In Clinical Practice

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Stephen G. Schwartz · Andrzej Grzybowski

Endophthalmitis in Clinical Practice

Springer

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ISSN 2199-6652 ISSN 2199-6660 (electronic)
In Clinical Practice
ISBN 978-3-319-66350-0 ISBN 978-3-319-66351-7 (eBook)
https://doi.org/10.1007/978-3-319-66351-7

Library of Congress Control Number: 2017957901

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Foreword

Over the past few decades, we have a better understanding of the pathophysiology of intraocular infections through clinical and microbiological studies, and we can initiate more prompt diagnosis and treatment to improve outcomes in the management of endophthalmitis. It is amazing to witness the changes in the differential diagnoses and management of endophthalmitis in recent years. With the increases in invasive ophthalmic procedures, there is a need for a concise, up-to-date reference on clinical endophthalmitis which includes options for antimicrobial therapy and the role of pars plana vitrectomy. This book, entitled *Endophthalmitis in Clinical Practice*, meets the need very well.

Multiple chapters in the book are dedicated to specific subtopics in endophthalmitis management. The background section includes historical information as well as details on the Endophthalmitis Vitrectomy Study, as well as controversies in the use of intracameral antibiotics during cataract surgery.

This follows a discussion on the various etiologies of endophthalmitis and includes initial treatment strategies in each subgroup. As part of diagnostic evaluation, sections include imaging for documentation of clinical features, echographic characteristics, and complications affecting visual outcomes. Management of more difficult cases may require retreatment after initial antimicrobials and uncommonly may require removal of the capsular bag and the intraocular lens in specific cases. Illustrations of pre- and posttreatment cases are shown from the authors' clinical practice.

Pars plana vitrectomy is often considered in more rapidly advancing cases, especially in endophthalmitis after cataract surgery in patients presenting with light perception visual acuity. The use of vitrectomy may be limited by corneal or media opacities, but small-gauge vitrectomy approaches may allow a simpler approach to core vitrectomy without the need for conjunctival dissection or suture placement.

Antimicrobial therapy is then discussed. This includes initial broad coverage of both gram-positive and gram-negative bacteria. Likewise, antifungal agents including amphotericin B and voriconazole can be utilized in suspected or confirmed endophthalmitis caused by fungi. Alternative agents for resistant organisms are reviewed and the tailoring of treatment for subsequent management.

The use of intravitreal injections for retinal diseases has become the leading ophthalmic procedure in the United States. In these patients, endophthalmitis can occur from solution contamination as well as from the injection procedure itself. These cases generally present early after injection and frequently involve oropharyngeal flora from contamination of the needle or the ocular surface during drug delivery. Streptococcus as well as other gram-positive organisms in these cases may have a more advanced clinical presentation with poor visual and anatomic outcomes.

This text will undoubtedly prove to be a valuable asset for clinical ophthalmologists as well as retinal specialists. The abundant clinical illustrations, concise tables, and reference material enhance its readability. With the exception of the Endophthalmitis Vitrectomy Study, there are no major randomized clinical trials on which to base definitive recommendations. Rather, the authors utilize published case series and their own experience to provide guidelines regarding the prompt and efficient management of endophthalmitis.

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Conflict of Interest

Funding/Grant Support - This work was supported in part by National Institutes of Health center core grant P30EY014801 and by unrestricted grant from the Institute for Research in Ophthalmology, Foundation for Ophthalmology Development, Poznan, Poland.

Financial Disclosures
Dr. Harry W. Flynn Jr. - None
Dr. Nidhi Relhan Batra - None
Dr. Stephen G. Schwartz discloses personal fees from Alimera, Bausch + Lomb, and Welch Allyn within the past 3 years.
Dr. Andrzej Grzybowski reports grants, personal fees and non-financial support from Bayer, grants and non-financial support from Novartis, non-financial support from Alcon, non-financial support from Thea, personal fees and non-financial support from Valeant, grants and personal fees from Pfizer, non-financial support from Santen, outside the submitted work.

How to Use This Book

Endophthalmitis remains an uncommon but serious cause of visual loss. Early diagnosis and treatment may restore useful vision for many patients. However, visual outcomes may be poor despite prompt and appropriate therapy in other patients. This book is intended to be a practical guide to the clinical management of patients with endophthalmitis.

The guidelines included in this book are based on the current peer-reviewed literature, as well as the authors' experience and opinions. Summary statements from published studies are adapted for inclusion in the current text. These adaptations are used to ensure that the exact message is conveyed since rephrasing of sentences may change the original message. The Endophthalmitis Vitrectomy Study (EVS) was a randomized clinical trial that has provided high-level evidence for endophthalmitis associated with cataract surgery or secondary intraocular lens (IOL) surgery between 1991 and 1994. However, many patients with endophthalmitis from other causes have a different spectrum of microbial etiologies, a different set of clinical features, and a different visual prognosis. The best available evidence for these patients consists of clinical case series and individual case reports.

This book provides guidance for an overall approach to the diagnosis and management of endophthalmitis, but the broad guidelines do not always apply to an individual patient, and treatment has to be individualized. The ultimate judgment regarding the care of an individual patient must be made by the treating physician, incorporating the specific clinical features, systemic risk factors, the microorganisms involved, and the wishes of the patient.

This book is not intended to be an all-inclusive document nor a medical-legal resource. It is intended to provide practical guidelines in the care of patients with endophthalmitis.

Contents

Endophthalmitis

Endophthalmitis is characterized by marked inflammation of intraocular fluids and tissues. Infectious endophthalmitis may be categorized by the apparent cause of the infection, including the onset of symptoms, the degree of inflammation, and other factors. The classification helps to plan further management and helps in predicting the treatment outcomes.

Endophthalmitis may be exogenous (caused by inoculation of microorganisms from the external environment) or endogenous (caused by hematogenous spread from other parts of the body). All categories of endophthalmitis are associated with variable degrees of marked intraocular inflammation, typically with hypopyon, in addition to visual loss, redness, and pain.

The diagnosis, treatment, and prophylaxis of endophthalmitis have been discussed in this book.

