Antibiotic prophylaxis of postoperative endophthalmitis after cataract surgery: Results of the 2014 ASCRS member survey

David F. Chang, MD, Rosa Braga-Mele, MD, Bonnie An Henderson, MD, Nick Mamalis, MD, Abhay Vasavada, MD, for the ASCRS Cataract Clinical Committee

A 2014 online survey of the American Society of Cataract and Refractive Surgery members indicated increasing use of intracameral antibiotic injection prophylaxis compared with a comparable survey from 2007. Forty-seven percent of respondents already used or planned to adopt this measure. One half of all surgeons not using intracameral prophylaxis expressed concern about the risks of noncommercially prepared antibiotic preparations. Overall, the large majority (75%) said they believe it is important to have a commercially available antibiotic approved for intracameral injection. Assuming reasonable cost, the survey indicates that commercial availability of Aprokam (cefuroxime) would increase the overall percentage of surgeons using intracameral antibiotic injection prophylaxis to nearly 84%. Although the majority used topical perioperative antibiotic prophylaxis, and gatifloxacin and moxifloxacin were still the most popular agents, there was a trend toward declining use of fourth-generation fluoroquinolones (60%, down from 81% in 2007) and greater use of topical ofloxacin and ciprofloxacin (21%, up from 9% in 2007).

J Cataract Refract Surg 2015; 41:1300–1305 © 2015 ASCRS and ESCRS

Supplemental material available at www.jcrsjournal.org.

In 2007,[1] the Cataract Clinical Committee of the American Society of Cataract and Refractive Surgery (ASCRS) surveyed the ASCRS membership regarding antibiotic prophylaxis for postoperative endophthalmitis after cataract surgery. The prospective randomized endophthalmitis prophylaxis trial of the European Society of Cataract and Refractive Surgeons (ESCRS) had just reported a 5-fold reduction in endophthalmitis rates with direct intracameral injection of cefuroxime at the conclusion of cataract surgery (0.07% versus 0.34% without intracameral cefuroxime).[2,3] The goal of the ASCRS survey was to evaluate member practice patterns regarding topical and intracameral antibiotic prophylaxis and to assess the impact of the ESCRS study. Sixteen percent of respondents were already injecting intracameral antibiotics before the study. Although 7% had recently started or planned to start injecting intracameral antibiotics, the ESCRS study apparently had not affected the practice of 77% of respondents who still did not plan to do so.

Since our 2007 survey, numerous large retrospective studies supporting the efficacy of intracameral cefuroxime have been published.[4–12] Both the 2011 American Academy of Ophthalmology (AAO) Cataract Preferred Practice Pattern Guidelines and a 2011 ASCRS Cataract Clinical Committee review of endophthalmitis prevention noted that there was stronger evidence supporting direct intracameral injection than for any other method of antibiotic prophylaxis.[13,14] In 2013,[15] the ESCRS published endophthalmitis prophylaxis guidelines that reviewed the evidence supporting the safety and efficacy of direct intracameral injection of cefuroxime. On the other

Submitted: November 20, 2014.
Final revision submitted: January 24, 2015.
Accepted: January 26, 2015.

From the University of California (Chang), San Francisco, California, Moran Eye Centre (Mamalis), University of Utah, Salt Lake City, Utah, and Department of Ophthalmology (Henderson), Tufts University School of Medicine, Boston, Massachusetts, USA; University of Toronto (Braga-Mele), Toronto, Ontario, Canada; Raghudeep Eye Clinic (Vasavada), Ahmedabad, India.

Corresponding author: David F. Chang, MD, 762 Altos Oaks Drive, Suite 1, Los Altos, California 94024, USA. E-mail: dceye@earthlink.net.

http://dx.doi.org/10.1016/j.jcrs.2015.01.014
0886-3350

hand, others continue to question whether intracameral antibiotic prophylaxis is effective or necessary.[16] Another significant development has been the approval of Aprokam, a commercial preparation of cefuroxime for intracameral injection, in 24 European countries.[15,17] Aprokam is a single-use vial containing 50 mg of cefuroxime powder. Five milliliters of sodium chloride 0.9% is used to reconstitute this, and then 0.1 mL (1 mg) is injected into the anterior chamber. Because of these developments, the ASCRS Cataract Clinical Committee decided to resurvey our membership regarding current endophthalmitis antibiotic prophylaxis practice patterns. Most of the same questions from the 2007 survey were repeated so that differences and trends could be analyzed.

