

Controversies, Consensuses, and Guidelines on Preventing, Diagnosing and Managing Acute-onset Bacterial Endophthalmitis after Cataract Surgery by the Academy of Asia-Pacific Professors of Ophthalmology (AAPPO), the Asia-Pacific Vitreo-retina Society (APVRS), and the Asia-Pacific Society of Ocular Inflammation and Infection (APSOII)



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### **Authors' contributions**

DSCL and NS conceptualized the study design and developed the methodology. SKR, AB and NS wrote the original draft. Data and materials were provided by all authors, in addition to existing literature. All authors contributed to the analysis and interpretation of the data, the review of the manuscript and consensus statements, voting on the consensus statements, manuscript revision and editing, and read and approved the final manuscript.

**Consent:** All Authors consent to be co-authors of this manuscript.

**Abstract**

Post-cataract surgery endophthalmitis is a serious but largely preventable clinical entity. The implementation of uniform pre-operative, intra-operative, and post-operative protocols is essential to reduce its incidence. In light of emerging evidence and considerable variability in clinical practices, a panel of international experts from the Academy of Asia-Pacific Professors of Ophthalmology (AAPPO), the Asia-Pacific Vitreo-retina Society (APVRS), and the Asia-Pacific Society of Ocular Inflammation and Infection (APSOII) convened to develop evidence-based guidelines addressing all phases of cataract surgery. This consensus manuscript is the product of a systematic review of the current literature, informed by the collective experience and expertise of the panel members. The panel engaged in structured discussions, critical evaluation of clinical data, and formal voting to establish agreement across three key domains: (1) pre-operative and intra-operative prophylactic strategies, (2) diagnostic approaches for early post-operative acute bacterial endophthalmitis, and (3) standardized management protocols. Voting on each proposed statement was conducted using a five-point Likert scale (strongly agree, agree, neutral, disagree, strongly disagree). Consensus was defined as  $\geq 75\%$  of experts voting either “strongly agree” or “agree.” A total of 45 consensus statements were evaluated, of which 21 (46.6%) achieved the predefined level of consensus. This document aims to establish standardized guidelines to improve cataract surgery outcomes by minimizing the risk of post-operative endophthalmitis. For areas where consensus was not achieved, the panel recommends further investigation and continued research to guide future updates to clinical practice.

Keywords: post-cataract surgery endophthalmitis, prophylaxis, diagnosis, management, AAPPO, APVRS, APSOII



## **Introduction**

Endophthalmitis remains an infrequent yet potentially sight-threatening postoperative complication across ocular surgeries. Reported incidence rates range from 0.03% to 0.2% following cataract extraction.<sup>1,2</sup> Notably, some epidemiological studies from Asia have documented higher rates, reaching up to 0.6%.<sup>3</sup> The risk of postoperative endophthalmitis is multifactorial, influenced by intraoperative asepsis protocols, hand hygiene compliance, the ocular adnexal microbiota, surgical technique, sterilization of instruments, the purity of intraocular solutions, wound integrity, and postoperative care.<sup>4</sup> Although topical antibiotic prophylaxis is frequently employed to mitigate this risk, its efficacy remains inconclusive, and adherence to treatment regimens poses additional challenges. Systemic prophylaxis with oral ciprofloxacin, in combination with preoperative povidone-iodine application and intracameral moxifloxacin, has been investigated but failed to demonstrate added protective benefit against endophthalmitis, leading to its disuse in the clinical setting.<sup>5</sup>

One of the primary reasons for developing the current consensus statements is to promote uniformity in cataract surgical practices. The statements aim to develop pre-operative practice guidelines and post-operative diagnostic and management strategies to minimize the incidence of post-operative endophthalmitis. The consensus document will serve as a valuable reference, consolidating best practices from seasoned surgeons worldwide to guide practitioners of all experience levels. Formulation of structured pre- and post-operative guidelines will help cataract surgeons modify their practise patterns to decrease the incidence of post-operative endophthalmitis and improve the overall surgical outcomes.

Considering the variability in the current practices for preventing, diagnosing, and managing acute-onset bacterial endophthalmitis, the Academy of Asia-Pacific Professors of Ophthalmology (AAPPO), the Asia-Pacific Vitreo-retina Society (APVRS) and the Asia-Pacific Society of Ocular Inflammation and Infection (APSOII) felt the need for such consensus statements. Two senior authors (DSCL and NS) of this manuscript were appointed to coordinate this consensus project. This consensus statement brings together evidence-based, real-world practice recommendations from leading global experts to support safe and effective clinical practice in cataract surgery to prevent, diagnose and manage acute-onset bacterial endophthalmitis following cataract surgery.

## **Methods**

Following the appointment of the two coordinators (DSCL and NS), the AAPPO formed an international panel of experts (IPE) consisting of 35 specialists from 13 countries/territories. From this panel, two more core group members (AB and SKR) were invited to join the two coordinators to form a core working to conduct a comprehensive literature review on bacterial endophthalmitis following cataract surgery. Literature search was done on PubMed using the terms bacterial endophthalmitis, cataract surgery, prevention, diagnosis, and management. Articles from the past 25 years were reviewed. The core group was tasked with drafting the initial version of the consensus statements, including detailed explanations and justifications. The statements were systematically categorized into 3 domains: preoperative strategies for the prevention of bacterial endophthalmitis associated with cataract surgery, diagnostic approaches for its early identification, and consensus-based recommendations for its clinical management.

Each panel member independently and anonymously reviewed each statement and provided comments to the core group. The core group then revised the feedback and comments and sent out the 2<sup>nd</sup> draft for further opinions. The process was repeated until the statements were finalized. Subsequently, each panel member voted on each statement anonymously in the final draft using a five-point Likert scale—ranging from strongly agree, agree, neutral, disagree, to strongly disagree.

A consensus was reached when at least 75% of the experts voted either 'agree' or 'strongly agree' for a statement.<sup>6</sup>

## **Controversies and Consensus Statements**

### **Section 1: Preventing Endophthalmitis**

Pre-operative prophylactic measures including application of betadine and pre-operative topical antibiotics help decrease the ocular commensal micro-organisms. Intra-operative and post-operative strategies including the use of intracameral and post-operative topical

antibiotics ensures optimal protective coverage against endophthalmitis. A 3-day pre-operative antibiotic regimen offers superior efficacy compared to shorter durations of 1 day or 1 hour, especially when enhanced by the synergistic action of povidone-iodine.<sup>7</sup> Povidone iodine is universally accepted and the only topical agent known to possess a bactericidal role by disrupting cellular membrane of the micro-organisms. Application of 5% betadine for at least 3 minutes effectively reduces the human conjunctival flora (including multidrug resistant microorganisms like *Enterococcus* sp.) and the risk of endophthalmitis by 3 to 5 fold within 1 minute of application.<sup>8-10</sup> Some studies report that addition of topical antibiotics to pre-operative application of periocular povidone-iodine (PVI) may not offer substantial additional benefits in terms of reducing conjunctival bacterial flora or preventing endophthalmitis in routine cataract surgeries. However, in patients at high risk of infection, combining 4<sup>th</sup> generation fluoroquinolones like levofloxacin with PVI may be considered. Thus, the most effective prophylactic regimen is yet to be established.<sup>11-19</sup>

*Consensus Statement 1.1: Prophylactic measures are considered to reduce the rates of post-cataract surgery acute-onset bacterial endophthalmitis. (Consensus score: 100% [strongly agree: 84.62%; agree: 15.38%; neutral: 0%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 1.2: A short course of topical antibiotics is considered as a part of the pre-operative regimen in all cases undergoing cataract surgery. (Consensus score: 23.07% [strongly agree: 7.69%; agree: 15.38%; neutral: 15.38%; disagree: 46.15%; strongly disagree 15.38%])*

*Consensus Statement 1.3: Pre-operative application of betadine on the periocular skin and ocular surface offers enhanced protection against acute-onset post-cataract surgery endophthalmitis. (Consensus score: 100% [strongly agree: 84.62%; agree: 15.38%; neutral: 0%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 1.4: As part of pre-operative preparation, a single application of 5% betadine on the ocular surface for a minimum of 3 minutes is commonly utilized. (Consensus score: 100% [strongly agree: 46.15%; agree: 53.85%; neutral: 0%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 1.5: Combining pre-operative application of topical antibiotics and betadine decreases the risk of acute-onset post-surgical endophthalmitis. (Consensus score:*

23.07% [*strongly agree: 15.38%; agree: 7.69%; neutral: 46.15%; disagree: 23.08%; strongly disagree 7.69%*])

Intracameral antibiotics are used by some for reducing the rates of post-cataract surgery endophthalmitis. There are various studies that have described use of intracameral drugs like vancomycin, cefuroxime and moxifloxacin.<sup>20–22</sup> A metanalysis by Kato et al, found all 3 to be comparable to each other.<sup>23</sup>

The administration of intracameral antibiotics can be considered in cases with an elevated risk of endophthalmitis including those with posterior capsular rupture (PCR), retained lens fragments, and systemic co-morbidities. However, it may lower the culture positivity of vitreous biopsy in cases developing post-surgical endophthalmitis.<sup>24</sup>

The use of intracameral and subconjunctival antibiotics has been described in paediatric cataract surgeries for prophylaxis of post-surgical endophthalmitis.