1. Classification of Endophthalmitis
2. Differential Diagnosis of Endophthalmitis
3. Making the Diagnosis of Endophthalmitis
4. Endophthalmitis Categories
5. Antimicrobial Treatment
6. Endophthalmitis Prophylaxis
7. Endophthalmitis and Retinal Detachment
8. Antibiotic Stewardship
9. Outcomes (Anatomical and Functional) and Complications of Treatment
10. Endophthalmitis: Miscellaneous Categories

Chapter 1
Endophthalmitis: Classification and Most Frequently Reported Organisms

1. Postoperative endophthalmitis
   (a) Following cataract surgery: Acute-onset postoperative endophthalmitis
      Coagulase (−) *Staphylococci, Staphylococcus aureus, Streptococcus,* gram-negative bacteria
   (b) Following cataract surgery: Delayed-onset postoperative endophthalmitis
      P. acnes, coagulase (−) *Staphylococci*, fungi
   (c) Following glaucoma surgery: Conjunctival filtering bleb-associated infection and endophthalmitis
      Streptococcus species, *Haemophilus influenzae*, *Staphylococcus* species
   (d) Following glaucoma surgery: Endophthalmitis associated with glaucoma drainage devices
   (e) Following elective corneal transplant
2. Posttraumatic endophthalmitis
   Bacillus species (30–40%), *Staphylococcus* species
3. Endogenous endophthalmitis
   Candida species, *Staphylococcus aureus*, gram-negative bacteria
4. Endophthalmitis associated with keratitis
   Pseudomonas, *Staphylococcus* species

H.W. Flynn Jr. et al., *Endophthalmitis in Clinical Practice*,
In Clinical Practice,
https://doi.org/10.1007/978-3-319-66351-7_1

5. Endophthalmitis associated with intravitreal injection *Staphylococcus*/*Streptococcus* species (Figs. 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 1.10, 1.11, 1.12, 1.13, 1.14, 1.15, 1.16, 1.17, 1.18, 1.19, 1.20, 1.21, 1.22, 1.23, 1.24, 1.25)

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Endophthalmitis Caused by methicillin-resistant
Staphylococcus epidermidis (MSSE)

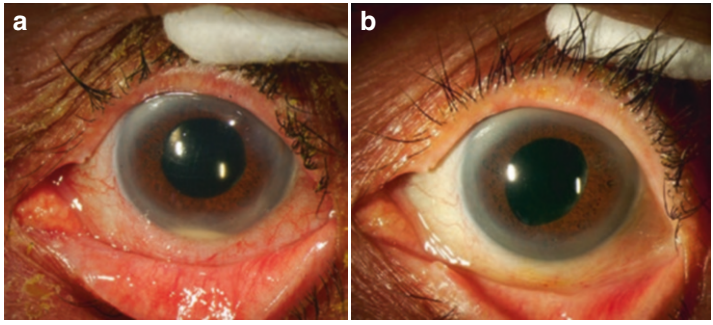

FIGURE 1.1 Acute-onset endophthalmitis. A 78-year-old male patient with acute-onset postoperative endophthalmitis following cataract surgery. (**a**) The patient presented with conjunctival congestion, mild corneal edema, hypopyon, hazy view to the posterior segment, and hand motions (HM) vision. Patient underwent vitreous tap and intraocular antibiotics (vancomycin and ceftazidime). The vitreous culture was positive for *Staphylococcus epidermidis* resistant to all fluoroquinolones and sensitive to vancomycin. (**b**) At 8-month follow-up, the patient regained best corrected visual acuity of 20/30

Endophthalmitis Caused by methicillin-susceptible
Staphylococcus aureus (MSSA)

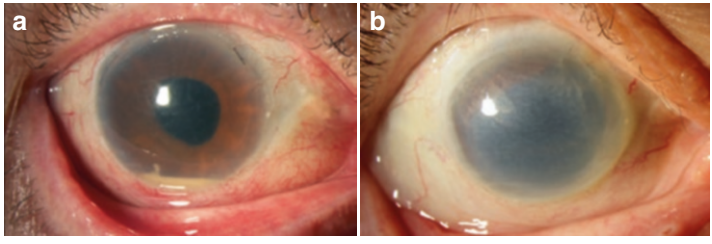

FIGURE 1.2 Acute-onset endophthalmitis. A 68-year-old male patient with acute-onset postoperative endophthalmitis following cataract surgery. (**a**) The patient presented with conjunctival congestion, mild corneal edema, hypopyon, and hand motions (HM) vision. Patient underwent vitreous tap and intraocular antibiotics and was culture positive for methicillin-resistant *Staphylococcus aureus* (MRSA) resistant to all fluoroquinolones. (**b**) At 6-month follow-up, the patient regained best corrected visual acuity of 2/200 with persistent corneal haze

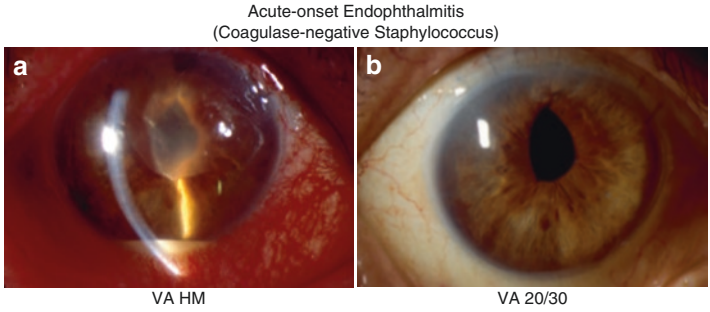

FIGURE 1.3 Acute-onset endophthalmitis. A 66-year-old male patient with acute-onset postoperative endophthalmitis following cataract surgery. (**a**) The patient presented with conjunctival congestion, fibrinous reaction in the anterior chamber, hypopyon, polypropylene suture at 12 o'clock to close a sector iridectomy, restricted view to the posterior segment, and hand motions (HM) vision. The patient underwent vitreous tap and intraocular antibiotics and was culture positive for coagulase-negative Staphylococcus. (**b**) At 1-year follow-up, the patient regained best corrected visual acuity of 20/30. The polypropylene suture was not removed at the time of treatment

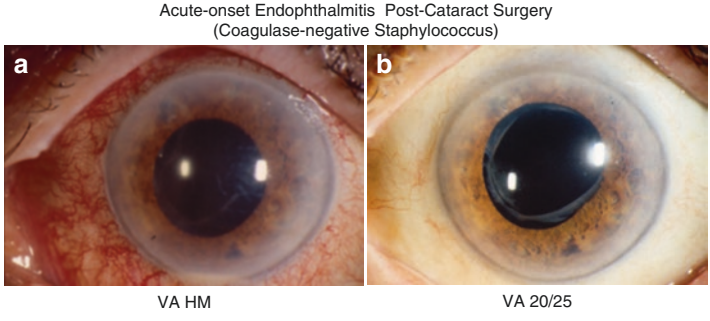

FIGURE 1.4 Acute-onset endophthalmitis. A 70-year-old male patient with acute-onset postoperative endophthalmitis following cataract surgery. (**a**) The patient presented with conjunctival congestion, mild corneal edema, hypopyon, and hand motions (HM) vision. Patient underwent vitreous tap and intraocular antibiotics and was culture positive for coagulase-negative Staphylococcus. (**b**) At 1-year follow-up, the patient regained best corrected visual acuity of 20/25

