Postoperative endophthalmitis is a rare, albeit serious, complication of cataract surgery. Over the years, preoperative and operative measures, such as lid hygiene, appropriate surgical draping, and improved surgical technique, have all decreased the incidence of postoperative endophthalmitis. Commonly used prophylactic measures include preoperative topical, intracameral, and postoperative topical antibiotics. Since the landmark study done by the endophthalmitis vitrectomy study group, treatment has usually consisted of intravitreal antibiotics with or without pars plana vitrectomy (depending on the patient population). In this review, we have focused on advances in the field of endophthalmitis within the last year. These include articles examining treatment and complications of diabetic patients and those with retinal detachments, bacterial adherence to lenses, prophylactic measures, and addition of steroids to conventional treatments of endophthalmitis. Curr Opin Ophthalmol 2002, 13:14–18 © 2002 Lippincott Williams & Wilkins, Inc.

Signs and symptoms
The most common presentation consists of reduced or blurred vision, conjunctival injection, red eye, pain, and lid swelling. According to the Endophthalmitis Vitrectomy Study (EVS), a hypopyon can be seen in nearly three-quarters of patients at presentation. In this study, ocular pain, which is widely regarded as diagnostic of endophthalmitis, was absent in 25% of patients [5]. Interestingly, the presence of diabetes, with its associated neuropathy, does not seem to affect the presence of pain at onset [6••].

A case of acute bacterial endophthalmitis was reported recently as presenting with retinal vasculitis five days postoperatively. Findings included diffuse, retinal hemorrhages and a posterior pole hypopyon. Very little inflammation was noted in the anterior portion of the vitreous and anterior chamber. The day after presentation, the patient developed the classic signs of postoperative endophthalmitis [7]. Other reported signs of early bacterial endophthalmitis have included both retinal periphlebitis and mid-peripheral retinal hemorrhages [8, 9].

Causes
Postoperative endophthalmitis can either be sterile, or infectious (approximately 69% of cases) [5]. In culture-positive cases of endophthalmitis, the ocular surface and adnexa are considered to be the primary sources of bacteria. Speaker et al. [10] noted an association between external bacterial flora and bacteria isolated from vitrectomy specimens in 82% of their patients. Similarly, in the EVS study group, isolates from intraocular and conjunctival specimens were indistinguishable in 67.7% of cases [11]. Bacteria are the most common cause of infectious endophthalmitis, with Staphylococcus epidermidis being the most likely organism. Approximately 70% of patients with positive cultures are infected with coagulase-negative microorganisms (mostly Staphylococcus epidermidis), 10% with Staphylococcus aureus, 9% with Streptococcus species, 2% with enterococcus, 3% with other gram-positive species, and finally 6% with gram-negative species [12–14]. The EVS has indicated that diabetics...
tend to have more virulent organisms, and are less likely to have culture-negative endophthalmitis [6••].

It seems that there is a correlation between clinical presentation and microbiologic spectrum. The EVS found that gram-positive, coagulase-negative micrococci tended to cause less severe infections compared with more virulent gram-negative, and “other” gram-positive organisms. More virulent organisms caused signs and symptoms of endophthalmitis to appear earlier. Other significant findings that correlated with a more severe infection included corneal infiltrate, cataract wound abnormalities, afferent pupillary defect, loss of red reflex, and initial light perception only vision. These findings are more highly associated with gram-negative or “other” gram-positive isolates [5]. Recent evidence has suggested that S. epidermidis carrying the ica (intercellular adhesion) locus may play a part in the pathogenesis of some forms of endophthalmitis. Other factors that may influence bacterial adhesion include lens materials, surface irregularities, and electrostatic charge [14].

Preoperative risk factors include blepharitis, conjunctivitis, cannuliculitis, lacrimal duct obstruction, contact lens wear, and an ocular prosthesis in the fellow orbit. The incidence of endophthalmitis increases during secondary IOL implantation, but is most likely caused by other associated risk factors, including diabetes, transcleral suture fixation of the posterior chamber IOL, polypropylene haptics, preoperative eyelid abnormalities, reentrance through a previous wound, and postoperative wound defects [15].