Intracameral moxifloxacin can be considered following cataract surgery. In an initial retrospective study in southern India, the use of intracameral moxifloxacin reduced the incidence of endophthalmitis from 0.07% to 0.02%.<sup>20</sup>

The Veterans Health Administration (VHA) meta-analysis of 14 comparative studies revealed that intracameral moxifloxacin was associated with a 73% reduction in the odds of developing endophthalmitis compared to standard care ( $p < 0.001$ ). Intracameral cefuroxime demonstrated comparable effectiveness to moxifloxacin.<sup>25</sup> However, most of these studies were not randomized or prospective. Furthermore, the preparation and use of intracameral antibiotics has been associated with contamination and toxic anterior segment syndrome

The dose of Intracameral moxifloxacin ranges from 100 to 500 µg, while the dose of cefuroxime is typically 1 mg.<sup>26</sup> In the only published prospective study by Melega et al, the prophylactic efficacy of 150 µg of intracameral moxifloxacin was evaluated. It was effective in reducing endophthalmitis from 0.38% to 0.05% ( $p=0.03$ ).<sup>27</sup>

*Consensus Statement 1.6: Intracameral antibiotics (moxifloxacin or cefuroxime or vancomycin) can be considered at the end of cataract surgery. (Consensus score: 84.62% [strongly agree: 61.54%; agree: 23.08%; neutral: 15.38%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 1.7: Intracameral antibiotics can be considered in cases with a higher risk of post-surgical endophthalmitis. (Consensus score: 100% [strongly agree: 76.92%; agree: 23.08%; neutral: 0%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 1.8: Instillation of intracameral antibiotics can be considered in paediatric cataract surgery. (Consensus score: 84.62% [strongly agree: 23.08%; agree: 61.54%; neutral: 15.38%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 1.9: Intracameral moxifloxacin can be considered for possibly reducing the rates of post-cataract surgery endophthalmitis. (Consensus score: 84.61% [strongly agree: 38.46%; agree: 46.15%; neutral: 15.38%; disagree: 0%; strongly disagree 0%])*

One study investigated the rate of post-operative endophthalmitis following immediate sequential bilateral cataract surgery and demonstrated a marked reduction in infection rates with the use of intracameral antibiotics. The incidence decreased to 1 in 14,352 cases (0.006%) when intracameral antibiotics were administered, compared to 1 in 5,759 cases (0.01%) without their use. Additionally, the risk of severe visual loss—defined as a final visual acuity equivalent to 20/200 or worse—due to post-operative endophthalmitis was exceedingly low with only 1 case per 18,000 operated eyes. However, the study was not randomized or prospective.<sup>28</sup> Though, immediate sequential bilateral cataract surgery is a cost effective alternative to delayed sequential bilateral cataract surgery, it may pose additional risk of post-surgical endophthalmitis.<sup>29</sup> Thus, senior surgeons may not recommend immediate sequential bilateral cataract surgery. (unpublished data as per Prof. Ke Yao's experience).

Intracameral cefuroxime, moxifloxacin, and vancomycin each possess a wide safety margin when used as prophylaxis for postoperative endophthalmitis, but they differ in their adverse effect profiles.<sup>30,31</sup> Cefuroxime is generally well-tolerated, with most studies reporting few side effects. Hypersensitivity reactions are rare but can occur, particularly in patients with penicillin allergies, occasionally leading to anaphylaxis. Overdose incidents have been

associated with ocular toxicity such as macular edema, retinal detachment, and corneal edema.<sup>32,33</sup>

Moxifloxacin which is available as a preservative-free formulation, is also considered for intraocular use. It shows no toxic effects on ocular structures even under stress conditions, though rare cases of hypersensitivity and anaphylaxis have been documented with topical use.<sup>22,34</sup> Vancomycin, while effective against gram-positive organisms like *S. epidermidis* and *S. aureus*, lacks a commercially available single use intracameral preparation, necessitating manual dilution. Although generally safe, it has been implicated in rare but severe cases of haemorrhagic occlusive retinal vasculitis (HORV), a presumed immune-mediated reaction causing irreversible vision loss. Given these risks, vancomycin is typically reserved for patients with beta-lactam allergies. Overall, while all 3 antibiotics have favourable safety profiles, cefuroxime and moxifloxacin have been preferred for routine use due to their lower incidence of serious adverse effects.<sup>35–39</sup> Intracameral moxifloxacin has been described in variable dosages (150 µg to 500 µg) and the higher doses have been reported to provide higher protection with no additional adverse effects. In a review by Arshinoff et al., a single case of endophthalmitis caused by moxifloxacin-resistant *Staphylococcus epidermidis* was reported among 3,430 surgeries where 100 µg/0.1 mL intracameral moxifloxacin was used. However, increasing the dosage to 450–600 µg and administering it as the final step of cataract surgery through the side port significantly reduced the risk of infection although there are concerns for reporting bias in this and other studies investigating intracameral antibiotics.<sup>40</sup>

Intracameral moxifloxacin is safe in post-operative settings. Studies have demonstrated favourable outcomes, including preserved specular endothelial cell count, stable central corneal thickness, and central macular thickness.<sup>41,42</sup> Thus, wound hydration with moxifloxacin may or may not pose any additional risk.

Furthermore, moxifloxacin has a short half-life in the aqueous humor, which is just over 1 hour. Yet it maintains a concentration above the minimum inhibitory concentration (MIC), even at a dosage of 150 µg/0.1 mL beyond 1 hour.<sup>43</sup>

*Consensus Statement 1.10:* Intracameral antibiotics can be considered in cases undergoing immediate sequential bilateral cataract surgery. (Consensus score: 100% [strongly agree: 53.85%; agree: 46.15%; neutral: 0%; disagree: 0%; strongly disagree 0%])

*Consensus Statement 1.11:* Adverse reactions of intracameral moxifloxacin, cefuroxime and vancomycin are comparable. (Consensus score: 30.77% [strongly agree: 7.69%; agree: 23.08%; neutral: 15.38%; disagree: 46.15%; strongly disagree 7.69%])

*Consensus Statement 1.12:* The reported safe dose of intracameral moxifloxacin for instillation after cataract surgery is 150 µg/0.1 mL. (Consensus score: 61.53% [strongly agree: 15.38%; agree: 46.15%; neutral: 7.69%; disagree: 23.08%; strongly disagree 7.69%])

*Consensus Statement 1.13:* Hydration of the corneal incisions may not post any additional risk. (Consensus score: 69.23% [strongly agree: 7.69%; agree: 61.54%; neutral: 23.08%; disagree: 7.69%; strongly disagree 0%])

In addition to intracameral and subconjunctival injection of antibiotics, addition of antibiotics like vancomycin and gentamycin in the irrigating solution have been reported to reduce the rate of post-cataract surgery endophthalmitis more than 10 times.<sup>44</sup> However, literature on this topic is limited and the practice has not been widely adopted due to risk of associated adverse effects with the drugs.<sup>39,45,46</sup>

Instruments should be autoclaved or sterilized using ethylene oxide (EtO) and not chemically sterilized. Operation theatre should be fumigated, and disinfection should be done using bacillocid, bacillol, virkon and UV irradiation. The airflow in OT and temperature (21<sup>0</sup> C) and humidity (20-60%) with positive pressure should be maintained.

There are various checklists for elective intraocular surgery which includes comprehensive ophthalmic evaluation prior to surgery, random blood sugar < 200, fasting blood sugar <140 and blood pressure < 160/95 mm Hg. The role of pre-operative topical antibiotics is controversial. Any contact procedure should be avoided. Use of povidone iodine 5% on periocular skin and conjunctival sac for 3 minutes is advisable. However, due to its epitheliotoxic nature, some surgeons believe concentration 1% or lower may be equally effective as 5% povidone iodine (*unpublished data as per Prof. Ke Yao's experience*). Further studies are warranted. Trimming of lashes prior to cataract surgery has not been

demonstrated to confer any benefit in decreasing the ocular microflora. However, adequately draping the eyelashes away from surgical field is essential.<sup>47–50</sup>

*Consensus Statement 1.14: Optimum OT sterilization techniques play an important role in reducing rates of post-surgical endophthalmitis. (Consensus score: 100% [strongly agree: 76.92%; agree: 23.08%; neutral: 0%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 1.15: Pre-operative check list for reducing rates of bacterial endophthalmitis is necessary. (Consensus score: 76.92% [strongly agree: 38.46%; agree: 38.46%; neutral: 7.69%; disagree: 7.69%; strongly disagree 7.69%])*

*Consensus Statement 1.16: Trimming eyelashes is not recommended practice prior to cataract surgery. (Consensus score: 76.92% [strongly agree: 46.15%; agree: 30.77%; neutral: 7.69%; disagree: 0%; strongly disagree 15.38%])*