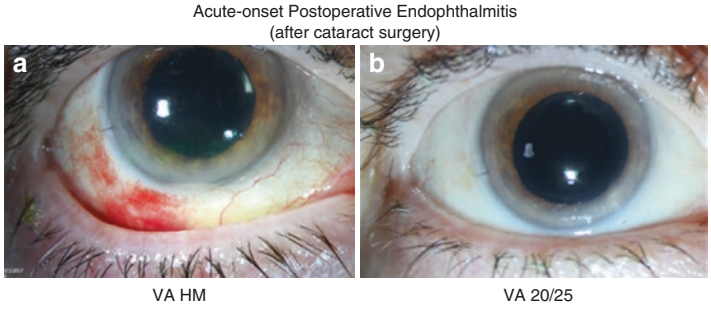

FIGURE 1.5 Acute-onset endophthalmitis. A 76-year-old female patient with acute-onset endophthalmitis following cataract surgery with intracameral moxifloxacin. (**a**) The patient presented with conjunctival congestion, fibrinous reaction in the anterior chamber, hazy view to the posterior segment, and hand motions (HM) vision. Patient underwent vitreous tap and intraocular antibiotics (vancomycin and ceftazidime) and was culture negative. (**b**) At 3-week follow-up, the patient regained best corrected visual acuity of 20/25 with resolution of inflammation

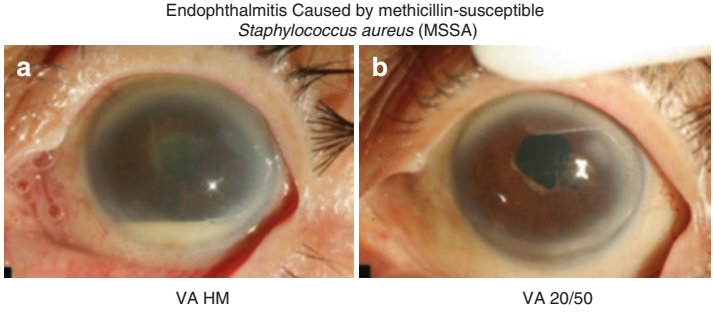

FIGURE 1.6 Acute-onset endophthalmitis. A 78-year-old male patient with acute-onset postoperative endophthalmitis following cataract surgery. (**a**) The patient presented with conjunctival congestion, mild corneal edema, hypopyon, fibrinous membrane in the anterior chamber, and hand motions (HM) vision. Patient underwent vitreous tap and intraocular antibiotics and was culture positive for methicillin-sensitive *Staphylococcus aureus* (MSSA) susceptible to fourth-generation fluoroquinolones. (**b**) At 6-month follow-up, the patient regained best corrected visual acuity of 20/50. The visual acuity reduction was associated with cystoid macular edema

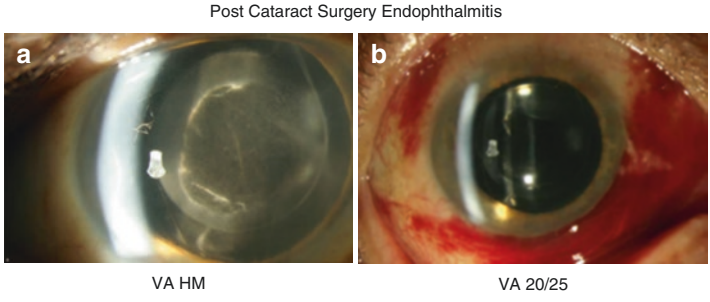

FIGURE 1.7 Acute-onset endophthalmitis. A 74-year-old male patient with acute-onset postoperative endophthalmitis following cataract surgery. (**a**) The patient presented with conjunctival congestion, fibrinous membrane in the anterior chamber over the intraocular lens, hazy view of the posterior segment, and hand motions (HM) vision. The patient underwent vitreous tap and intraocular antibiotics. (**b**) At 2-week follow-up, the patient regained best corrected visual acuity of 20/25 with resolving inflammation and infection

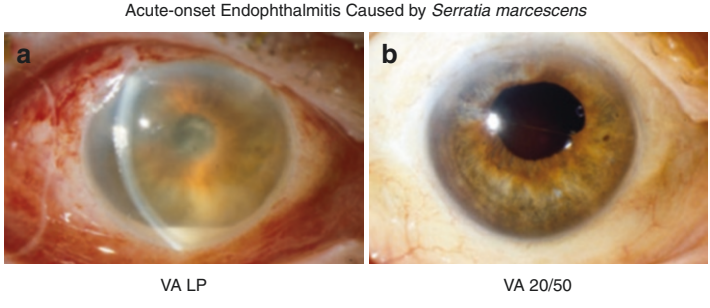

FIGURE 1.8 Acute-onset endophthalmitis. A 78-year-old male patient with acute-onset postoperative endophthalmitis 1 day following cataract surgery. (**a**) The patient presented with conjunctival congestion, mild corneal edema, hypopyon, fibrinous membrane in the anterior chamber, hazy view of the posterior segment, and light perception (LP) vision. The patient underwent pars plana vitrectomy and intraocular antibiotics. The vitreous culture was positive for *Serratia marcescens*. (**b**) At 1-year follow-up, the patient regained best corrected visual acuity of 20/50

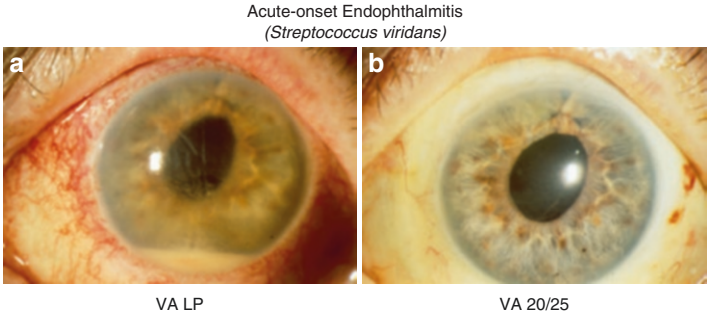

FIGURE 1.9 Acute-onset endophthalmitis. A 65-year-old male patient with acute-onset postoperative endophthalmitis following cataract surgery. (**a**) The patient presented with conjunctival congestion, mild corneal edema, hypopyon, polypropylene suture in the iris superiorly, fibrinous membrane in the anterior chamber, hazy view of the posterior segment, and light perception (LP) vision. The patient underwent vitreous tap and intraocular antibiotics. The vitreous culture was positive for *Streptococcus viridans*. (**b**) At 1-year follow-up, the patient regained best corrected visual acuity of 20/25