MATERIALS AND METHODS

In August 2014, a link to an online survey was sent to 7677 ASCRS member e-mail addresses on file. The online anonymous survey consisted of 18 questions that took approximately 3 minutes to complete. A unique response link was generated so that it was impossible to complete the survey more than once. The questionnaire is reprinted in Appendix A (available at: http://jcrsjournal.org).

RESULTS

The questionnaire was completed by 15% (1147 members), which was similar to the 18% response rate in 2007. The majority of respondents (65% [740/1144]) were from the United States, with only 9% (101/1144) from Europe (Table 1). The entire spectrum of low- to high-volume surgeons was well represented, and two thirds of respondents performed at least 300 cases a year (Table 2). Respondents were asked to list their rate of infectious endophthalmitis per 10 000; the results are shown in Figure 1. Of note, 81% of the respondents had 0 to 2 cases per 10 000. Only 7% of the respondents reported a rate higher than 0.05% (5/10 000).

The vast majority of surgeons (90% [1029/1140]) used topical perioperative antibiotic prophylaxis at the time of cataract surgery (Table 3). Of respondents prescribing topical antibiotics, the majority preferred the fourth-generation fluoroquinolones gatifloxacin or moxifloxacin (60% [621/1029]), followed by ofloxacin or ciprofloxacin (21% [215/1029]), levofloxacin (3% [35/1029]), and other antibiotics (15% [158/1029]) (Table 4). Among 698 U.S. respondents prescribing topical antibiotics, the rates were 58% (403/698), 25% (174/698), 2% (14/698), and 15% (107/698), respectively. This represents a shift from the 2007 survey, for which the distribution among all respondents was 81% (968/1194), 9% (108/1194), 3% (38/1194), and 7% (80/1194), respectively (Table 4).

Eight-five percent (973/1145) of ASCRS surgeons initiated topical antibiotics preoperatively (Table 3). As was the case in 2007, roughly one half of them started antibiotics 3 days before surgery (48% [470/973]), while the other half initiated them on the day of surgery (20% [189/973]) or 1 day before surgery (32% [314/973]) (Table 5). Virtually all surgeons (97% [1108/1146]) prescribed topical antibiotics postoperatively (Table 3). Of the surgeons, 72% (796/1108) stopped postoperative antibiotics by 1 week (Table 6); 21% (237/1108) used postoperative antibiotics for several weeks without tapering, and 7% (75/1108) tapered them over several weeks. These patterns of postoperative topical antibiotics use are virtually unchanged from 2007 (Table 6).

As in 2007, the great majority of surgeons (93% [1067/1144]) were administering some type of antibiotic at the conclusion of cataract surgery (Table 7). The majority were instilling a topical antibiotic (69% [788/1067]). Compared with 2007, the percentage of surgeons injecting an intracameral antibiotic increased from 14% (179/1311) to 36% (411/1144). Looking at U.S. respondents only, 30% (221/737) were injecting intracameral antibiotic at the end of surgery compared with 70% (70/100) of European respondents. Fewer respondents were using a subconjunctival injection (8% [95/1144]) or a collagen shield (1% [14/1144]). These percentages total more than 100 because some surgeons use multiple methods of antibiotic delivery.

The percentage of surgeons using any type of intracameral antibiotic rose to 50%, compared with 30% in

Table 1. Distribution of respondents by practice location.

Region	Number (%) 2014 Survey	2007 Survey
United States	740 (65)	910 (69)
Europe	101 (9)	138 (11)
Canada	54 (5)	52 (4)
Latin/South America/Mexico	152 (13)	109 (8)
Australia/Asia	10 (1)	98 (7)
Africa	87 (8)	0

Table 2. Distribution of respondents by cataract volume.

Annual Cataract Volume	Number (%) 2014 Survey	2007 Survey
<100 cases	66 (6)	143 (11)
100 to 300 cases	315 (27)	446 (34)
300 to 500 cases	301 (26)	361 (28)
>500 cases	465 (41)	362 (28)