*Consensus Statement 1.17: Instead of trimming eyelashes, adequate draping eyelashes from surgical field is an acceptable practical practice. (Consensus score: 100% [strongly agree: 61.54%; agree: 38.46%; neutral: 0%; disagree: 0%; strongly disagree 0%])*

Oral antibiotics have not been observed to add additional benefit in terms of decreasing the rate of post-surgical endophthalmitis. Topical antibiotics should be initiated within 4–6 hours after surgery, coinciding with the decline in effectiveness of intracameral or subconjunctival antibiotics. Fluoroquinolones are the preferred agents for postoperative use and are commonly administered for a duration of 1–4 weeks. However, there is no conclusive evidence supporting their role in reducing rates of postsurgical endophthalmitis. To minimize the risk of developing antibiotic resistance, topical antibiotics should be discontinued rather than tapered.<sup>51</sup>

*Consensus Statement 1.18: A short course of pre- and post-operative (peri-operative) oral antibiotics is not proven beneficial for high-risk cases such as one-eye patients (the other eye blind already) to prevent post-surgical endophthalmitis. (Consensus score: 92.31% [strongly agree: 23.08%; agree: 69.23%; neutral: 7.69%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 1.19: The use of topical antibiotics for 1 to 2 weeks after surgery is commonly utilized. (Consensus score: 76.92% [strongly agree: 15.38%; agree: 61.54%; neutral: 15.38%; disagree: 7.69%; strongly disagree 0%])*



The risk factors for post-cataract surgery endophthalmitis includes age >80- years, poor general health, immunocompromised states, periocular septic foci, blepharitis, and a history of penetrating trauma. The intra-operative and post-operative factors include posterior capsular rupture, large incision extracapsular extraction, absence of prophylactic measures, forceps-inserted foldable intraocular lens (IOL), silicone and polymethacrylate (PMMA) IOL material, additional intravitreal injection, late application of topical antibiotics and use of older-generation fluoroquinolones.<sup>52–62</sup>

A cluster Infection Is defined as the occurrence of 2 or more postoperative infections on the same day from a single operating theatre or the repeated occurrence of infections over time. In 2018 Kumar A et al analysed the causes of cluster endophthalmitis. The usual causes were attributed to contaminated irrigating fluids, unclean Phacoemulsification tubing, improper ventilation systems, poor operation room hygiene, and improper storage of bevacizumab.<sup>63–</sup>

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In case of an outbreak, effective management includes prompt confirmation of the diagnosis and thorough investigation to identify the source of the outbreak. This includes obtaining cultures, tracing the batch numbers of all solutions used, and reviewing the surgical logbook, operative notes, and the entire setup of the operating environment.<sup>26</sup>

The commercially available antibiotics preparation is more cost effective than those prepared through compounding pharmacies.<sup>24</sup> Thus, countries with limited resources may prefer them over fortified drops. The other possible causes of non-usage of reconstituted antibiotics include errors in dilution, break in the sterility chain, or other logistic reasons.<sup>66</sup>

*Consensus Statement 1.20:* The rates of endophthalmitis are higher in extracapsular cataract extraction than phacoemulsification. (Consensus score: 53.84% [strongly agree: 7.69%; agree: 46.15%; neutral: 30.77%; disagree: 15.38%; strongly disagree 0%])

*Consensus Statement 1.21:* Diabetic patients with well controlled blood sugars are not at higher risk of post-surgical endophthalmitis. (Consensus score: 53.84% [strongly agree: 23.08%; agree: 30.77%; neutral: 0%; disagree: 46.15%; strongly disagree 0%])

*Consensus Statement 1.22: Cluster endophthalmitis is a preventable entity. (Consensus score: 92.31% [strongly agree: 23.08%; agree: 69.23%; neutral: 0%; disagree: 7.69%; strongly disagree 0%])*

*Consensus Statement 1.23: The major limiting factor for usage of intracameral antibiotics is the cost factor in developing countries. (Consensus score: 38.46% [strongly agree: 0%; agree: 38.46%; neutral: 46.15%; disagree: 15.38%; strongly disagree 0%])*

## Section 2: Diagnosing Endophthalmitis

The most common presenting symptom of endophthalmitis is progressive vision loss, followed by pain—which may be absent in up to 25% of cases—and conjunctival injection. In the landmark multi-centric Endophthalmitis Vitrectomy Study (EVS) study, one-fourth of eyes had vision limited to light perception (PL); however, the actual incidence of such poor vision may be higher, as eyes with no PL and significant anterior chamber opacification were excluded from the study. In addition to decreased visual acuity, common clinical signs include lid edema, conjunctival chemosis, corneal edema, anterior chamber cells and fibrin, hypopyon (present in 85% of cases), vitritis, retinitis, retinal periphlebitis (an early indicator), and blunting of the red reflex.<sup>67</sup>

The ESCRS study group define the terms ‘presumed’ and ‘proven’ endophthalmitis. Presumed endophthalmitis was diagnosed in any patient who presented with ocular pain or decreased vision following surgery, where the clinical findings were suggestive of intraocular infection. Proven endophthalmitis was considered if there was microbiological evidence (vitreal staining or culture or polymerase chain reaction positive for micro-organism) in addition to clinical symptoms and signs of endophthalmitis.<sup>21,67,68</sup>

Culture positivity in cases of endophthalmitis is variable ranging from 34% to 58%. The most commonly isolated micro-organism are gram positive bacteria, particularly coagulase negative Staphylococcus (CoNS). Outcomes in cases caused gram positive bacteria are superior compared to those caused by other micro-organisms.<sup>69,70</sup>

Postoperative follow-up on day 1 and week 1 are essential for all post-cataract surgery patients. Early scheduled follow-up may help in timely diagnosis of early-onset endophthalmitis.<sup>56</sup>

*Consensus Statement 2.1: The most common symptom of acute-onset endophthalmitis is loss of visual acuity. (Consensus score: 92.31% [strongly agree: 30.77%; agree: 61.54%; neutral: 7.69%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 2.2: Both presumed and proven endophthalmitis should be managed similarly. (Consensus score: 100% [strongly agree: 53.85%; agree: 46.15%; neutral: 0%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 2.3: Culture positivity of vitreous biopsy is an important prognostic factor in post-surgical endophthalmitis. (Consensus score: 100 [strongly agree: 41.67%; agree: 58.33%; neutral: 0%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 2.4: The 1-week post-operative visit is important for diagnosing acute-onset bacterial endophthalmitis. (Consensus score: 69.23% [strongly agree: 30.77%; agree: 38.46%; neutral: 15.38%; disagree: 15.38%; strongly disagree 0%])*

Both clinical presentation and microbiological evidence are prognostic of outcomes in post-cataract surgery endophthalmitis. A meta-analysis by Cioana et al determined that the greatest improvement in visual acuity occurred in cases caused by coagulase-negative staphylococci, followed by gram-negative bacteria, and then other gram-positive organisms such as streptococci and enterococci. The outcomes aligned with the results of the Endophthalmitis Vitrectomy Study despite advancements in surgical techniques and microbial changes over time.<sup>71,72</sup> A study by Rahimi et al, suggested that the “gram-positive coagulase-negative” and no growth” groups had the best visual outcome. In addition, cases of endophthalmitis associated with keratitis and those avoiding intraocular steroids were associated with risk of evisceration.<sup>10</sup> Furthermore, antibiotic resistance is a predictor of poor visual outcomes.<sup>73</sup>

The described clinical presentation of acute-onset bacterial endophthalmitis has been comparable between landmark endophthalmitis studies. The most common presenting symptom in these was blurred visual acuity with pain, media haze, and hypopyon.<sup>21,72</sup>

When evaluating suspected endophthalmitis, it is essential to consider differential diagnoses such as toxic anterior segment syndrome (TASS), residual lens material, noninfectious uveitis, and vitreous haemorrhage. TASS can closely mimic infectious endophthalmitis, presenting with severe corneal edema and hypopyon, but lacks vitreous involvement. Differentiation is crucial, as TASS typically shows anterior chamber inflammation without posterior segment signs. Confirming the diagnosis involves isolating the causative organism through gram stain, culture, and PCR testing, particularly in resistant cases. Empiric broad-spectrum intravitreal antibiotics should be initiated promptly. In culture-negative cases (~30%), B-scan ultrasonography helps assess vitreous opacities and retinal or choroidal detachment.<sup>74-76</sup>

*Consensus Statement 2.5: The clinical features and microbiology report of acute-onset endophthalmitis are important in management. (Consensus score: 100% [strongly agree: 53.85%; agree: 46.15%; neutral: 0%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 2.6: Post-operative endophthalmitis with keratitis is associated with worse clinical outcomes. (Consensus score: 100% [strongly agree: 38.46%; agree: 61.54%; neutral: 0%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 2.7: Toxic anterior shock syndrome (TASS) is clinically distinct from acute-onset endophthalmitis in most cases. (Consensus score: 76.92% [strongly agree: 30.77%; agree: 46.15%; neutral: 15.38%; disagree: 7.69%; strongly disagree 0%])*

In acute-onset endophthalmitis after cataract surgery the microbiological analysis of aqueous and vitreous samples reveal a good positivity rate (up to 61%) with a higher prevalence of gram-positive isolates.<sup>10</sup>

In 2019 Duan F. et al aimed to identify the microbial etiology of acute-onset endophthalmitis in isolates at an eye hospital in South China. In postsurgical endophthalmitis, all infections were bacterial.<sup>77</sup>

Mollan et al. reported an acute-onset endophthalmitis incidence of 0.09% in the United Kingdom with gram-positive bacteria being the predominant causative organisms, identified in 93.4% of culture-positive cases. They recommended performing both anterior chamber tap

and vitreous biopsy or PPV in suspected cases to aid in microbiological diagnosis and guide appropriate treatment.<sup>69</sup>

Pars plana vitrectomy with instillation of antibiotics is an option for management of acute-onset endophthalmitis. It helps in debulking the infection, clearing the visual axis to allow for visual rehabilitation and a serial funduscopy examination, collecting adequate vitreous specimens for culture to guide management, and allowing better distribution of intravitreal antibiotics.