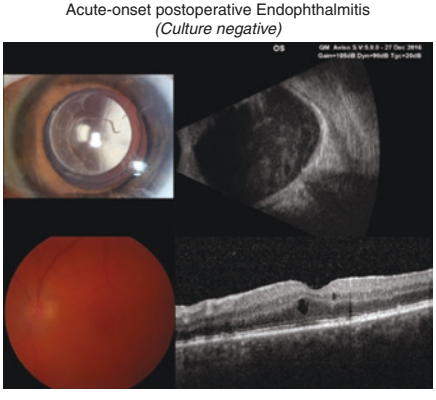

FIGURE 1.10 Acute-onset endophthalmitis. A 76-year-old female patient with acute-onset endophthalmitis following cataract surgery with intracameral moxifloxacin. Presenting features 4 days after cataract surgery include fibrin in anterior chamber, hazy view of the vitreous cavity, and cystic retinal thickness on OCT

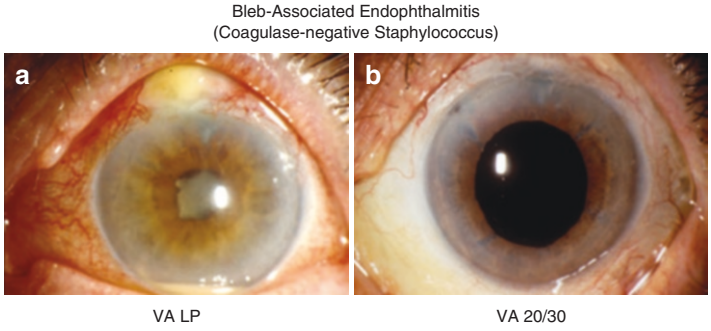

FIGURE 1.11 Bleb-associated endophthalmitis. A 66-year-old male patient with bleb-associated endophthalmitis following trabeculectomy. (**a**) The patient presented with conjunctival congestion, purulent blebitis, mild corneal edema, hypopyon, fibrinous membrane in the anterior chamber and pupillary area, hazy view to the posterior segment, and hand motions (HM) vision. The patient underwent pars plana vitrectomy and intraocular antibiotics. The vitreous culture was positive for coagulase-negative Staphylococcus. (**b**) At 6-month follow-up, the patient regained best corrected visual acuity of 20/30 with resolution of endophthalmitis

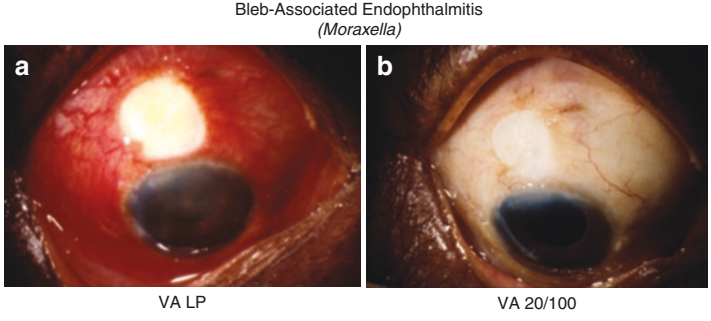

FIGURE 1.12 Bleb-associated endophthalmitis. A 66-year-old male patient with bleb-associated endophthalmitis following trabeculectomy. (**a**) The patient presented with conjunctival congestion, bleb infection, mild corneal edema, hazy view to the posterior segment, and light perception (LP) vision. The patient underwent pars plana vitrectomy and intraocular antibiotics. The vitreous culture was positive for *Moraxella* species. (**b**) At 6-month follow-up, the patient regained best corrected visual acuity of 20/100 with resolution of endophthalmitis

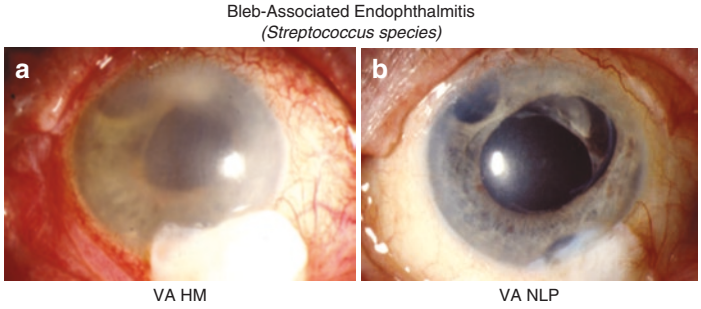

FIGURE 1.13 Bleb-associated endophthalmitis. A 72-year-old female patient with bleb-associated endophthalmitis following trabeculectomy. (**a**) At presentation the patient had conjunctival congestion, bleb infection, corneal edema, hazy view to the posterior segment, and hand motions (HM) vision. The patient underwent pars plana vitrectomy and intraocular antibiotics. The vitreous culture was positive for *Streptococcus* species. (**b**) At 1-year follow-up, the patient had resolution of endophthalmitis, but the visual acuity deteriorated to light perception (NLP)

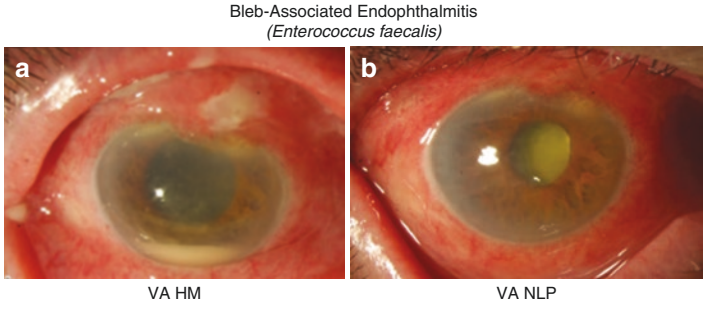

FIGURE 1.14 Bleb-associated endophthalmitis. A 72-year-old female patient with bleb-associated endophthalmitis following trabeculectomy. (**a**) At presentation patient had conjunctival congestion, bleb infection, corneal edema, hypopyon, fibrinous membrane in the anterior chamber and pupillary area, hazy view to the posterior segment, and light perception (LP) vision. The patient underwent vitreous tap and intraocular antibiotics. The vitreous culture was positive for *Enterococcus faecalis*. (**b**) At 2-month follow-up, the inflammation and infection started resolving, but the visual acuity deteriorated to no light perception (NLP)

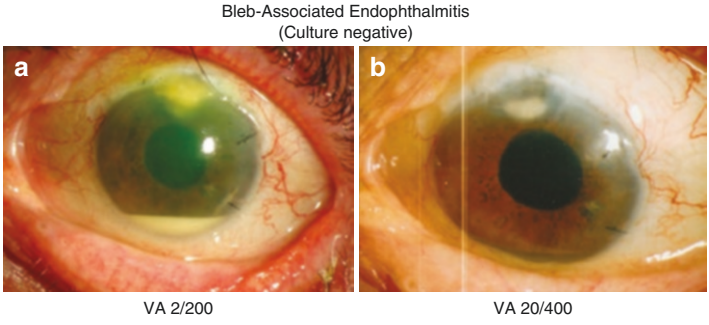

FIGURE 1.15 Bleb-associated endophthalmitis. A 66-year-old female patient with bleb-associated endophthalmitis following trabeculectomy. (**a**) At presentation the patient had conjunctival congestion, bleb infection, corneal edema, hypopyon, hazy view to the posterior segment, and 2/200 visual acuity. The patient underwent vitreous tap and intraocular antibiotics. The vitreous culture was negative for any organism. (**b**) At 6-month follow-up, the patient had complete resolution of endophthalmitis and best corrected visual acuity improved to 20/400