Intraocular contamination seems to be relatively common after uncomplicated cataract surgery. Anterior chamber aspirates have been found to be positive 13.7 to 43% of the time after cataract surgery [16, 17]. Interestingly enough, no patients in either of these studies developed postoperative endophthalmitis. There must be other factors in a patient’s history, and aspects of the cataract surgery itself that have a bearing on the development of postoperative endophthalmitis. Such aspects include wound abnormalities, use of an IOL without a heparinized surface, and immunosuppression [18]. A survey, performed in Germany, found that scleral incisions, diabetes mellitus, occlusion of the lacrimal sac, and skin diseases were regarded as risk factors for endophthalmitis by survey respondents [19].

Intraoperative risk factors that have been found to be associated with an increased incidence of postoperative endophthalmitis, include inadequate disinfection of the eyelid or conjunctiva, surgery longer than sixty minutes, vitreous loss, use of prolene haptic IOLs, and unplanned or inapparent ocular penetration [20]. Other risk factors that may be related to an increased incidence of postoperative endophthalmitis include wound leak or dehis-cence, incarceration of the vitreous into the surgical wound, inadequately buried sutures or suture removal, and a postoperative filtering bleb. In a retrospective chart review, Colleaux et al. found that the incidence of endophthalmitis did not differ with clear corneal versus scleral tunnel incisions [21].

**Treatments**

Historically, intravenous antibiotics and pars plana vitrectomy have been used to treat postoperative endophthalmitis. In 1995, the endophthalmitis vitrectomy study (EVS) evaluated the roles of systemic antibiotics and pars plana vitrectomy in the treatment of endophthalmitis following cataract surgery. They found that systemic antibiotics were not useful adjuncts to intravitreal antibiotics in either acute or subacute postoperative endophthalmitis. Although there still exists some controversy over potential limitations of the study design, most clinicians feel that to reduce toxic side effects, cost, and length of hospital stay, systemic antibiotics should not be used [5, 22]. The conclusions about whether to do a vitrectomy tended to vary according to patient subgroups. Vitrectomy was advocated originally as a way to remove vitreous membranes, debris, and possibly the infecting organism and associated toxins. The EVS group found that immediate vitrectomy in patients with hand motion or better vision, was not beneficial. Interestingly, patients with light perception only vision had a three-fold increase chance of achieving 20/40 vision if they received a vitrectomy [5].

The EVS group recently published an article looking at their diabetic population, and noted a different trend. Patients with light perception only at baseline seemed to do better with a vitrectomy at all visual thresholds, though this was not statistically significant (33% with vitrectomy achieved 20/40; 0% with tap/biopsy achieved 20/40). Of the diabetics with better than light perception vision at baseline, 57% of those who received a vitrectomy achieved 20/40 vision, whereas only 40% of those who underwent tap and biopsy achieved 20/40 vision. Although these results might imply that vitrectomy is superior to tap and biopsy in both diabetic subgroups, this difference was not statistically significant. In fact, 324 more diabetic patients would have to have been added to the study to increase the power enough to detect a true difference in those patients with better than light perception vision at baseline. As a result, the EVS authors concluded that until a study is performed that includes enough patients, intraocular antibiotics with either vitreous tap/biopsy, or vitrectomy is reasonable [6••].

In an effort to achieve the greatest concentration of antibiotic within the eye, the primary method of administering antibiotics is via intravitreal injection. As the offending organism is not usually known at the time of
injection, the antibiotics used must cover both gram-positive and gram-negative bacteria. The mainstay in treatment of gram-positive bacteria is vancomycin, 1mg/0.1ml. In a recent small trial, Haider et al.[23] found that after injection of both 1 or 2 mg of vancomycin, concentrations were above the minimal bactericidal levels at 48 and 72 hours for PMMA adherent coagulase negative Staphylococcus. Unfortunately, the vancomycin concentrations ranged quite a bit. Antibiotic concentrations were occasionally above the retinotoxic levels previous defined in rabbits, especially when a 2 mg injection was used. The EVS group found that 100% of the gram-positive organisms were sensitive to vancomycin, including methicillin-resistant staph aureus [24].