Advancements in diagnostic technologies, such as real-time PCR (RT-PCR) and mass spectrometry, offer significant potential for enhancing the detection and identification of microorganisms in endophthalmitis, enabling more accurate and timely diagnosis.<sup>10</sup>

In 2018, Mishra D et al studied the utility of broad range 16 S rRNA PCR assay versus conventional methods and re-emphasised that the positivity from routine culture was much lower (conventional culture positivity = 8.7 %) as compared to automated culture (30.76 %) and PCR (65.13 %).<sup>78</sup> In 2022, Low et al demonstrated the utility of whole genome sequencing to detect pathogens and even bacteriophages in both culture-positive and culture-negative cases of endophthalmitis.<sup>79</sup>

There have been studies reporting the emergence of multidrug-resistant micro-organisms. Jindal A et al in 2013 and 2015 evaluated medical records of all patients with Gram-negative bacterial endophthalmitis resistant to both amikacin and ceftazidime between 2005 and 2010 at L. V. Prasad Eye Institute, a tertiary care ophthalmic Centre in South India.<sup>80,81</sup> *Pseudomonas* was the most common Gram-negative bacteria resistant to both amikacin and ceftazidime. The emergence of MDR bacteria causing endophthalmitis was addressed as a matter of concern in India. Globally, Schwartz S G et al in 2014 mentioned emergence of multidrug resistant organisms causing endophthalmitis.<sup>82</sup>

Post-cataract surgery endophthalmitis may be caused by break in OT sterility and cold chain of consumables. It may or may not be associated with post-operative endophthalmitis. In a study by Satpathy G et al, *P. aeruginosa* isolates obtained from the patients of post-cataract surgery endophthalmitis were phenotypically similar and genetically close to those obtained

from the corresponding phacoemulsification machine.<sup>83</sup> Thus the association needs to be evaluated in future studies.

*Consensus Statement 2.8: Aqueous tap and PPV have equivalent value in establishing the diagnosis of endophthalmitis. (Consensus score: 30.77% [strongly agree: 0%; agree: 30.77%; neutral: 23.08%; disagree: 30.77%; strongly disagree 15.38%])*

*Consensus Statement 2.9: Performing pars plana vitrectomy and instillation of intravitreal antibiotics is the first line treatment option in cases of endophthalmitis. (Consensus score: 53.84%[strongly agree: 15.38%; agree: 38.46%; neutral: 7.69%; disagree: 38.46%; strongly disagree 0%])*

*Consensus Statement 2.10: Polymerase chain reaction (PCR) testing of vitreous may be useful if available. (Consensus score: 100% [strongly agree: 50%; agree: 50%; neutral: 0%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 2.11: There has been emergence of MDR (multi-drug resistant) micro-organism over time as causative agents for endophthalmitis.(Consensus score: 83.33% [strongly agree: 25%; agree: 58.33%; neutral: 8.33%; disagree: 0%; strongly disagree 0%])*

*Consensus Statement 2.12: The factors contributing to cluster endophthalmitis may differ from those associated with isolated cases. (Consensus score: 100%[strongly agree: 16.67%; agree: 83.33%; neutral: 0%; disagree: 0%; strongly disagree 0%])*

### Section 3: Management of Endophthalmitis

Antibiotics given oral or intravenous have poor penetration into the vitreous cavity. Therefore, intravitreal antibiotics are mainstay of treatment.<sup>84</sup>

The role of systemic antibiotics in treating postoperative endophthalmitis remains controversial. Systemic administration of amikacin and ceftazidime has shown no significant impact on final visual outcomes, likely due to their poor penetration across the blood-ocular barrier. In contrast, fluoroquinolones such as ciprofloxacin and moxifloxacin may have better intraocular penetration. Though intravenous drugs may achieve higher concentration in the blood stream, oral administration of these drugs has been preferred due to lower risk of systemic adverse effects.<sup>85</sup>

When managing severe bacterial postoperative endophthalmitis, intravitreal injection of unpreserved dexamethasone with broad-spectrum antibiotics can be considered. The first-line treatment typically involves an intravitreal vancomycin-ceftazidime combination. Other combinations include ceftazidime-tazobactam, ceftazidime-imipenem, and vancomycin-amikacin.<sup>86,87</sup>

The antibiotic combination covers both gram-positive and gram-negative bacteria. The parameters guiding the frequency of repeat administration of antibiotics are clinical response, half-life, drug clearance from the eye, and surgical status of the eye. The aim of repeat dosing should be to optimize the duration of drug exposure to concentrations above the minimum inhibitory concentration (MIC), rather than to aim for higher peak levels. Adequate and safe antibiotic levels can be better achieved by more frequent rather than higher dosages.<sup>88</sup>

Since intravitreal antibiotic levels drop rapidly within 24 to 48 hours following injection, a single injection may not be sufficient, particularly of vancomycin or ceftazidime based on culture results and clinical response. Drugs like amikacin are typically avoided if possible due to potential retinal toxicity. Repeat antibiotic selection is guided by culture results.

In cases of multidrug resistant microorganisms causing endophthalmitis, alternate antibiotic regimens like intravitreal piperacillin/tazobactam and imipenem have been reported to be safe and comparable to each other.<sup>86,89–94</sup>

The pharmacokinetics of various drugs have been studied and usually a drug combination which tends to stay in the vitreous cavity and covers both gram-positive and negative microorganisms is chosen for injection. The large molecules like vancomycin are known to leave the eye predominantly by the passive diffusion across the vitreous to the anterior chamber and through Schlemm's canal. Smaller drug molecules like beta-lactams, clindamycin and fluoroquinolones are cleared posteriorly by active transport in the capillaries and the retinal pigment epithelium (RPE).<sup>95</sup>

The drugs eliminated through the anterior route have a faster clearance in an inflamed eye.<sup>96</sup> For drugs mainly eliminated by the posterior route (beta-lactams, cephalosporins, and clindamycin), drug clearance is retarded in an inflamed eye due to compromise of the RPE pump or active transport. Thus, their half-life is extended.<sup>88</sup>

The microbiological profile of post-cataract surgery endophthalmitis has remained stable over the past few decades. In fact, it has not changed much from the Endophthalmitis Vitrectomy Study. The predominant etiological agents are gram-positive bacteria followed by gram-negative bacteria and fungi. Overall the most common causative species is coagulase negative *Staphylococcus*. Similar outcomes have been observed throughout different geographical zones.<sup>56,77,97-99</sup> However, there are few isolated reports identifying newer causative agents for post-surgical endophthalmitis.<sup>50,52</sup>

*Consensus Statement 3.1:* Intravenous antibiotics do not have an important role in management of acute-onset bacterial endophthalmitis. (*Consensus score: 76.92% [strongly agree: 38.46%; agree: 38.46%; neutral: 23.08%; disagree: 0%; strongly disagree 0%]*)

*Consensus Statement 3.2:* There is no definite role of oral antibiotics in cases of acute-onset bacterial endophthalmitis. (*Consensus score: 100% [strongly agree: 15.38%; agree: 84.62%; neutral: 0%; disagree: 0%; strongly disagree 0%]*)

*Consensus Statement 3.3:* The ideal intravitreal antibiotic regimen for management of acute bacterial endophthalmitis is a combination of drugs covering both gram-positive and gram-negative bacteria. (*Consensus score: 100% [strongly agree: 83.33%; agree: 16.67%; neutral: 0%; disagree: 0%; strongly disagree 0%]*)

*Consensus Statement 3.4:* A repeat intravitreal antibiotic injection is not recommended in cases that show a favourable response to the initial injection. (*Consensus score: 75% [strongly agree: 16.67%; agree: 58.33%; neutral: 8.33%; disagree: 16.67%; strongly disagree 0%]*)

*Consensus Statement 3.5:* The choice of antibiotics for intravitreal injection is based on the pharmacokinetics of the drugs. Injections usually do need to be repeated. (*Consensus score: 66.67% [strongly agree: 16.67%; agree: 50%; neutral: 25%; disagree: 8.33%; strongly disagree 0%]*)

*Consensus Statement 3.6:* The microbiological profile of the most common etiological agents causing acute bacterial endophthalmitis has not changed over 2 decades. (*Consensus score:*



61.54% [strongly agree: 0%; agree: 61.54%; neutral: 30.77%; disagree: 7.69%; strongly disagree 0%])

The predictors for poor visual outcomes include old age, poor presenting visual acuity at presentation, gram-negative bacteria on culture and acute-onset endophthalmitis.<sup>100</sup> In a study by Ting et al, 66.7% cases of post-surgical endophthalmitis attained best corrected visual acuity better than 6/36.<sup>10</sup>

The Endophthalmitis Vitrectomy Study laid the basic principles for the management of endophthalmitis. It addressed major points like the role of initial visual acuity on the timing of PPV and the lack of benefit of systemic antibiotics. However, with advancements in surgical machines and techniques, early primary vitrectomy is often indicated in acute-onset endophthalmitis today. It decreases the infectious load at an earlier stage. Additionally, has been demonstrated to decrease the need for repeated interventions and shorten the treatment period and recovery time for endophthalmitis.