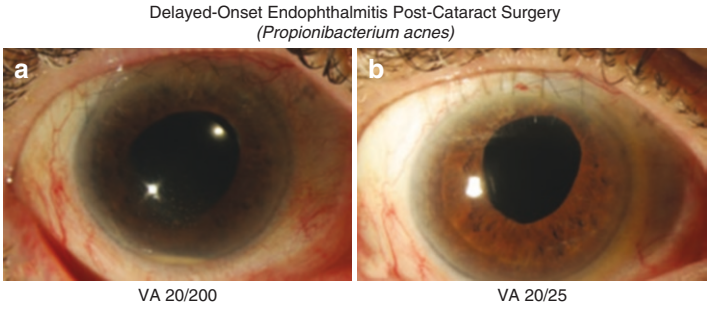

FIGURE 1.16 Chronic/delayed-onset postoperative endophthalmitis. A 69-year-old male patient with delayed-onset postoperative endophthalmitis following cataract surgery. (**a**) The patient presented with gradual painless decrease in vision, conjunctival congestion, hypopyon, inflammatory cells in the anterior chamber, and 20/200 visual acuity. Patient underwent pars plana vitrectomy and intraocular antibiotics injection. The vitreous culture was positive for *Propionibacterium acnes*. A repeat pars plana vitrectomy, removal of the intraocular lens, and intraocular antibiotics injection were performed. (**b**) At 6-month follow-up, the patient regained best corrected visual acuity of 20/25 with resolution of inflammation

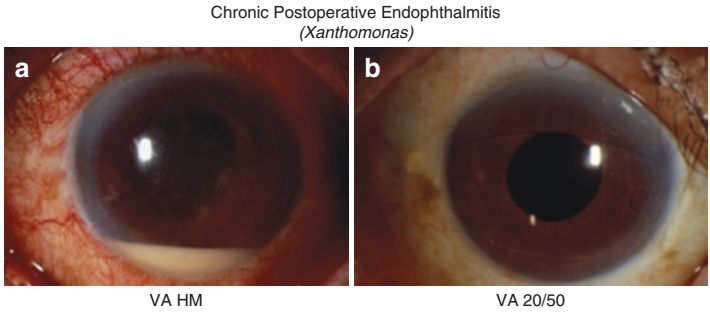

FIGURE 1.17 Chronic/delayed-onset postoperative endophthalmitis. A 77-year-old female patient with delayed-onset postoperative endophthalmitis following cataract surgery. (**a**) The patient presented with gradual painless decrease in vision, conjunctival congestion, hypopyon, fibrinous membrane in the anterior chamber, and hand motions (HM) vision. The patient underwent pars plana vitrectomy and intraocular antibiotics injection. The vitreous culture was positive for *Xanthomonas* species. (**b**) At 1-year follow-up, the patient regained best corrected visual acuity of 20/50 with resolution of inflammation

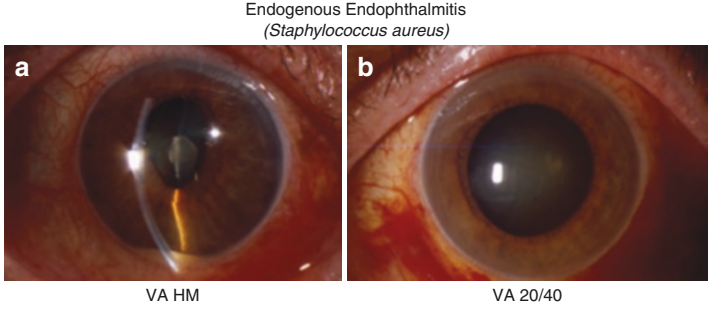

FIGURE 1.18 Endogenous endophthalmitis. (**a**) A 60-year-old female patient with uncontrolled diabetes mellitus presented with sudden blurring of vision, vitreous floaters, and hand motions (HM) vision. The fundus examination showed hyperemic disc and presence of subretinal exudates at the posterior pole. The patient underwent vitreous tap and intraocular antibiotics. The vitreous culture was positive for *Staphylococcus aureus*. (**b**) At 1-month follow-up, the inflammation and infection started resolving with best corrected visual acuity improving to 20/40

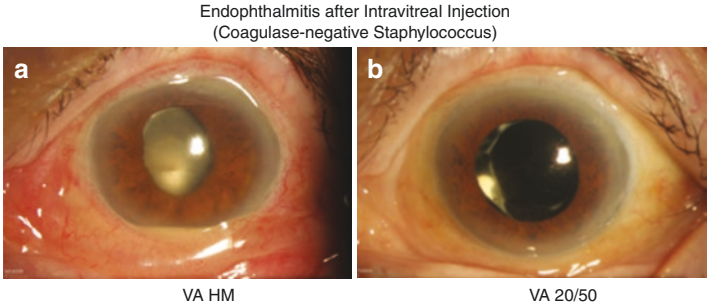

FIGURE 1.19 Endophthalmitis after intravitreal injection. A 56-year-old male patient presented 1 day after intravitreal anti-VEGF injection for age-related macular degeneration (AMD) with sudden painful decrease in vision. (**a**) The patient presented with conjunctival congestion, conjunctival chemosis, hypopyon, fibrinous membrane in the anterior chamber, hazy view of the posterior segment, and hand motions (HM) vision. The patient underwent vitreous tap and intraocular injection (vancomycin, ceftazidime, and dexamethasone). The vitreous culture was positive for coagulase-negative Staphylococcus. (**b**) At 1-year follow-up, the inflammation and infection resolved with best corrected visual acuity improved to 20/50

Endophthalmitis after Intravitreal Injection
(Culture negative)

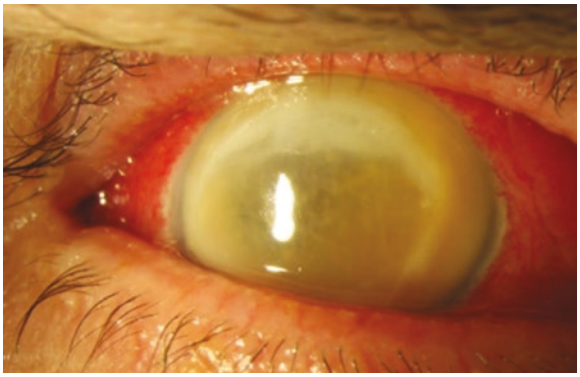

FIGURE 1.20 Endophthalmitis after intravitreal injection. A 60-year-old male patient with neovascular age-related macular degeneration (AMD) presented 1 day after intravitreal aflibercept injection with sudden painful decrease in vision. The patient presented with conjunctival congestion, corneal edema, hypopyon, fibrinous reaction in the anterior chamber, hazy view of the posterior segment, and light perception (LP) vision. The patient underwent pars plana vitrectomy and intraocular injection (vancomycin and ceftazidime). The vitreous culture was culture negative