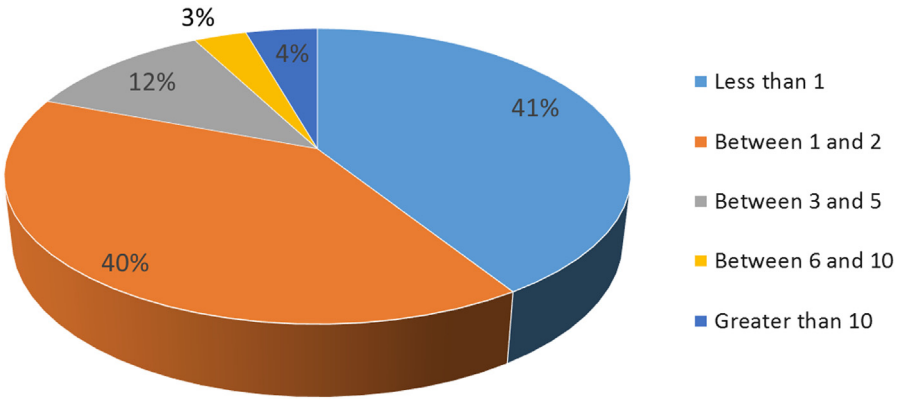

Figure 1. Number of infectious endophthalmitis cases per 10 000.

2007 (Table 3). Of these users, only 16% (93/570) were placing the antibiotic in the irrigating bottle compared 48% (187/389) in 2007. Table 8 shows the antibiotic preferences of those using intracameral antibiotic prophylaxis. Moxifloxacin was used by 33% (189/570), vancomycin by 37% (211/570), and cefuroxime by 26% (145/570). If Aprokam was not used, the intracameral antibiotics were prepared by the operating room nursing staff (65% [368/564]), by a pharmacy (24% [133/564]), or by the surgeon (6% [34/564]) (Table 9).

Nineteen percent (213/1135 respondents) indicated that they had initiated intracameral antibiotic injections within the past 2 years or planned to initiate them in the next 6 months. Twenty-eight percent (317/1135) said that they were already injecting antibiotic before 2 years ago. For the 53% (605/1135) who were not injecting intracameral antibiotic, the stated reasons were cost (19% [112/602]), mixing or compounding risk (49% [297/602]), or the lack of convincing evidence (65% [394/602]) (Table 10). These results were similar to those in 2007 except that 89% in this group (599/672) cited lack of convincing evidence in the first survey. The percentages total more than 100 because some surgeons cited multiple reasons.

Asked to rate the importance of intracameral antibiotic prophylaxis, 19% (216/1144) were not sure, 14% (158/1144) said it was unnecessary, 41% (469/1144) said it was "very important," and 26% (301/1144) said that it was "important, but other antibiotic prophylaxis methods were sufficient." However, 75% (864/1146) said they now believe that it is important to have a commercially approved and formulated antibiotic for direct intracameral injection; 9% (105/1146) said it was not important, and 15% (177/1146) were not sure (Table 11). Respondents currently without access to Aprokam were asked whether they would use it if were approved (Table 11). Sixty-nine percent (722/1047) said that they would assuming reasonable cost, 15% (152/1047) would use a different intracameral antibiotic, and 17% (173/1047) said that they would still not use any intracameral antibiotic. Among U.S. respondents only, 53% (384/726) said they believe that the U.S. Food and Drug Administration (FDA) should approve Aprokam based on the European clinical trials and usage (no new trial). The rest said that the FDA should require a new clinical trial showing safety and efficacy (31% [224/726]) or safety only (16% [118/726]).

The survey asked whether surgeons had ever experienced a complication from using noncommercially prepared intracameral antibiotics. Of those using intracameral antibiotics, 94% (487/520) said no. Six percent of those using intracameral antibiotics (33 respondents) reported having had complications ranging from infection (3/33), inflammation/toxic anterior segment syndrome (TASS) (24/33), corneal endothelial injury (10/33), to other (5/33).

Table 3. Perioperative use of antibiotic prophylaxis.

	2014		2007	
Regimen	Use (%)	Do Not Use (%)	Use (%)	Do Not Use (%)
Perioperative topical antibiotics	90	10	91	9
Preoperative topical antibiotics	85	15	88	1
Postoperative topical antibiotics	97	3	98	2
Intracameral antibiotics	50	50	30	70
Irrigation vs direct injection				
Direct injection	84	—	52	—
Irrigation bottle	16	—	48	—

Table 4. Preferred perioperative topical antibiotic.*

Antibiotic	2014 Survey (%)	2007 Survey (%)
Gatifloxacin or moxifloxacin	60	81
Ofloxacin or ciprofloxacin	21	9
Levofloxacin	3	3
Other	15	7