The EVS did not discuss the use of steroids in these cases. Since most case of acute-onset endophthalmitis are due to bacterial infection, steroids may help in managing the intraocular inflammation.<sup>100</sup> In a recent retrospective long-term study, it was observed that current practise patterns are different from those employed by the EVS study.<sup>101</sup>

The prognosis of acute-onset endophthalmitis depends on the etiology and intervention method. Poor prognostic factors include delayed presentation beyond 6 days, virulent pathogens (*Pseudomonas* sp.), pre-existing retinal detachment, and corneal disease.<sup>102</sup> The management involves vitreous tap with injection of intravitreal antibiotics. Pars plana vitrectomy with intravitreal antibiotics is often preferred in eyes with poor vision or non-response to intravitreal antibiotics.

One-quarter to one-half of the routine dose of intravitreal antibiotics is preferred in cases of endophthalmitis with silicone oil in-situ to prevent retinal toxicity as the drug is confined to the limited aqueous-filled space surrounding the oil bubble and has a longer elimination time.<sup>103</sup>

*Consensus Statement 3.7:* In cases of post-cataract surgery endophthalmitis, <10% eyes have poor visual outcomes. (Consensus score: 33.33% [strongly agree: 0%; agree: 33.33%; neutral: 16.67%; disagree: 41.67%; strongly disagree 8.33%])

*Consensus Statement 3.8:* The management principles of the Endophthalmitis Vitrectomy Study are still valid. (Consensus score: 41.67% [strongly agree: 0%; agree: 41.67%; neutral: 33.33%; disagree: 25%; strongly disagree 0%])

*Consensus Statement 3.9:* The final outcomes of post-surgical endophthalmitis are dependent on multiple factors. (Consensus score: 100% [strongly agree: 61.54%; agree: 38.46%; neutral: 0%; disagree: 0%; strongly disagree 0%])

*Consensus Statement 3.10:* Eyes with post-cataract surgery endophthalmitis in the presence of silicone oil tamponade require a lower dose of intravitreal antibiotics. (Consensus score: 100% [strongly agree: 50%; agree: 50%; neutral: 0%; disagree: 0%; strongly disagree 0%])

## Result of Voting and Discussion

Table 1 provides a summary of the key consensus statements along with the corresponding voting results.

Section	Consensus Statement	C Score	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
<b>1. Preventing Endophthalmitis</b>							
1.1	Prophylactic measures are considered to reduce the rates of post-cataract surgery acute-onset bacterial endophthalmitis.	<b>100%</b>	84.62%	15.38%	0%	0%	0%
1.2	A short course of topical antibiotics is considered as a part of the pre-operative regimen in all cases undergoing cataract surgery.	<u>23.07%</u>	7.69%	15.38%	15.38%	46.15%	15.38%
1.3	Pre-operative application of betadine on the periocular skin and ocular surface offers enhanced protection against acute-onset post-cataract surgery endophthalmitis.	<b>100%</b>	84.62%	15.38%	0%	0%	0%
1.4	As part of pre-operative preparation, a single application of 5% betadine on the ocular surface for a minimum of 3 minutes is commonly utilized.	<b>100%</b>	46.15%	53.85%	0%	0%	0%
1.5	Combining pre-operative application of topical antibiotics and betadine decreases the risk of acute-onset post-surgical endophthalmitis.	<u>23.07%</u>	15.38%	7.69%	46.15%	23.08%	7.69%
1.6	Intracameral antibiotics (moxifloxacin or cefuroxime or vancomycin) can be considered at the end of cataract surgery.	<b>84.62%</b>	61.54%	23.08%	15.38%	0%	0%

1.7	Intracameral antibiotics can be considered in cases with a higher risk of post-surgical endophthalmitis.	<b>100%</b>	76.92%	23.08%	0%	0%	0%
1.8	Instillation of intracameral antibiotics can be considered in paediatric cataract surgery.	<b>84.62%</b>	23.08%	61.54%	15.38%	0%	0%
1.9	Intracameral moxifloxacin can be considered for possibly reducing the rates of post-cataract surgery endophthalmitis.	<b>84.61%</b>	38.46%	46.15%	15.38%	0%	0%
1.10	Intracameral antibiotics can be considered in cases undergoing immediate sequential bilateral cataract surgery.	<b>100%</b>	53.85%	46.15%	0%	0%	0%
1.11	Adverse reactions of intracameral moxifloxacin, cefuroxime and vancomycin are comparable.	<u>30.77%</u>	7.69%	23.08%	15.38%	46.15%	7.69%
1.12	The reported safe dose of intracameral moxifloxacin for instillation after cataract surgery is 150 µg/0.1 mL.	<u>61.53%</u>	15.38%	46.15%	7.69%	23.08%	7.69%
1.13	Hydration of the corneal incisions may not post any additional risk.	<u>69.23%</u>	7.69%	61.54%	23.08%	7.69%	0%
1.14	Optimum OT sterilization techniques play an important role in reducing rates of post-surgical endophthalmitis.	<b>100%</b>	76.92%	23.08%	0%	0%	0%
1.15	Pre-operative check list for reducing rates of bacterial endophthalmitis is necessary.	<b>76.92%</b>	38.46%	38.46%	7.69%	7.69%	7.69%
1.16	Trimming eyelashes is not recommended practice prior to cataract surgery.	<b>76.92%</b>	46.15%	30.77%	7.69%	0%	15.38%
1.17	Instead of trimming eyelashes, adequate draping eyelashes from surgical field is an acceptable practical practice.	<b>100%</b>	61.54%	38.46%	0%	0%	0%
1.18	A short course of pre- and post-operative (peri-operative) oral antibiotics is not proven beneficial for high-risk cases such as one-eye patients (the other eye blind already) to prevent post-surgical endophthalmitis.	<b>92.31%</b>	23.08%	69.23%	7.69%	0%	0%
1.19	The use of topical antibiotics for 1 to 2 weeks after surgery is commonly utilized.	<b>76.92%</b>	15.38%	61.54%	15.38%	7.69%	0%
1.20	The rates of endophthalmitis are higher in extracapsular cataract extraction than phacoemulsification.	<u>53.84%</u>	7.69%	46.15%	30.77%	15.38%	0%
1.21	Diabetic patients with well controlled blood sugars are not at higher risk of post-surgical endophthalmitis.	<u>53.84%</u>	23.08%	30.77%	0%	46.15%	0%
1.22	Cluster endophthalmitis is a preventable entity.	<b>92.31%</b>	23.08%	69.23%	0%	7.69%	0%
1.23	The major limiting factor for usage of intracameral antibiotics is the cost factor in developing countries.	<u>38.46%</u>	0%	38.46%	46.15%	15.38%	0%
<b>2. Diagnosing Endophthalmitis</b>							
2.1	The most common symptom of acute-onset endophthalmitis is loss of visual acuity.	<b>92.31%</b>	30.77%	61.54%	7.69%	0%	0%
2.2	Both presumed and proven endophthalmitis should be managed similarly.	<b>100%</b>	53.85%	46.15%	0%	0%	0%
2.3	Culture positivity of vitreous biopsy is an important prognostic factor in post-surgical endophthalmitis.	<b>100%</b>	41.67%	58.33%	0%	0%	0%