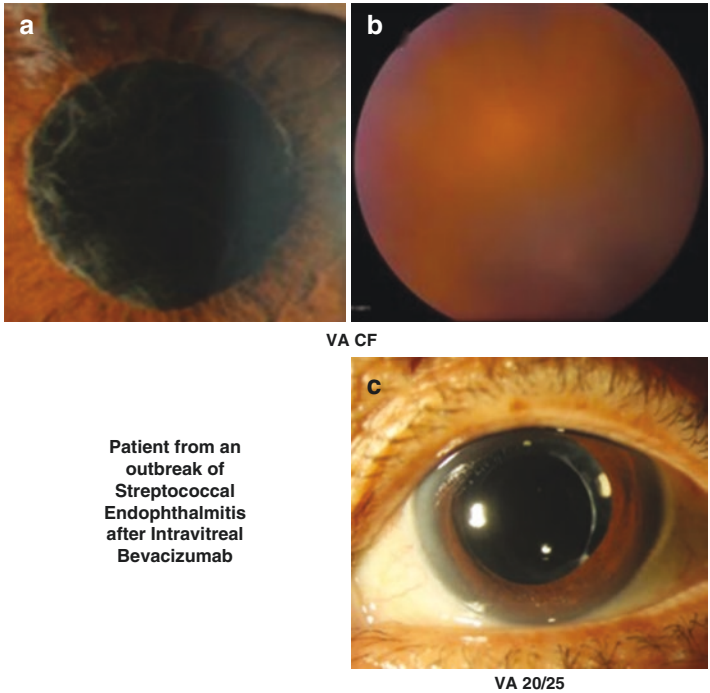

FIGURE 1.21 60-year-old male patient with age-related macular degeneration (AMD) received compounded intravitreal bevacizumab. Two days after injection, the patient presented with pain, redness, and counting fingers (CF) vision. (**a**) Slit lamp examination showed the presence of fibrin in anterior chamber. (**b**) Posterior segment was hazy with no clarity of fundus details. The patient underwent vitreous tap and intraocular injection of antibiotics. (**c**) At 6 months follow-up, the inflammation and infection resolved and best-corrected visual acuity improved to 20/25. The patient was one of the 12 patients among an outbreak of Streptococcus endophthalmitis after compounded intravitreal bevacizumab

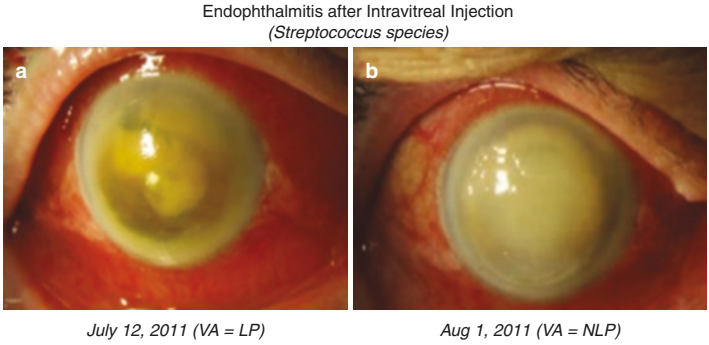

FIGURE 1.22 Endophthalmitis after intravitreal injection. A 60-year-old male patient with central retinal vein occlusion/neovascular glaucoma (CRVO/NVG) presented 2 days after intravitreal aflibercept injection with sudden painful decrease in vision. (**a**) The patient presented with conjunctival congestion, corneal edema, exudates filling the anterior chamber, no view of the posterior segment, and light perception (LP) vision. The patient underwent vitreous tap and intraocular injection. (**b**) At 3-week follow-up, the inflammation and infection persisted, and visual acuity deteriorated to no light perception (NLP). The patient underwent evisceration, and the specimen culture was positive for *Streptococcus* species

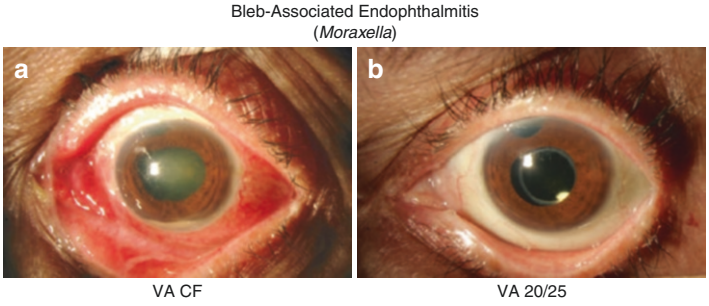

FIGURE 1.23 A 72-year-old male patient with bleb-associated endophthalmitis following trabeculectomy. (**a**) The patient presented with conjunctival congestion, bleb infection, mild corneal edema, hypopyon, cataract, hazy view to the posterior segment and counting fingers (CF) vision. Patient underwent vitreous tap and intraocular antibiotics. The vitreous culture was positive for Moraxella species. (**b**) At 6-month follow-up, the patient regained best corrected visual acuity of 20/25 after subsequent cataract surgery

