Postoperative endophthalmitis remains a serious clinical problem in ophthalmology, with an incidence of ~0.5%. Prognosis is largely determined by the virulence of the offending organism. The Endophthalmitis Vitrectomy Study (EVS) was a prospective, randomized trial comparing various diagnostic and treatment modalities in cases of endophthalmitis that followed cataract surgery. The EVS found that vitrectomy was only beneficial for patients presenting with very poor visual acuity and that intravenous antibiotic treatments had no additional benefit, compared with intravitreal antibiotic therapy alone. However, weaknesses of the EVS leave these conclusions open to modification in the future. Preoperative application of povidone-iodine preparation to the skin and conjunctiva is the only proven endophthalmitis prophylaxis. Endophthalmitis may be chronic and may follow glaucoma surgery and intravitreal injection of gas and drugs. The EVS did not study these issues, although they are associated with specific features that may require alterations in patient management.

Postoperative endophthalmitis, a potentially devastating complication associated with intraocular surgery, can now be treated effectively, with preservation of useful vision in most patients. However, the major randomized trial on the subject, the Endophthalmitis Vitrectomy Study (EVS) [1], leaves many questions unanswered. Also, there is evidence that a popular cataract surgery technique may be responsible for an increased incidence of this complication.

**CLINICAL PRESENTATION**

The classic signs of endophthalmitis are hypopyon (i.e., layering of WBCs in the anterior chamber of the eye), lid swelling, vitreous opacification, and loss of vision. Pain is a common presenting symptom but may be absent. Symptoms typically appear 24–48 h after surgery. In general, eyes with more-virulent bacteria have a quicker onset of endophthalmitis. Endophthalmitis may have unusual manifestations, such as vitreous hemorrhage [2].

**MICROBIOLOGICAL DATA**

Staphylococcus epidermidis is the most common organism recovered from patients with culture-proven endophthalmitis (~60% of cases). Staphylococcus aureus, streptococci, and enterococci are each found in 5%–10% of cases, and other gram-negative species are found in 6%. Culturing of intraocular fluid (aqueous and vitreous) specimens obtained by direct aspiration is critical to the proper diagnosis and management of endophthalmitis. Frequently, results of culture of the aqueous and vitreous fluids are negative and positive, respectively. Therefore, culturing of specimens obtained from both chambers is essential. Although there may be a correlation between preoperative conjunctival flora and the causative agent in cases of endophthalmitis, in the presence of established endophthalmitis, conjunctival cultures have no diagnostic value. For >30% of patients with presumed bacterial endophthalmitis, results of both aqueous and vitreous cultures are negative. In contrast to postoperative endophthalmitis, traumatic endophthalmitis is more likely to be caused by more-virulent bacteria, especially Bacillus species [3].

**PROPHYLAXIS**

Because endophthalmitis fortunately remains a rare problem, meaningful data on prophylaxis are elusive. There is no question that preexisting conditions, such as conjunctivitis, dacryocystitis, and blepharitis, should be diagnosed and treated.
before any intraocular surgery is performed. In the absence of a specific infectious condition, preoperative antibiotics—although they may reduce conjunctival bacterial flora—have not been shown to reduce the incidence or severity of postoperative bacterial endophthalmitis.

There is general agreement that application of povidone-iodine to skin and conjunctiva is the best surgical preparation technique, because this treatment has been shown to reduce bacterial flora and the incidence of endophthalmitis [4, 5]. Although commonly used, most authorities do not recommend adding antibiotics to the infusion fluid used during surgery.

There is some evidence that clear corneal incision cataract surgery [6] and topical anesthesia [7] may be associated with a higher incidence of endophthalmitis. The clear corneal sutureless incision is usually made temporally. More conventional incisions are made superiorly at the corneoscleral limbus, where there may be some protection of the wound by the upper eyelid. Pressure on the posterior lip of a temporal corneal incision by the patient may cause the wound to leak. It is thought that this late leakage can allow bacteria in the tears to access the anterior chamber of the eye.

In one of the largest studies (12,317 eyes), the incidence of endophthalmitis associated with a temporal corneal incision was 0.29%, compared with an incidence of 0.05% associated with a superior corneoscleral incision [5]. Caution in interpreting these reports is suggested. Several years ago, I managed a disproportionate number of endophthalmitic patients from one group of surgeons who used temporal corneal techniques. After the problem was identified, the surgeons used greater care in preoperative treatment of external eye infections and educated patients in postoperative hygiene measures, such as hand washing. For 5 years, no case of endophthalmitis has occurred in patients treated by this group, even though these surgeons continue to use the same surgical technique. Nevertheless, cataract surgeons need to be aware that temporal corneal incision techniques may be associated with a higher risk of endophthalmitis, and they should balance this risk against presumed benefits of the technique.