2.4	The 1-week post-operative visit is important for diagnosing acute-onset bacterial endophthalmitis.	<u>69.23%</u>	30.77%	38.46%	15.38%	15.38%	0%
2.5	The clinical features and microbiology report of acute-onset endophthalmitis are important in management.	<b>100%</b>	53.85%	46.15%	0%	0%	0%
2.6	Post-operative endophthalmitis with keratitis is associated with worse clinical outcomes.	<b>100%</b>	38.46%	61.54%	0%	0%	0%
2.7	Toxic anterior shock syndrome (TASS) is clinically distinct from acute-onset endophthalmitis in most cases.	<b>76.92%</b>	30.77%	46.15%	15.38%	7.69%	0%
2.8	Aqueous tap and PPV have equivalent value in establishing the diagnosis of endophthalmitis.	<u>30.77%</u>	0%	30.77%	23.08%	30.77%	15.38%
2.9	Performing pars plana vitrectomy and instillation of intravitreal antibiotics is the first line treatment option in cases of endophthalmitis.	<u>53.84%</u>	15.38%	38.46%	7.69%	38.46%	0%
2.10	Polymerase chain reaction (PCR) testing of vitreous may be useful if available.	<b>100%</b>	50%	50%	0%	0%	0%
2.11	There has been emergence of MDR (multi-drug resistant) micro-organism over time as causative agents for endophthalmitis.	<b>83.33%</b>	25%	58.33%	8.33%	0%	0%
2.12	The factors contributing to cluster endophthalmitis may differ from those associated with isolated cases.	<b>100%</b>	16.67%	83.33%	0%	0%	0%
<b>3. Management of Endophthalmitis</b>							
3.1	Intravenous antibiotics do not have an important role in management of acute-onset bacterial endophthalmitis.	<b>76.92%</b>	38.46%	38.46%	23.08%	0%	0%
3.2	There is no definite role of oral antibiotics in cases of acute-onset bacterial endophthalmitis.	<b>100%</b>	15.38%	84.62%	0%	0%	0%
3.3	The ideal intravitreal antibiotic regimen for management of acute bacterial endophthalmitis is a combination of drugs covering both gram-positive and gram-negative bacteria.	<b>100%</b>	83.33%	16.67%	0%	0%	0%
3.4	A repeat intravitreal antibiotic injection is not recommended in cases that show a favourable response to the initial injection.	<b>75%</b>	16.67%	58.33%	8.33%	16.67%	0%
3.5	The choice of antibiotics for intravitreal injection is based on the pharmacokinetics of the drugs. Injections usually do need to be repeated.	<u>66.67%</u>	16.67%	50%	25%	8.33%	0%
3.6	The microbiological profile of the most common etiological agents causing acute bacterial endophthalmitis has not changed over 2 decades.	<u>61.54%</u>	0%	61.54%	30.77%	7.69%	0%
3.7	In cases of post-cataract surgery endophthalmitis, <10% eyes have poor visual outcomes.	<u>33.33%</u>	0%	33.33%	16.67%	41.67%	8.33%
3.8	The management principles of the Endophthalmitis Vitrectomy Study are still valid.	<u>41.67%</u>	0%	41.67%	33.33%	25%	0%
3.9	The final outcomes of post-surgical endophthalmitis are dependent on multiple factors.	<b>100%</b>	61.54%	38.46%	0%	0%	0%

3.10	Eyes with post-cataract surgery endophthalmitis in the presence of silicone oil tamponade require a lower dose of intravitreal antibiotics.	<b>100%</b>	50%	50%	0%	0%	0%
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*Consensus Score (C Score) was defined as the value of the summation of the 'strongly agree', and 'agree' percentages; C Score  $\geq 75\%$  was considered 'consensus achieved' and C Score  $< 75\%$  was 'consensus not reached'. Fifteen statements were 'consensus not achieved' (with unbold and underline).*

Post-cataract surgery endophthalmitis is a rare but potentially devastating complication that can lead to significant vision loss. This consensus manuscript represents a comprehensive synthesis of current scientific literature, enriched by the collective expertise of leading international specialists in the field. The primary objective was to establish evidence-based recommendations for the prevention, early diagnosis, and effective management of post-operative endophthalmitis to optimize patient outcomes.

The consensus development process was methodologically rigorous, incorporating an extensive review of existing literature alongside structured expert deliberation. A panel of 35 experts from the Academy of Asia-Pacific Professors of Ophthalmology (AAPPO), the Asia-Pacific Vitreo-retina Society (APVRS), and the Asia-Pacific Society of Ocular Inflammation and Infection (APSOII) participated in the voting process, providing their agreement on a series of consensus statements.

The outcomes of this collaborative effort is the formulation of standardized, practical guidelines aimed at assisting cataract surgeons in minimizing the incidence and improving the management of post-surgical endophthalmitis across diverse clinical settings. The consensus statements have been divided into those with high ( $>75\%$ ), borderline (50-74%) and poor ( $<50\%$ ) acceptance.

### Highly Accepted Statements

Table 2 summarizes the statements which are highly accepted by the international panel of experts ( $>75\%$ ).

Section	Consensus Statement	C Score	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
<b>1. Preventing Endophthalmitis</b>							

1.1	Prophylactic measures are considered to reduce the rates of post-cataract surgery acute-onset bacterial endophthalmitis.	<b>100%</b>	84.62%	15.38%	0%	0%	0%
1.3	Pre-operative application of betadine on the periocular skin and ocular surface offers enhanced protection against acute-onset post-cataract surgery endophthalmitis.	<b>100%</b>	84.62%	15.38%	0%	0%	0%
1.4	As part of pre-operative preparation, a single application of 5% betadine on the ocular surface for a minimum of 3 minutes is commonly utilized.	<b>100%</b>	46.15%	53.85%	0%	0%	0%
1.6	Intracameral antibiotics (moxifloxacin or cefuroxime or vancomycin) can be considered at the end of cataract surgery.	<b>84.62%</b>	61.54%	23.08%	15.38%	0%	0%
1.7	Intracameral antibiotics can be considered in cases with a higher risk of post-surgical endophthalmitis.	<b>100%</b>	76.92%	23.08%	0%	0%	0%
1.8	Instillation of intracameral antibiotics can be considered in pediatric cataract surgery.	<b>84.62%</b>	23.08%	61.54%	15.38%	0%	0%
1.9	Intracameral moxifloxacin can be considered for possibly reducing the rates of post-cataract surgery endophthalmitis.	<b>84.61%</b>	38.46%	46.15%	15.38%	0%	0%
1.10	Intracameral antibiotics can be considered in cases undergoing immediate sequential bilateral cataract surgery.	<b>100%</b>	53.85%	46.15%	0%	0%	0%
1.14	Optimum OT sterilization techniques play an important role in reducing rates of post-surgical endophthalmitis.	<b>100%</b>	76.92%	23.08%	0%	0%	0%
1.15	Pre-operative check list for reducing rates of bacterial endophthalmitis is necessary.	<b>76.92%</b>	38.46%	38.46%	7.69%	7.69%	7.69%
1.16	Trimming eyelashes is not recommended practice prior to cataract surgery.	<b>76.92%</b>	46.15%	30.77%	7.69%	0%	15.38%
1.17	Instead of trimming eyelashes, adequate draping eyelashes from surgical field is an acceptable practical practice.	<b>100%</b>	61.54%	38.46%	0%	0%	0%
1.18	A short course of pre- and post-operative (peri-operative) oral antibiotics is not proven beneficial for high-risk cases such as one-eye patients (the other eye blind already) to prevent post-surgical endophthalmitis.	<b>92.31%</b>	23.08%	69.23%	7.69%	0%	0%
1.19	The use of topical antibiotics for 1 to 2 weeks after surgery is commonly utilized.	<b>76.92%</b>	15.38%	61.54%	15.38%	7.69%	0%
1.22	Cluster endophthalmitis is a preventable entity.	<b>92.31%</b>	23.08%	69.23%	0%	7.69%	0%
<b>2. Diagnosing Endophthalmitis</b>							
2.1	The most common symptom of acute-onset endophthalmitis is loss of visual acuity.	<b>92.31%</b>	30.77%	61.54%	7.69%	0%	0%
2.2	Both presumed and proven endophthalmitis should be managed similarly.	<b>100%</b>	53.85%	46.15%	0%	0%	0%
2.3	Culture positivity of vitreous biopsy is an important prognostic factor in post-surgical endophthalmitis.	<b>100%</b>	41.67%	58.33%	0%	0%	0%

2.5	The clinical features and microbiology report of acute-onset endophthalmitis are important in management.	<b>100%</b>	53.85%	46.15%	0%	0%	0%
2.6	Post-operative endophthalmitis with keratitis is associated with worse clinical outcomes.	<b>100%</b>	38.46%	61.54%	0%	0%	0%
2.7	Toxic anterior shock syndrome (TASS) is clinically distinct from acute-onset endophthalmitis in most cases.	<b>76.92%</b>	30.77%	46.15%	15.38%	7.69%	0%
2.10	Polymerase chain reaction (PCR) testing of vitreous may be useful if available.	<b>100%</b>	50%	50%	0%	0%	0%
2.11	There has been emergence of MDR (multi-drug resistant) micro-organism over time as causative agents for endophthalmitis.	<b>83.33%</b>	25%	58.33%	8.33%	0%	0%
2.12	The factors contributing to cluster endophthalmitis may differ from those associated with isolated cases.	<b>100%</b>	16.67%	83.33%	0%	0%	0%
<b>3. Management of Endophthalmitis</b>							
3.1	Intravenous antibiotics do not have an important role in management of acute-onset bacterial endophthalmitis.	<b>76.92%</b>	38.46%	38.46%	23.08%	0%	0%
3.2	There is no definite role of oral antibiotics in cases of acute-onset bacterial endophthalmitis.	<b>100%</b>	15.38%	84.62%	0%	0%	0%
3.3	The ideal intravitreal antibiotic regimen for management of acute bacterial endophthalmitis is a combination of drugs covering both gram-positive and gram-negative bacteria.	<b>100%</b>	83.33%	16.67%	0%	0%	0%
3.4	A repeat intravitreal antibiotic injection is not recommended in cases that show a favorable response to the initial injection.	<b>75%</b>	16.67%	58.33%	8.33%	16.67%	0%
3.9	The final outcomes of post-surgical endophthalmitis are dependent on multiple factors.	<b>100%</b>	61.54%	38.46%	0%	0%	0%
3.10	Eyes with post-cataract surgery endophthalmitis in the presence of silicone oil tamponade require a lower dose of intravitreal antibiotics.	<b>100%</b>	50%	50%	0%	0%	0%