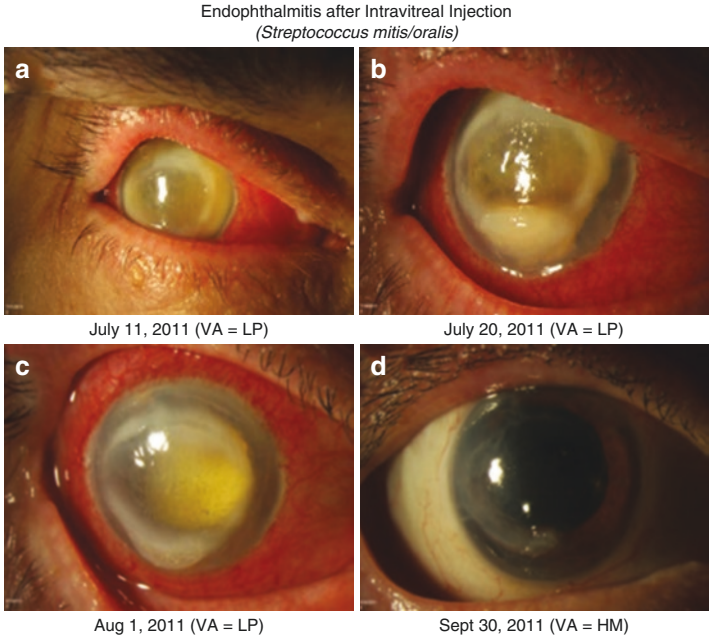

FIGURE 1.24 Endophthalmitis after intravitreal injection. A 60-year-old male patient with neovascular age-related macular degeneration (AMD) presented 2 days after intravitreal ranibizumab injection with sudden painful decrease in vision. (**a**) Slit-lamp examination showed conjunctival congestion, corneal edema, hypopyon, infectious exudates in the anterior chamber, no view of the posterior segment, and light perception (LP) vision. The patient underwent vitreous tap and intraocular antibiotic injection. The vitreous culture was positive for *Streptococcus mitis/oralis*. (**b**, **c**) Inflammation and infection remained uncontrolled. (**d**) Two weeks after pars plana vitrectomy, lensectomy, and silicone oil injection, inflammation and infection reduced. However, 6 months later, the patient underwent enucleation for the painful blind eye

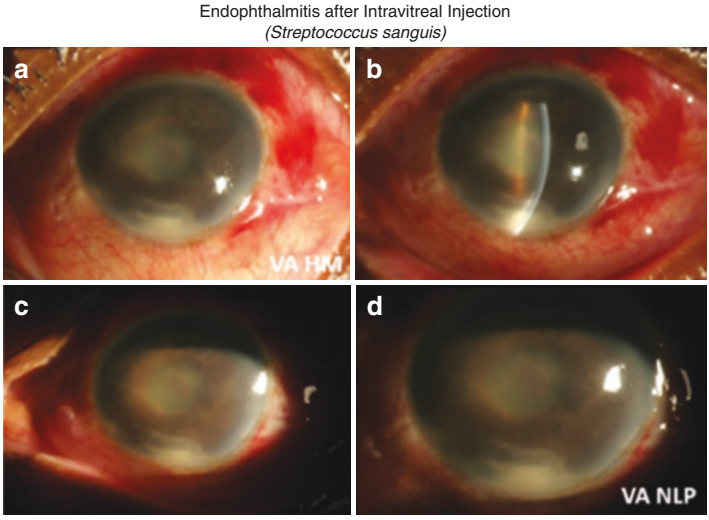

FIGURE 1.25 Endophthalmitis after intravitreal injection. A 60-year-old male patient with neovascular age-related macular degeneration (AMD) presented 1 day after intravitreal ranibizumab injection with sudden painful decrease in vision. (**a**) Slit-lamp examination showed conjunctival congestion, corneal edema, hypopyon, fibrinous membrane in the anterior chamber, no view of the posterior segment, and hand motions (HM) vision. The patient underwent vitreous tap and intraocular antibiotic injection. The vitreous culture was positive for *Streptococcus sanguis*. (**b**–**d**) Inflammation and infection persisted and vision became no light perception (NLP)

Chapter 2
Differential Diagnosis of Endophthalmitis

Endophthalmitis is a clinical diagnosis, confirmed with subsequent laboratory testing. Endophthalmitis must be distinguished from noninfectious inflammation as well as noninflammatory cellular infiltration, including hemorrhage and tumor cells. Endophthalmitis with negative intraocular cultures is relatively common, reported in the range of about 20% following intraocular surgery and up to 50% following intravitreal injection.

It is important to consider the various conditions which may mimic as infectious endophthalmitis. The following are some conditions which should be differentiated from infectious endophthalmitis:

(a) Toxic anterior segment syndrome (TASS)
(b) Retained lens material
(c) Flare-up of preexisting uveitis
(d) Chronic vitreous hemorrhage
(e) Retinoblastoma (in children)
(f) Retained triamcinolone acetonide
(g) Viral retinitis
(h) Pseudoendophthalmitis from intravitreal injections

H.W. Flynn Jr. et al., *Endophthalmitis in Clinical Practice*,
In Clinical Practice,
https://doi.org/10.1007/978-3-319-66351-7_2

Toxic Anterior Segment Syndrome (Fig. 2.1)

Toxic anterior segment syndrome (TASS) is an acute postoperative sterile inflammation of the anterior segment which occurs due to toxic effects on corneal endothelium (Fig. 2.1). The following are characteristic features of TASS:

- *Usually identified on the first day following cataract surgery*—Symptoms of TASS characteristically appear 12–48 h after the surgery.
- *Prominent corneal edema is observed from limbus to limbus*—Corneal edema with limbus to limbus involvement is noted in most cases. Inflammation in the anterior segment is severe with fibrinous reaction.
- *Prominent anterior chamber cells (usually without hypopyon)*—The inflammation usually does not involve the vitreous.

The most common symptom of TASS is blurred vision. Patients may present with blurred vision and mild pain on the same day of the surgery or within 24 hours after the surgery.

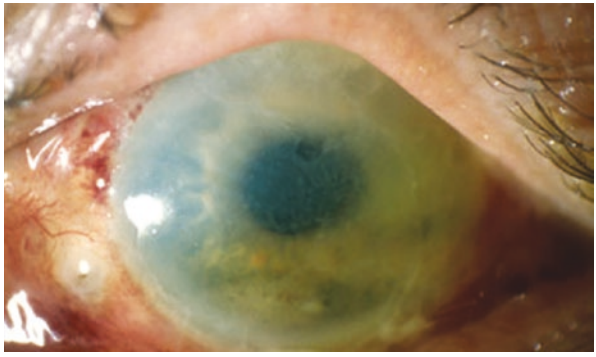

FIGURE 2.1 Toxic anterior segment syndrome (TASS) with limbus to limbus corneal edema

In addition, the iris may be irregular with unreactive pupil. Damage to the trabecular meshwork may result in secondary glaucoma. Differentiating features between TASS and endophthalmitis are shown in the Table 2.1.

Table 2.1 Differences between toxic anterior segment syndrome (TASS) and endophthalmitis

Differences between TASS and endophthalmitis		
	TASS	**Endophthalmitis**
Cause	Noninfectious reaction to toxic agent present in: • BSS solution • Antibiotic injection • Endotoxin • Residue	Bacterial, fungal, or viral infection
Onset	12–24 h	4–7 days
Signs/symptoms (*distinguishing features as reported in literature)	Blurry vision	Decreased VA
	Pain: None or mild to moderate	Pain (25% have no pain), lid swelling with edema
	Corneal edema: Diffuse, limbus to limbus*	Conjunctival injection, hyperemia
	Pupil: Dilated, irregular, nonreactive*, increased IOP*	Anterior chamber: Marked inflammatory response with hypopyon
	Anterior chamber: Mild to severe reaction with cells, flare, hypopyon, fibrin	Inflammation in entire ocular cavity*—vitreous involvement present
	Signs and symptoms are limited to anterior chamber*	
	Gram stain and culture negative	

(continued)

Table 2.1 (continued)

Differences between TASS and endophthalmitis		
	TASS	**Endophthalmitis**
Treatment	Rule out infection Daily observation Intensive corticosteroids Monitor IOP closely for signs of damage to trabecular meshwork and side effects of steroids	Culture anterior chamber and vitreous fluid Intravitreal and topical antibiotics Vitrectomy in selected cases

TASS can be treated with frequent administration of topical steroids. Toxic substances which have been shown in studies to cause damage to corneal endothelial cells are preoperative disinfectant, intraocular irrigating solution, highly concentrated intraocular medicine, preservatives, remnants of cleaning solutions for surgical devices, hydrogen peroxide, or the insertion of air into the anterior segment.