Gram-negative organisms usually are treated with an aminoglycoside, amikacin, at a dose of 0.4 mg/0.1 ml. Although amikacin is somewhat less toxic than other aminoglycosides, there is still a potential for toxicity. Ceftazidime (2.25 mg/0.1 ml), a third-generation cephalosporin, has been used as a more recent alternative to amikacin because of its broader coverage and decreased potential for retinotoxicity. In a study of endophthalmitis caused by gram-negative organisms, 100% of the gram-negative isolates were sensitive to ceftazidime, whereas only 97% were sensitive to amikacin [25]. Of special note, ceftazidime and vancomycin must be injected in separate syringes to avoid precipitation out of solution when combined. If the patient has not shown signs of clinical improvement or if worsening is noted within the first 48 to 72 hours following initial injection, a repeat vitreous tap and injection of antibiotics plus a pars plana vitrectomy (if this was not originally done) should be considered [26].

Topical and subconjunctival antibiotics are often used to supplement intravitreal injections. This supplementation is done in an attempt to increase the concentration of antibiotics within the anterior segment of the eye. However, topically administered antibiotics do not penetrate the vitreous well, and subconjunctival injection is riskier, and more highly associated with pain. Presently recommended dosages of supplemental topical antibiotics include fortified vancomycin (50 mg per ml) with the drops with either fortified amikacin (20 mg per ml) or ceftazidime (100 mg per ml), all used hourly [5, 27].

Corticosteroid therapy may be used in conjunction with antibiotics either topically, intravitreally, or systemically to help reduce the inflammation and its possible destructive effects on the retina. Intravitreal corticosteroid injection has been shown in some studies to reduce the intraocular inflammatory process and secondary complications associated with infectious endophthalmitis [28, 29], but also has been shown to have no effect on visual outcome [1]. In a retrospective, nonrandomized comparative trial by Shah et al.[30•], intravitreal steroids were even found to be detrimental with a decreased visual acuity compared with those who did not receive intravitreal antibiotics. Some controversy exists about how to interpret these results given the nonrandomized nature of the study, and the fact that there was a nonsignificant (P=0.7) baseline difference between treatment groups (those receiving steroids and worse vision to begin with) [31]. Recommended corticosteroid therapy, if used, consists of dexamethasone (400 mg grams per 0.1 ml) and is given at the time of vitrectomy or biopsy. Prednisolone acetate, at 1%, can be used as the topical corticosteroid of choice, and prednisone 30 mg per day for 5 to 10 days as the oral dose. This was the regimen used by the EVS [5].

Outcomes

Patients tend to have poor visual acuity when presenting with postoperative endophthalmitis. Eighty-six percent of EVS patients had an initial acuity of less than 5/200, and 26% were light perception only. At three months, 41% percent of patients achieved 20/40, and 69% had better than 20/100 vision. Between 9 and 12 months, 53% of patients in the EVS achieved a visual acuity of 20/40, and 74% were better than 20/100. According to the EVS, poor outcomes were associated with worse initial vision, small pupil size after maximal dilation, presence of rubeosis irides, and an absence of a red reflex. Diabetics tend to have worse vision after treatment of endophthalmitis; only 56% of diabetics achieved 20/100 in the EVS population (versus 77% of nondiabetics) [6••]. Other associated factors include a history of glaucoma, afferent pupillary defect, corneal infiltrate, ring ulcer, abnormal intraocular pressure, and microbiologic factors [5]. The EVS noted that a final visual acuity of 20/100 was achieved with gram-positive, coagulase-negative micrococci 84% of the time; followed by staph aureus, 50%; streptococci, 30%; enterococci, 14%; and gram-negative organisms, 56%. The visual acuity at initial presentation appeared to be more useful than biologic factors in predicting visual outcome and favorable response to vitrectomy in acute bacterial endophthalmitis [24].

Complications within the first 36 to 60 hours include dislocated intraocular lenses, retinal detachments, macular infarctions, and expulsive hemorrhages. In the EVS, 6 to 7% of patients needed an additional procedure secondary to such complications (regardless of initial procedure). Diabetics tended to have an increase in early additional procedures [6]. Recently, the EVS published additional data that found that 8.3% of eyes in their patients developed retinal detachment after initial treatment [32••]. The rate of retinal detachment was found to be related to microbial pathogens (higher rates with gram-negative, and “other” gram positive organisms), presenting visual acuity, open posterior capsule, age greater than 75, and need for an additional procedure early in the postoperative course. Of note, the rate of retinal detachment was not related to initial manage-
ment, (vitrectomy or tap biopsy), or presence of diabetes. Not surprisingly, retinal detachment resulted in a poorer visual outcome with only 27% of patients achieving 20/40 visual acuity versus 55% of patients without detachment. If patients were able to undergo surgery for the detachment, their chance of achieving 20/40 increased to 38%. In the EVS, this consisted of scleral buckling, with or without vitreotomy, or retinopexy.