Statements which had gained clear majority (>75%) were considered highly accepted consensus statements. The majority of experts agreed that prophylactic measures are essential to prevent post-cataract surgery bacterial endophthalmitis. There was strong agreement on the use of intracameral antibiotics in patients at higher risk of post-surgical endophthalmitis and in those undergoing immediate sequential bilateral cataract surgery. Intracameral antibiotic use was considered safe in paediatric age group. There was strong agreement on the use of intracameral antibiotics in patients at higher risk of post-surgical endophthalmitis and in those undergoing immediate sequential bilateral cataract surgery.

Oral antibiotics, whether administered pre- or post-operatively, were not considered to provide additional benefit, even in high-risk scenarios such as monocular cataract surgery.

Optimal operating theatre (OT) sterilization protocols were universally regarded as critical for minimizing the risk of infection. Implementation of a comprehensive pre-operative checklist was deemed essential for the prevention of bacterial contamination. Most experts believed that rather than trimming eyelashes, adequately draping them away from the surgical field was a safe and effective practice. A post-operative regimen of topical antibiotics for one to two weeks was considered sufficient for routine prophylaxis.

The practice of changing surgical gloves after each procedure and using a sterile gown for each patient has been found to be comparable in efficacy to disinfecting the same gloves between cases without patient gowning.<sup>104</sup>

Cluster endophthalmitis was viewed as a largely preventable complication, contingent on stringent infection control measures. Acute bacterial endophthalmitis typically presents with progressive visual loss, pain, redness, and lid swelling. Decrease in visual acuity was considered the most common presenting symptom as per experience of the experts.

Both presumed and microbiologically confirmed cases of endophthalmitis should be managed using similar protocols, with emphasis on clinical presentation and laboratory findings. Culture positivity from vitreous biopsy remains an important prognostic indicator, influencing both therapeutic decisions and expected outcomes. A one-week post-operative follow-up is critical for the early detection of acute bacterial endophthalmitis. Endophthalmitis associated with keratitis typically results in worse clinical outcomes. Although toxic anterior segment syndrome (TASS) may mimic infectious endophthalmitis, it is usually distinguishable based on clinical presentation. When accessible, polymerase chain reaction (PCR) testing of vitreous samples is recommended for rapid and accurate microbial identification.

Majority of experts believed that the emergence of multi-drug resistant (MDR) organisms as causative agents has added complexity to the management of post-operative endophthalmitis. Notably, the etiological factors for cluster outbreaks often differ from those implicated in isolated cases, underscoring the need for tailored preventive and investigative approaches.

While the EVS included systemic therapy in the study, it found no benefit of systemic antibiotics in acute post-cataract bacterial endophthalmitis. Therefore, the current consensus suggests that systemic antibiotics may not be necessary in routine endophthalmitis



management. Moreover, cases showing clinical improvement after a single dose of intravitreal antibiotics may not require repeat administration. Selection of intravitreal antibiotics was primarily based on broad-spectrum coverage against both gram-positive and gram-negative organisms, rather than on pharmacokinetics. Over the past two decades, there has been a notable shift in the microbiological spectrum of causative organisms, further distancing current practice from EVS-era recommendations.

The prognosis was believed to be influenced by multiple factors, including patient age, initial visual acuity, microbial virulence, timing of vitrectomy, culture positivity, and underlying retinal or corneal pathology. In patients with prior vitreoretinal surgery and silicone oil in situ, the dose of intravitreal antibiotics should be reduced to one-quarter to one-half of the standard amount to minimize retinal toxicity.

### Borderline Accepted Statements

Table 3 summarizes the statements which are borderline accepted by the international panel of experts (50-74%).

Section	Consensus Statement	C Score	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
<b>1. Preventing Endophthalmitis</b>							
1.12	The reported safe dose of intracameral moxifloxacin for instillation after cataract surgery is 150 µg/0.1 mL.	<u>61.53%</u>	15.38%	46.15%	7.69%	23.08%	7.69%
1.13	Hydration of the corneal incisions may not post any additional risk.	<u>69.23%</u>	7.69%	61.54%	23.08%	7.69%	0%
1.20	The rates of endophthalmitis are higher in extracapsular cataract extraction than phacoemulsification.	<u>53.84%</u>	7.69%	46.15%	30.77%	15.38%	0%
1.21	Diabetic patients with well controlled blood sugars are not at higher risk of post-surgical endophthalmitis.	<u>53.84%</u>	23.08%	30.77%	0%	46.15%	0%
<b>2. Diagnosing Endophthalmitis</b>							
2.4	The 1-week post-operative visit is important for diagnosing acute-onset bacterial endophthalmitis.	<u>69.23%</u>	30.77%	38.46%	15.38%	15.38%	0%
2.9	Performing pars plana vitrectomy and instillation of intravitreal antibiotics is the first	<u>53.84%</u>	15.38%	38.46%	7.69%	38.46%	0%

	line treatment option in cases of endophthalmitis.						
<b>3. Management of Endophthalmitis</b>							
3.5	The choice of antibiotics for intravitreal injection is based on the pharmacokinetics of the drugs. Injections usually do need to be repeated.	<u>66.67%</u>	16.67%	50%	25%	8.33%	0%
3.6	The microbiological profile of the most common etiological agents causing acute bacterial endophthalmitis has not changed over 2 decades.	<u>61.54%</u>	0%	61.54%	30.77%	7.69%	0%

Few statements had more than 50% response score but still could not achieve clear majority. These topics remain subjects of ongoing debate and may require prospective studies to establish definitive clinical outcomes.

The dosage of intracameral moxifloxacin, 150 µg/0.1 mL, was found to be acceptable to most experts but not majority of them. This suggests that a proportion of surgeons prefer higher dosage of moxifloxacin for prophylaxis of post-cataract surgery endophthalmitis. The hydration of corneal incisions with moxifloxacin was not considered a preferable technique. Some experts believe this may be due to a potential risk of endothelial toxicity. The consensus was also divided on whether well-controlled diabetic patients face a similar risk of endophthalmitis compared to non-diabetic patients. It remains uncertain whether patients with short-term glycaemic control but poor long-term blood sugar management are at increased risk of post-cataract surgery endophthalmitis. Among cataract surgical techniques, extracapsular cataract extraction (ECCE) was expected to be associated with a higher incidence of post-operative endophthalmitis compared to phacoemulsification. ECCE involves a larger incision and more sutures; however, despite decades of advancements in cataract surgery techniques, the consensus on its relative drawbacks remains unclear.

While the majority of experts considered the first postoperative week follow-up to be important, this view was not universally shared. In cases of early endophthalmitis, vitreous biopsy and intravitreal antibiotic administration were not always deemed necessary as first-line management, especially in milder presentations. The selection of antibiotics was primarily based on microbial coverage rather than pharmacokinetic properties. Many experts believed that the microbiological profile of organisms causing post-surgical endophthalmitis

has remained largely unchanged over the past two decades; however, strong consensus was lacking due to emerging etiological agents and varying patterns of antibiotic susceptibility.

### Poorly Accepted Statements

Table 4 summarizes the statements which are poorly accepted by the international panel of experts (<50%).

Section	Consensus Statement	C Score	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
<b>1. Preventing Endophthalmitis</b>							
1.2	A short course of topical antibiotics is considered as a part of the pre-operative regimen in all cases undergoing cataract surgery.	<u>23.07%</u>	7.69%	15.38%	15.38%	46.15%	15.38%
1.5	Combining pre-operative application of topical antibiotics and betadine decreases the risk of acute-onset post-surgical endophthalmitis.	<u>23.07%</u>	15.38%	7.69%	46.15%	23.08%	7.69%
1.11	Adverse reactions of intracameral moxifloxacin, cefuroxime and vancomycin are comparable.	<u>30.77%</u>	7.69%	23.08%	15.38%	46.15%	7.69%
1.23	The major limiting factor for usage of intracameral antibiotics is the cost factor in developing countries.	<u>38.46%</u>	0%	38.46%	46.15%	15.38%	0%
<b>2. Diagnosing Endophthalmitis</b>							
2.8	Aqueous tap and PPV have equivalent value in establishing the diagnosis of endophthalmitis.	<u>30.77%</u>	0%	30.77%	23.08%	30.77%	15.38%
<b>3. Management of Endophthalmitis</b>							
3.7	In cases of post-cataract surgery endophthalmitis, <10% eyes have poor visual outcomes.	<u>33.33%</u>	0%	33.33%	16.67%	41.67%	8.33%
3.8	The management principles of the Endophthalmitis Vitrectomy Study are still valid.	<u>41.67%</u>	0%	41.67%	33.33%	25%	0%

The statements with consensus score <50% were considered poorly accepted, suggesting the uncertainty or controversy on the topic among experts. Although these topics lacked sufficient evidence to support formal recommendations, they revealed a general ambivalence among experts.