*Of those using a perioperative topical antibiotic

DISCUSSION

The 2007 ASCRS endophthalmitis prophylaxis survey was performed after publication and dissemination of the ESCRS prospective study results.[1] The latter was the first and so far only large multicenter prospective randomized controlled trial to evaluate direct intracameral antibiotic injection and reported a significant reduction in the rate of post-cataract infectious endophthalmitis with intracameral cefuroxime.[2,3] A total of 1312 members responded to the 2007 online survey (18% response rate). The vast majority (91%) were using preoperative and postoperative topical fluoroquinolone prophylaxis. Of the 30% who were using intracameral antibiotics, there was a 50:50 split between those placing the antibiotic in the infusion bottle versus those injecting it directly. Vancomycin was the most popular agent, preferred by 61% of those using an intracameral antibiotic. Only 6% of respondents were injecting intracameral cefuroxime. The survey showed that 77% of all respondents were still not injecting intracameral antibiotics, but 82% of all respondents indicated that they would use a commercially available antibiotic for direct injection if it were reasonably priced.

As was the case in 2007, perioperative topical antibiotic prophylaxis continues to be used by the overwhelming majority of surgeons. It was used preoperatively by 85%, postoperatively by 97%, and at the conclusion of surgery by 69%. There was a shift from using gatifloxacin and moxifloxacin (60%, down from 81% in 2007) to greater use of ofloxacin and ciprofloxacin (21%, up from 9% in 2007). This could reflect cost considerations associated with insurance coverage, availability of generics, and the reduction in topical drug samples provided to patients in the U.S.

Table 5. When respondents started preoperative topical antibiotic.*

Antibiotic	2014 Survey (%)	2007 Survey (%)
3 days before surgery	48	52
1 day before surgery	32	26
Upon arrival for surgery	20	22

*Of those using a perioperative topical antibiotic

Since 2007, multiple multinational retrospective studies have been published that support the safety and efficacy of direct intracameral antibiotic prophylaxis.[4–12] Among the more recent studies published in 2013, the 6-year incidence of endophthalmitis from the Swedish National Cataract Register (where intracameral cefuroxime is standard) was reported to be 0.029%.[10] In the U.S., a retrospective study that took place at Kaiser Permanente[9] documented a 22-fold decrease in endophthalmitis rates over a 5-year period when intracameral antibiotic injection was routinely used with cataract surgery.

Perhaps as a result, the current ASCRS survey found a significant shift in opinion and practice regarding intracameral antibiotic use compared with 2007. Direct intracameral antibiotic injection at the conclusion of surgery was used by 36% in the 2014 survey compared with 14% in 2007. The percentage of surgeons using any intracameral antibiotic increased from 30% to 50%, and the majority of these surgeons said they now use direct injection compared with placing antibiotic in the irrigating solution (84% versus 16% in 2014; 52% versus 48% in 2007). Unlike the stronger preference for vancomycin (61%) in 2007, moxifloxacin (33%), cefuroxime (26%), and vancomycin (37%) were somewhat more evenly used intracamerally in 2014.

Reflecting the smaller percentage of European respondents in the ASCRS survey, commercial

Table 6. Duration of postoperative topical antibiotic use.*

Regimen	2014 Survey (%)	2007 Survey (%)
1 week or less	72	73
Several weeks (no taper)	21	19
Several weeks (taper)	7	8

*Of those using a postoperative topical antibiotic

Table 7. Method of antibiotic administration at the conclusion of surgery.*

Method	2014 Survey (%)	2007 Survey (%)
Topical	69	75
Intracameral injection	36	14
Subconjunctival injection	8	11
Collagen shield	1	3
None	7	10

*Percentages total more than 100 as respondents could check more than 1 method.

Table 8. Distribution of drugs and routes for those using intracameral antibiotic prophylaxis.

Route	Distribution (%)
Direct intracameral antibiotic injection	
Moxifloxacin (mixed from Vigamox)	29
Moxifloxacin (compounded)	4
Vancomycin	22
Aprokam (commercial)	12
Cefuroxime (non-Aprokam)	14
Other	3
Antibiotic placed in irrigation bottle	
Vancomycin	15
Other	1

Table 9. Who prepares the intracameral antibiotic.*

	2014 Survey		2007 Survey
Preparer	Global	U.S. Only	Global
Operating room nursing staff	65	66	77
Surgeon	6	1	5
Aprokam (commercial)	5	0	0
Pharmacy	24	32	18
Hospital vs compounding pharmacy			
Hospital	14	18	—
Compounding	9	14	—

*Of those using a preoperative topical antibiotic

Aprokam was used by only 5% of respondents. Far more Europeans (70%) compared with those in the U.S. (30%) were injecting intracameral antibiotics at the conclusion of surgery. These results are consistent with a smaller ESCRS survey reporting that 75% usually or always use intracameral antibiotic.[17] In the global ASCRS survey, the majority of intracameral antibiotic continued to be prepared by operating room nurses (65% versus 77% in 2007); however, there is a trend toward greater reliance on pharmacies (24% versus 18% in 2007).