Prevention

Several methods have been advocated to decrease the incidence of endophthalmitis using either preoperative or operative measures to decrease the presence of bacteria on the operative field. Examples of prophylaxis include antisepsis (adequate draping of eyelid, lashes, and lid margins), topical preoperative antibiotics, intracameral antibiotics, subconjunctival antibiotics, systemic antibiotics, and postoperative antibiotics. Multiple studies have shown a decreased bacterial load with prophylaxis, but no definitive decrease in endophthalmitis [33].

Application of topical 5% povidone-iodine solution on the conjunctival sac in the immediate preoperative period, for three consecutive days preoperatively, or at the conclusion of surgery has been shown to decrease the conjunctival bacterial load, and possibly reduce the incidence of surgery [19,34–36,37]. This year, Mendivil et al. [38] published a randomized control trial that did not find any difference in culture results between patients treated with preoperative topical povidone-iodine and those given a placebo.

Dilute antibiotics have been used in the irrigating fluid during surgery to try and decrease bacterial load. Vancomycin tends to be the antibiotic of choice given its spectrum against gram-positive organisms. Mendivil et al., in a randomized control trial, found that the half-life of vancomycin after cataract surgery was less than two hours: levels decreased from 20.1 µg/ml to 9.4 µg/ml (minimum inhibitory concentration between 0.5 and 2.0 mg/ml). Even though the time of antibiotic exposure was low, they found that the number of positive intraocular cultures had decreased two hours after surgery in those patients who had received intracameral vancomycin. No patients in this study developed endophthalmitis [38]. Two published surveys have noted a decrease in endophthalmitis but are flawed given the fact that they are surveys in themselves [19,39].

Vancomycin prophylaxis continues to be fiercely debated. There is a theoretical risk of increasing antibiotic resistance with routine use of vancomycin [40]. In 1995, after noting an increased incidence of vancomycin resistant bugs, the CDC issued guidelines discouraging use of prophylactic vancomycin in surgical procedures. Vancomycin might be theoretically useful, and until sufficient studies are done to fully evaluate the subsequent incidence of endophthalmitis, the decision will be based on surgeon preference [41••]. Recently, the effects of cefotaxime on the corneal endothelium was examined, and was found to be safe [42]. Although this drug does not have as good gram-positive coverage as the first generation cephalosporins, it does have a greater extended spectrum than vancomycin, and may be an alternative for infection prophylaxis.

In the hopes of preventing endophthalmitis, antibiotics have been applied subconjunctivally and topically, both in the preoperative and postoperative periods. There is a distinct lack of good data proving any benefit for postoperative topical antibiotics despite widespread use among ophthalmologists. In a recent retrospective chart review, Colleaux et al. [21] found that preoperative topical antibiotics did not make a statistical difference in the incidence of endophthalmitis. On the other hand, they did find that immediate postoperative subconjunctival antibiotics decreased the incidence of endophthalmitis. All of their surgeons used topical antibiotics postoperatively, thus making any conclusion about its usefulness impossible.

Factors that should be considered when choosing prophylactic antibiotics include the spectrum of activity, and the toxic or allergenic potential. Fluoroquinolones have less toxicity, and a broader spectrum of activity against gram-positive and gram-negative organisms than the aminoglycosides. To help prevent resistance, topical antibiotics, should be applied on a qid dosing schedule, continued for not more than five to seven days, and should not be tapered [43].

Conclusions

Endophthalmitis continues to be a serious complication of cataract surgery. Significant advances have been made, which have decreased the incidence of endophthalmitis and improved subsequent outcomes. Unfortunately, given the rarity of endophthalmitis, researchers will continue to have difficulty producing studies with sufficient power to fully investigate future treatment and prophylactic measures. Acknowledgements: Supported in part by a grant from Research to Prevent Blindness, Inc., New York, New York, to the Department of Ophthalmology, University of Utah, Salt Lake City, Utah, USA.

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