The use of pre-operative antibiotics is not a standard or widely accepted prophylactic measure for cataract surgery among the practicing ophthalmologists. It was not believed to offer additional advantage for preventing post-operative endophthalmitis. There was no uniform consensus on whether the combined use of topical antibiotics and povidone-iodine offered additional protection. Specific strategies such as a single pre-operative application of 5% povidone-iodine on the periocular skin and ocular surface for at least three minutes, along with a short course of pre-operative topical antibiotics, were not considered sufficiently effective in significantly reducing the incidence of post-operative endophthalmitis.

There was variability in expert opinion regarding the adverse effects of commonly used intracameral antibiotics such as moxifloxacin, cefuroxime, and vancomycin, suggesting that these agents are not interchangeable in terms of safety profiles. Intracameral antibiotics though offer significant advantage, moxifloxacin was considered safer and preferable over cefuroxime and vancomycin.

The major reason for non-usage of intracameral antibiotics is debatable with majority experts casting a neutral reply. There was no clear agreement on the limiting factors for the use of intracameral antibiotics in developing countries; however, high cost was not considered a primary barrier. Other factors, such as errors in dilution, breaches in sterility, logistical constraints and lack of suitable commercially available preparations were identified as more likely contributors to non-usage of reconstituted antibiotics.

Aqueous tap and PPV have no diagnostic role in endophthalmitis. The expert panel also stressed that in the modern era, the management principles of Endophthalmitis vitrectomy study do not stand valid. The concept of early vitrectomy with advances in vitrectomy system and newer antibiotics and usage of steroids has revolutionized the old age principles. These observations suggest that the traditional guidelines outlined in the Endophthalmitis Vitrectomy Study (EVS) may no longer be fully applicable in contemporary practice. The Chinese expert consensus on endophthalmitis proposes a classification system that stratifies the condition into stages based on the severity of anterior chamber inflammation, the presence or absence of hypopyon, and the degree of vitreous opacification. Management is implemented in a stepwise approach, incorporating subconjunctival and systemic antibiotic therapy, intravitreal antimicrobial agents, and adjunctive treatments. In cases exhibiting rapid progression, frequent clinical monitoring is essential, and therapeutic strategies are dynamically adjusted according to the disease stage.<sup>105</sup>

Despite best management practices, the visual outcomes in post-operative endophthalmitis remain suboptimal, with more than 10% of affected eyes experiencing poor outcomes.

There are certain limitations of this study. It being a consensus article is based on expert opinions and existing literature, which means it does not include new experimental or large-scale clinical trials to validate the recommendations. This limits the ability to definitively confirm the efficacy of some proposed strategies. On the other hand, it provides a more practical working guideline. Additionally, there may be geographical bias. While the expert panel was international, certain recommendations may be more applicable in regions with access to advanced technology and resources. The applicability of these guidelines in resource limited settings may be challenging, especially for practices with limited access to intracameral antibiotics or advanced imaging technologies. This consensus also highlights certain points which have low acceptance or majority, further exposing areas of controversy and potential research to provide clearer guidelines.

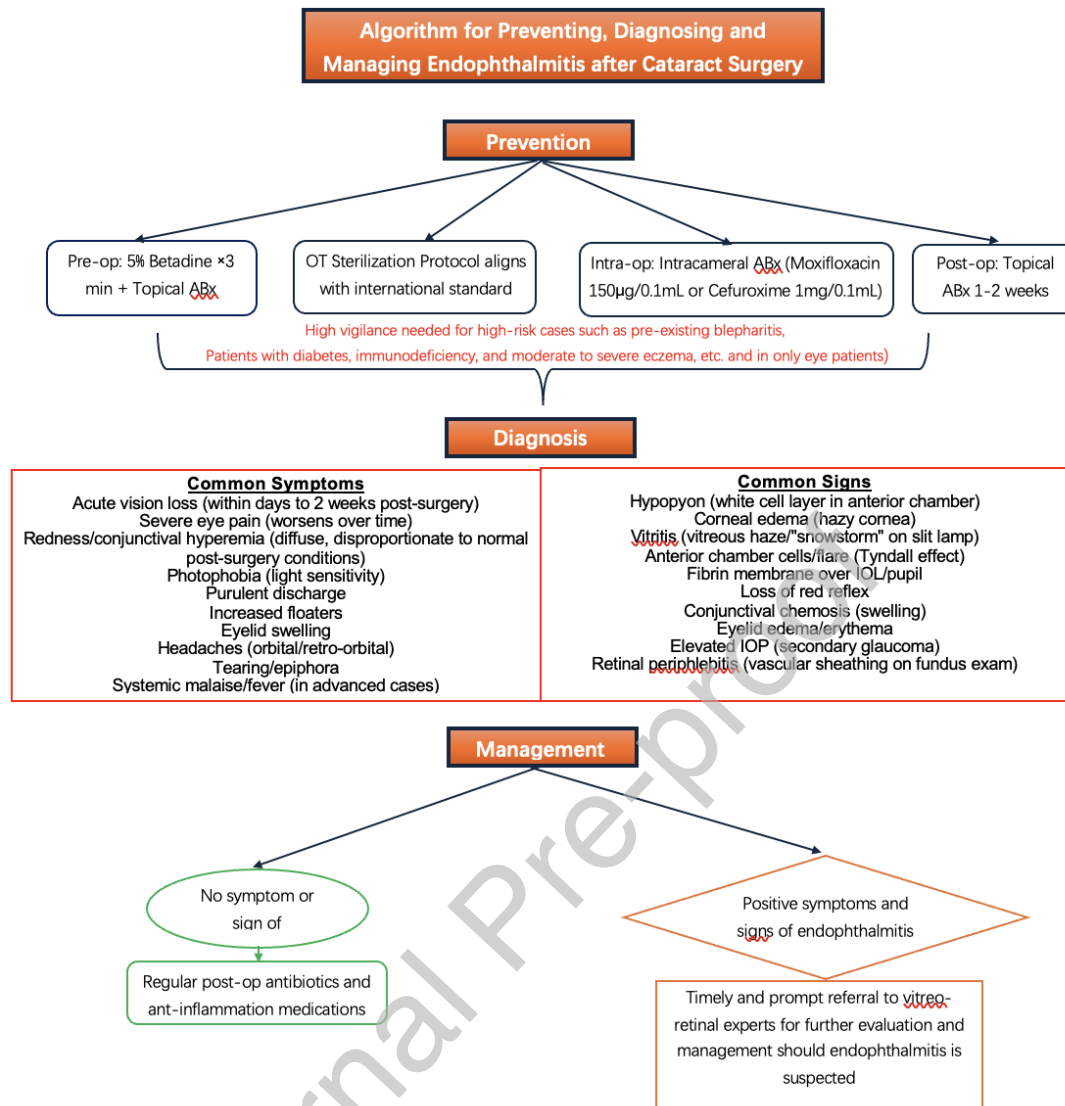


Figure 1. Management algorithm for endophthalmitis after cataract surgery.

## Conclusion

Acute-onset endophthalmitis after cataract surgery is a serious and uncommon complication. A consensus statement on the prevention, diagnosis, and management of post-surgical endophthalmitis is crucial to harmonize clinical practices, enhance patient safety, and uphold the standards of cataract surgery worldwide. The formulation of such statements should be a priority for professional ophthalmic organizations, promoting collaboration among experts to address this vision-threatening complication comprehensively. The development of a consensus statement is not merely a procedural formality, but a vital step toward improving patient care. By standardizing these guidelines, it enables early and accurate diagnosis while

optimizing the final outcomes. Furthermore, it helps to identify and bridge existing knowledge gaps and updates outdated frameworks, such as those outlined in the Endophthalmitis Vitrectomy Study (EVS), which may no longer fully align with current practices. As cataract surgery continues to evolve with advancements in surgical techniques and technology, the establishment of updated, evidence-based consensus guidelines will be instrumental in ensuring safer procedures and improved visual outcomes for patients globally.

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#### Table of Contents Statement

Post-cataract surgery endophthalmitis is a serious but largely preventable clinical entity. Its prevention, diagnosis and management have considerable variability in clinical practices. A panel of 35 international experts from 13 countries/regions was formed to establish consensus. This paper is the product of a systematic review of current literature, informed by the panel's collective experience and expertise. It aims to establish standardized guidelines to improve cataract surgery outcomes by minimizing the risk of post-operative endophthalmitis.

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