Two thirds of respondents (67%) said they believe intracameral antibiotic prophylaxis is very important or important as an option. Of those not using intracameral antibiotics, half expressed concerned about the risk for a mixing or compounding error, with the underlying possibility of TASS. The clear majority (75.5%) said they now believe that it is important to have an approved and commercially formulated antibiotic for direct intracameral use. This is a significant increase from 54% in 2007. The likely adoption of intracameral antibiotic use if a reasonably priced approved product became commercially available remains equally strong. Were this to happen, only 16.5% said they would still not use an intracameral antibiotic, compared with 18% in 2007. In the ESCRS survey,[17] 8% of 193 surgeons said they would still not use an intracameral antibiotic if it were commercially available.

These latter responses underscore the strong need for approved commercial antibiotic formulations for intracameral prophylaxis in cataract surgery. Compounding and mixing risk continues to be an important deterrent for at least one half of surgeons not using intracameral antibiotics. However, our survey clearly shows that increasing numbers of surgeons (47%) are using or planning to use antibiotics for direct intracameral injection, despite the need to prepare this off-label in the absence of commercially approved products. In most cases, this means mixing vancomycin or cefuroxime labeled for parenteral use or using moxifloxacin (Vigamox) labeled for topical use.[18] As of 2014, Aprokam was approved in approximately 2 dozen European countries, and more than 1.3 million units had been used worldwide with no significant incidence of reported adverse events. As noted in AAO's 2011 Cataract Preferred Practice Pattern,[13] the ASCRS Cataract Clinical Committee's 2011 white paper,[14] and the 2013 ESCRS guidelines for prevention

Table 10. Reasons for not using direct intracameral injection.*

Reason	2014 Survey (%)	2007 Survey (%)
Mixing/compounding risk	49	45
Cost	19	17
Not convinced of need	65	89

*Asked of those who do not and were not planning to inject intracameral antibiotic. Percentages total more than 100 because respondents could check more than 1 reason.

Table 11. Is it important to have a commercially available antibiotic approved and formulated for direct IC injection?*

Response	2014 Survey (%)	2007 Survey (%)
Yes	75	54
No	9	11
Not sure	15	35
Would use it	21*	47
Would use it if cost reasonable	48*	35
Would not use any IC antibiotic	17*	18
Would use another IC antibiotic	15*	—

IC = intracameral
*Asked of those currently without access to Aprokam

of endophthalmitis,[15] the published evidence for antibiotic prophylaxis efficacy is strongest for direct intracameral injection. With such a strong consensus among ophthalmologists regarding the efficacy, importance, and desirability of commercially approved antibiotics for intracameral injection, we call on the pharmaceutical industry and the FDA to collaborate in making such products available for our patients.