**ACUTE-ONSET POSTOPERATIVE ENDOPTHALMITIS (AOPE)**

AOPE occurs most frequently after cataract surgery, the most common intraocular procedure, with an incidence of ~0.05% [8]. AOPE is more common after secondary intraocular lens implantation (0.20% of cases) and less common after vitrectomy (0.03% of cases). The clinical presentation described above usually occurs on the first or second postoperative day. However, presentation ≥ 3 days after surgery may occur, especially in patients with sutureless cataract incisions.

Treatment of AOPE improved greatly with the introduction of intravitreal antibiotics in the 1970s. Animal studies were critical to the establishment of guidelines concerning safe and effective doses of intravitreal antibiotics. Pars plana vitrectomy, also introduced in the 1970s, was quickly added to the treatment regimen. The advantages were obvious: a large sample of fluid was easily obtainable, making culture and Gram staining easier. The vitrectomy procedure essentially drained the vitreous abscess, resulting in removal of infected material and clearance of opacities.

The EVS was a prospective, multicenter, randomized trial studying treatment of AOPE associated with cataract surgery [1]. The efficacy of vitrectomy was compared with that of “vitreous tap” and “biopsy,” and the efficacy of systemic antibiotic administration was compared with that of local therapy only. The major EVS findings were as follows. First, for patients presenting with a visual acuity of light perception or worse, vitrectomy was superior to tap biopsy, with 33% of patients in the vitrectomy group achieving final vision of 20/40 or better, compared with only 11% of those who underwent vitreous tapping. When results were calculated using 20/100 as a benchmark, 56% of those in the vitrectomy group achieved this level, compared with 30% in the vitreous tap group. Second, for patients presenting with visual acuity of hand motions or better, the efficacy of tap biopsy was equal to that of vitrectomy when final visual results were measured. Overall, 55% of patients achieved a final visual acuity of 20/40 or better. However, the vitrectomy group had quicker recovery of vision. Finally, systemic (intravenous) antibiotics were of no value.

On the basis of these results, the patient should be referred for vitrectomy if the visual acuity is light perception or worse. If the visual acuity is hand motions or better, the ophthalmologist has the option of performing a “tap,” which may be an office-based needle aspiration of vitreous fluid, or a “vitreous biopsy,” in which automated vitrectomy equipment is used in the operating room to obtain a vitreous sample. Instruments have been designed to allow office-based vitreous biopsy [9]. However, I prefer to use the hospital operating room for all vitreous biopsies, because the microbiology laboratory is immediately available for plating the specimens, and the hospital pharmacy can accurately prepare the intravitreal antibiotics. In remote areas, however, office management of AOPE may be preferable to a significant delay in treatment of the patient.

The major impact of the EVS was to reduce drastically the use of intravenous antibiotics for treating AOPE. Cost savings due to the elimination of systemic antibiotics have been touted as a major benefit of the EVS. However, these analyses have assumed that intravenous therapy required inpatient hospitalization [10], although outpatient intravenous therapy is of course readily available. A Canadian study found that the major
recommendations of the EVS were widely ignored, with many surgeons using vitrectomy in patients with a visual acuity that was better than light perception [11]. When the EVS isolated the diabetic population, results showed that, at all presenting levels of visual acuity, 57% of patients who underwent vitrectomy achieved 20/40 vision or better, compared with 40% of the patients in the tap biopsy group. These results were not statistically significant, however [12].

Two points regarding the EVS merit further discussion. First, although the EVS was designed to compare vitreous tapping with vitrectomy, many of the patients who were noted to have undergone vitreous tapping in fact underwent a mechanical vitrectomy in the operating room, which is also called a vitreous biopsy. In effect, many of these patients underwent a vitrectomy, but it was a subtotal procedure. Thus, the study did not fully answer the question of the relative effectiveness of a needle tap of the vitreous fluid with antibiotic injection versus that of pars plana vitrectomy and antibiotic injection [13]. In a later publication, the EVS authors reported that severe visual loss (i.e., a visual acuity of less than 5/200) was significantly more common in patients who underwent “tapping” than in patients who underwent “vitreous biopsy” (24% vs. 11%) [14]. Second, another later EVS report showed that retinal detachment was twice as common (11.2% vs. 5.3%) in patients who did not receive systemic antibiotics [15]. Because there was no clinical hypothesis to explain the finding, Doft et al. [15] attributed the difference to chance.

Gatifloxacin, a fourth-generation fluoroquinolone, may achieve significant intraocular levels, even with oral administration [16]. Another newer fluoroquinolone, moxifloxacin, has been shown to achieve bactericidal levels in the vitreous fluid after intravenous administration, especially when the blood-ocular barrier has been broken down by intraocular inflammation [17]. Notwithstanding the EVS recommendations, systemic administration of these new fluoroquinolones could improve treatment of AOPE. Further research is needed to prove or disprove this hypothesis.

