or better. In a 1994 report on late-onset, bleb-associated endophthalmitis, 8 (44%) of 18 patients achieved a final visual acuity of 20/400 or better.[4] Twelve (67%) of the

Table 5. Initial and Final Visual Outcomes

Patient No.	Visual Acuity			Follow-Up (mos)
	Pretreatment	*Posttreatment*	*Final*	
1	LP	HM	HM	31
2	LP	LP	NLP	12
3	HM	4/200	20/100	2
4	LP	LP	NLP	9
5	HM	HM	HM	10
6	HM	20/30	20/30	13
7	20/400	20/25	20/30	27
8	LP	1/200	NLP	26
9	20/400	3/200	3/200	34
10	HM	20/60	20/200	23
11	LP	20/80	20/80	24
12	LP	NLP	NLP	21
13	HM	20/80	20/60	5
14	LP	LP	NLP	8
15	LP	LP	NLP	15
16	20/200	20/60	20/60	6
17	20/400	20/200	20/200	1.5
18	20/300	20/30	20/25	18
19	HM	HM	5/200	9
20	20/400	20/30	20/50	9
21	LP	9/200	20/200	2
22	20/70	20/60	20/40	36
23	1/200	20/400	5/200	48
24	HM	NLP	NLP	12
25	LP	1/200	HM	13
26	LP	LP	LP	1
27	20/400	3/200	20/100	10
28	20/200	20/40	20/50	8
29	1/200	20/100	20/100	6
30	NLP	Eviscerated	NLP	54
31	NLP	Eviscerated	NLP	19
32	NLP	Eviscerated	NLP	28

LP = light perception; HM = hand motion; NLP = no light perception.

18 patients had positive intraocular cultures, but only 4 (36%) of 11 had Streptococcal species cultured from the eye. None of these four patients achieved a final visual acuity of 20/400 or better. Other recent series also are included in Table 6.[12–14] In the current study, the final recorded visual acuity was 20/400 or better in 6 (40%) of 15 patients with Streptococcal species and in 15 (47%) of 32 overall.

The value of adjunctive intravitreal steroids in the treatment of endophthalmitis has not been established.[15,16] Two previous nonrandomized studies showed no deleterious effects and better visual acuity outcomes with intravitreous steroids.[15,16] Intravitreal steroids were not used in the previous bleb-associated endophthalmitis report by Mandelbaum et al[3] or Phillips et al.[4] In the current study, 24 (75%) of 32 patients received intravitreal steroids. Thirteen (54%) of 24 achieved 20/400 or better compared to 2 (25%) of 8 in patients receiving no intravitreal steroids. The number of patients in each treatment group was small, and the differences in outcomes were not statistically significant ($P = 0.31$, chi square).

The Endophthalmitis Vitrectomy Study evaluated outcomes of treatment for acute-onset endophthalmitis after cataract or secondary intraocular lens surgery.[17] In the Endophthalmitis Vitrectomy Study at 9 to 12 months after treatment, 53% of patients achieved a visual acuity of 20/40 or better, 74% achieved 20/100 or better, and 15% had acuity worse than 5/200. In the current study, only 13% of patients achieved 20/40 or better, 34% achieved 20/100 or better, and 47% had acuity worse than 5/200. In the current study, eyes treated by immediate pars plana vitrectomy had slightly better visual acuity outcomes compared to those with vitreous tap eyes, but the difference was not statistically significant ($P = 0.41$, chi square).

In summary, delayed-onset endophthalmitis associated with conjunctival filtering blebs is a current and future concern, especially with the increasing use of mitomycin C.[18] In the current study, the Streptococcal species was the most common infecting organism. There was a trend in our results for a better outcome with vitrectomy and with intraocular steroid injection, but a larger sample size would be needed to have sufficient power to confirm advantage to these treatments. Despite current treatment of bleb-associated endophthalmitis, the visual acuity outcomes generally are worse than in patients with acute-onset endophthalmitis after cataract surgery.

Table 6. Comparison of Larger and More Recently Reported Series of Patients with Delayed-onset Endophthalmitis Associated with Conjunctival Filtering Blebs

Author (year)	No. of Cases Reported	No. (%) of Positive Intraocular Cultures	No. (%) of Streptococcal Species	Overall Final Visual Acuity of ≥20/400 [no. (%)]	Streptococcal Species Final Visual Acuity of ≥20/400 [no. (%)]
Mandelbaum et al (1985)	36	30 (83)	17/30 (57)	11/36 (31)	3/17 (18)
Phillips et al (1994)	18	12 (67)	4/12 (33)	8/18 (44)	0/5
Fluorouracil study (1996)	3	2 (67)	1/3 (33)	3/3 (100)	1/1 (100)
Higginbotham et al (1996)	6	5 (83)	2/6 (33)	4/6 (67)	1/2 (50)
Caronia et al (1996)	12	8 (67)	0/12 (0)	Not available	Not available
Current study (1996)	32	31 (97)	15/32 (47)	15/32 (47)	6/15 (40)

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XIth Congress of the European Society of Ophthalmology Budapest, Hungary, June 1–5, 1997

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