REFERENCES

1. Chang DF, Braga-Mele R, Mamalis N, Masket S, Miller KM, Nichamin LD, Packard RB, Packer M; for the ASCRS Cataract Clinical Committee. Prophylaxis of postoperative endophthalmitis after cataract surgery; results of the 2007 ASCRS member survey. J Cataract Refract Surg 2007; 33:1801–1805
2. Barry P, Seal DV, Gettinby G, Lees F, Peterson M, Revie CW; for the ESCRS Endophthalmitis Study Group. ESCRS study of prophylaxis of postoperative endophthalmitis after cataract surgery; preliminary report of principal results from a European multicenter study. J Cataract Refract Surg 2006; 32:407–410; erratum, 709
3. ESCRS Endophthalmitis Study Group. Prophylaxis of postoperative endophthalmitis following cataract surgery: results of the ESCRS multicenter study and identification of risk factors. J Cataract Refract Surg 2007; 33:978–988
4. Lundström M, Wejde G, Stenevi U, Thorburn W, Montan P. Endophthalmitis after cataract surgery; a nationwide prospective study evaluating incidence in relation to incision type and location. Ophthalmology 2007; 114:866–870
5. García-Sáenz MC, Arias-Puente A, Rodríguez-Caravaca G, Bañuelos JB. Effectiveness of intracameral cefuroxime in preventing endophthalmitis after cataract surgery; ten-year comparative study. J Cataract Refract Surg 2010; 36:203–207
6. Behndig A, Montan P, Stenevi U, Kugelberg M, Lundström M. One million cataract surgeries: Swedish National Cataract Register 1992–2009. J Cataract Refract Surg 2011; 37:1539–1545
7. Tan CSH, Wong HK, Yang FP. Epidemiology of postoperative endophthalmitis in an Asian population: 11-year incidence and effect of intracameral antibiotic agents. J Cataract Refract Surg 2012; 38:425–430
8. Barreau G, Mounier M, Marin B, Adenis J-P, Robert P-Y. Intracameral cefuroxime injection at the end of cataract surgery to reduce the incidence of endophthalmitis: French study. J Cataract Refract Surg 2012; 38:1370–1375
9. Shorstein NH, Winthrop KL, Herrinton LJ. Decreased postoperative endophthalmitis rate after institution of intracameral antibiotics in a Northern California eye department. J Cataract Refract Surg 2013; 39:8–14
10. Friling E, Lundström M, Stenevi U, Montan P. Six-year incidence of endophthalmitis after cataract surgery: Swedish national study. J Cataract Refract Surg 2013; 39:15–21
11. Rodríguez-Caravaca G, García-Sáenz MC, Villar-del-Campo MC, Andrés-Alba Y, Arias-Puente A. Incidence of endophthalmitis and impact of prophylaxis with cefuroxime on cataract surgery. J Cataract Refract Surg 2013; 39:1399–1403
12. Beselga D, Campos A, Castro M, Fernandes C, Carvalheira F, Campos S, Mendes S, Neves A, Campos J, Violante L, Sousa JC. Postcataract surgery endophthalmitis after introduction of the ESCRS protocol: a 5-year study. Eur J Ophthalmol 2014; 24:516–519
13. American Academy of Ophthalmology. Cataract in the Adult Eye; Preferred Practice Pattern. San Francisco, CA, American Academy of Ophthalmology, 2011. Available at http://one.aao.org/Assets/8d66318f-ff50-408e-9bb1-73d277cf14ce/636496436146230000/cataract-in-the-adult-eye-pdf. Accessed March 21, 2015
14. Packer M, Chang DF, Dewey SH, Little BC, Mamalis N, Oetting TA, Talley-Rostov A, Yoo SH; for the ASCRS Cataract Clinical Committee. Prevention, diagnosis, and management of acute postoperative bacterial endophthalmitis. J Cataract Refract Surg 2011; 37:1699–1714
15. Barry P, Cordovés L, Gardner S. ESCRS Guidelines for Prevention and Treatment of Endophthalmitis Following Cataract Surgery: Data, Dilemmas and Conclusions. Dublin, Ireland, European Society of Cataract and Refractive Surgeons, 2013. Available at http://www.escrs.org/downloads/Endophthalmitis-Guidelines.pdf. Accessed March 21, 2015
16. Schimel AM, Alfonso EC, Flynn HW Jr. Endophthalmitis prophylaxis for cataract surgery. Are intracameral antibiotics necessary? [Viewpoint]. JAMA Ophthalmol 2014; 132:1269–1270
17. Barry P. Adoption of intracameral antibiotic prophylaxis of endophthalmitis following cataract surgery; update on the ESCRS Endophthalmitis Study. J Cataract Refract Surg 2014; 40:138–142
18. Braga-Mele R, Chang DF, Henderson BA, Mamalis N, Talley-Rostov A, Vasavada A; for the ASCRS Clinical Cataract Committee. Intracameral antibiotics: safety, efficacy, and preparation. J Cataract Refract Surg 2014; 40:2134–2142. Available at: http://www.ascrs.org/sites/default/files/resources/JCRS_December_2014.pdf. Accessed March 21, 2015

FINANCIAL DISCLOSURES

Dr. Chang is a consultant to Abbott Medical Optics Inc., Clarity, Power Vision, Calhoun, Icon, and Transcend. Dr. Braga-Mele is a consultant to Alcon and Abbott Medical Optics Inc. Dr. Henderson is a consultant to Alcon, Bausch & Lomb, Abbott Medical Optics Inc., and Genzyme. Dr. Vasavada is a consultation to Alcon. Dr. Mamalis has no financial or proprietary interest in any material or method mentioned.