Whether vitrectomy or tapping is done, AOPE following cataract surgery is always treated with intravitreal antibiotics. At the time of writing, vancomycin (1 mg) and ceftazidime (2.25 mg) are the preferred therapeutic agents. Vancomycin has effectiveness against many methicillin-resistant gram-positive organisms. Bactericidal concentrations of vancomycin after a 1–2-mg intravitreal dose persist in most cases for 48–72 h [18]. Ceftazidime seems to provide adequate coverage of gram-negative organisms and does not have the unpredictable retinal toxicity of the 2 aminoglycosides, amikacin and gentamicin [19]. There is conflicting research on whether intraocular steroids should be given at the time of initial treatment of AOPE, and the EVS did not address this question. Removal of the intraocular lens is usually not required for treating AOPE.

After initial treatment, the patient is observed closely. Antibiotic treatment can be adjusted on the basis of culture and susceptibility test results. A second dose of intravitreal antibiotics is usually given 2–3 days after the initial treatment, if warranted by the clinical course. We usually do this in the operating room, along with obtaining additional vitreous and aqueous aspirates for repeated microbiologic analysis.

Prognosis in cases of AOPE that follow cataract surgery depends largely on the presenting visual acuity and the organism isolated. Permanent loss of vision in patients with AOPE can occur through a variety of mechanisms, including retinal detachment, hypotony, and corneal opacity. Aggressive management of these complications, such as replacement of the vitreous fluid with silicon oil, may improve the results [20].

**CHRONIC POSTOPERATIVE ENDOPHTHALMITIS (CPE)**

CPE may present with nonspecific inflammatory signs weeks or months following surgery. The patient may have mild cells and flare in the anterior chamber, vitreous inflammation, and/or cystoid macular edema. Frequently, these entities are responsive to corticosteroid treatment. The diagnosis of CPE is suspected when these inflammatory problems are recurrent or unresponsive to corticosteroid treatment. *Propionibacterium acnes* is the most commonly isolated organism in cases of CPE [21], but many other bacteria, mostly with low virulence, have been implicated in the syndrome.

A relatively specific sign of CPE is a cellular white opacity around the intraocular lens, usually coating the posterior lens capsule. Sequestration of bacteria within the lens capsule bag may explain the atypical clinical course of CPE. Although intraocular lens removal is almost never required for management of AOPE, it sometimes is needed to cure CPE.

Although CPE was not directly addressed in the EVS, treatment is similar to that of AOPE. Vitreous tap, vitrectomy, and intravitreal antibiotics are the mainstays of therapy. Recurrences are common after treatment of CPE. Removal of the capsular bag surrounding the lens implant or removal of the lens implant itself may be necessary to effect a complete cure [22].

**FILTERING BLEB–ASSOCIATED ENDOPHTHALMITIS (FBE)**

In surgery for glaucoma (i.e., trabeculectomy), a defect in the eye wall is created. Aqueous fluid then filters into the subconjunctival space, causing an elevated blister, or filtering bleb. Thus, the normal barrier effect of the eye wall (cornea and
sclera) is lost in this area. External bacteria can then pass through the conjunctiva, causing FBE. Sometimes, FBE presents as typical postoperative endophthalmitis. At other times, the intraocular inflammation is localized to the filtering bleb area (referred to as “blebitis”) [23].

The antimetabolites mitomycin C and 5-fluorouracil are frequently used to prevent unwanted closure of the filtering defect. Use of these drugs may increase the risk of FBE, with an incidence of 2% after mitomycin C filtering operations, which may increase to 13% for cases in which the filtering bleb is located on the inferior limbus, away from the protection of the upper lid [24]. Permanent tubes or setons are increasingly used in glaucoma surgery. FBE associated with this procedure usually is severe and may require removal of the seton implant or enucleation of the globe [25].

**INTRAVITREAL INJECTION–ASSOCIATED ENDOPHTHALMITIS (IEE)**

Because the blood-ocular barrier presents a significant impediment to drug penetration into the eye, some agents must be administered by intravitreal injection. Intravitreal triamcinolone (Kenalog; Bristol-Myers Squibb) has been shown to have promising effectiveness for many retinal conditions, such as chronic diabetic macular edema, cystoid macular edema, and age-related macular degeneration [26, 27]. New classes of anti-angiogenesis drugs are being tested in promising clinical trials. Most of these agents require intravitreal injection. Also, intravitreal injections of air and other gases are commonly used in the treatment of retinal detachment. Many of these injections are performed in the physician’s office, sometimes under semisterile conditions.

Because the eye wall is penetrated with a needle during these intravitreal injections, IIE is to be expected and has been reported [28, 29]. Although the incidence of IIE after office-based intravitreal injection is probably low, this procedure will become a major cause of endophthalmitis in the future, simply because of the enormous number of these procedures being done.

Intravitreal crystalline triamcinolone (Kenalog; Bristol-Myers Squibb) may be associated with sterile IIE (i.e., inflammation with negative culture results) or “pseudohypopyon,” in which the crystals precipitate in the inferior part of the anterior chamber, simulating a hypopyon. Close observation with topical corticosteroid treatment may be appropriate for such patients [30].

**SUMMARY**

Postoperative endophthalmitis remains a significant problem, with an incidence of at least 0.03%. The EVS provides a basis for treatment, but therapy must evolve as new research on the subject emerges.

**References**