References: Toxic Anterior Segment Syndrome (TASS)

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Retained Lens Fragments (Figs. 2.2 and 2.3)

Patients with retained lens fragments after cataract surgery may develop marked intraocular inflammation with hypopyon in the absence of infection (Figs. 2.2 and 2.3). However, concomitant endophthalmitis also may be present and it is important to make the correct diagnosis. It is possible that the

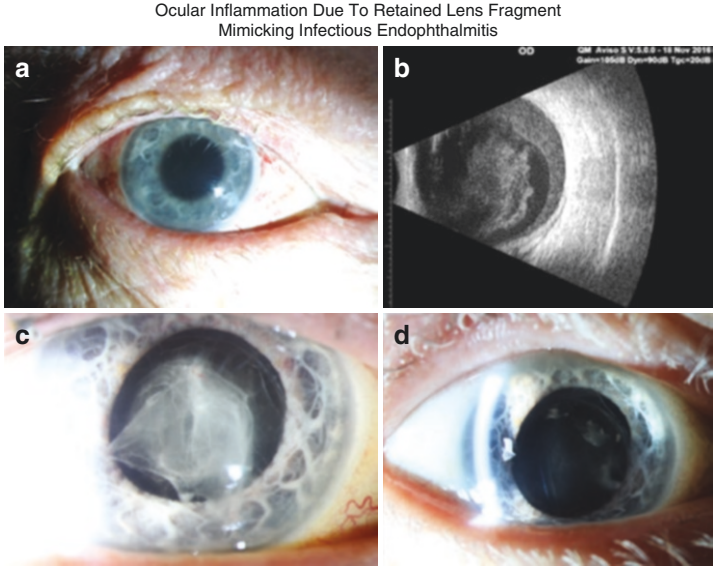

Figure 2.2 Retained lens fragments. A 79-year-old man with acute-onset postoperative endophthalmitis. (**a**) Slit-lamp examination revealed conjunctival congestion, corneal edema, and an anterior chamber inflammation with small hypopyon. (**b**) Ultrasound B-scan showed moderate density echogenic vitreous opacities filling the globe suggestive of membranes with vitreous debris. The patient underwent tap and intravitreal injections (vancomycin, ceftazidime, dexamethasone) followed by gradual resolution of inflammation. Microbiology culture report was negative. (**c**) Slit-lamp photograph at day 2 after intravitreal antibiotics shows contracting fibrin in the anterior chamber. (**d**) Two weeks follow-up exam showed quiet conjunctiva, clear cornea with resolution of anterior chamber inflammation. At 1-year follow-up, the visual acuity was 20/30

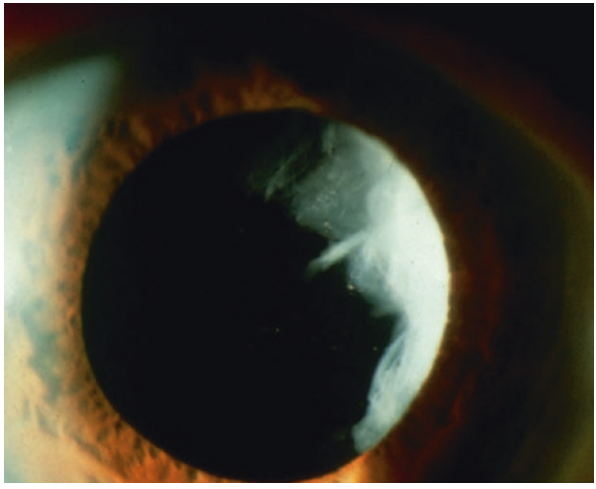

FIGURE 2.3 Retained lens fragments

eyes with retained lens fragments may be at increased risk for endophthalmitis. Neither the presence of pain nor the duration of time after surgery are absolute differentiating points between retained lens fragments and endophthalmitis.

Diagnostic ultrasound is a useful tool in evaluating eyes with dense vitritis after cataract extraction when retained lens material is suspected. Lens material typically appears as reflective, mobile material in the vitreous cavity. Lens material may be involved with extensive epiretinal inflammatory membranes, however, and may not be mobile at the time of examination.

References: Retained Lens Material

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Flare-Up of Preexisting Uveitis

Patients with preexisting uveitis may have exacerbation of their uveitis after cataract surgery and may mimic endophthalmitis (Fig. 2.4). Diagnosis, control of inflammation, preoperative management, particularities of the surgical techniques, and postoperative complications in patients with a history of uveitis are essential to good vision.

Inflammation should be controlled in patients with preexisting uveitis before proceeding with elective intraocular surgery. Frequent administration of topical anti-inflammatory drugs as well as systemic administration of corticosteroids or corticosteroid-sparing agents may be utilized in such cases once endophthalmitis is ruled out.

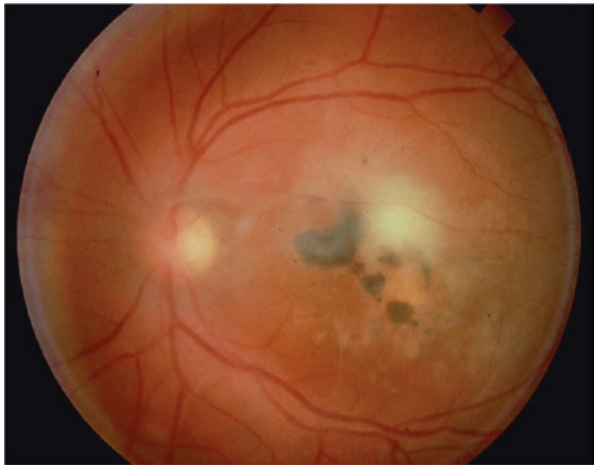

FIGURE 2.4 Flare-up of preexisting uveitis. A 70-year-old female patient with urinary tract infection and initial early diagnosis of endogenous endophthalmitis presented with painless decrease in vision and vitreous floaters. The fundus examination showed presence of pigmented scars (from toxoplasmosis) at the posterior pole with active patch of retinitis and creamy-white opacities in the vitreous

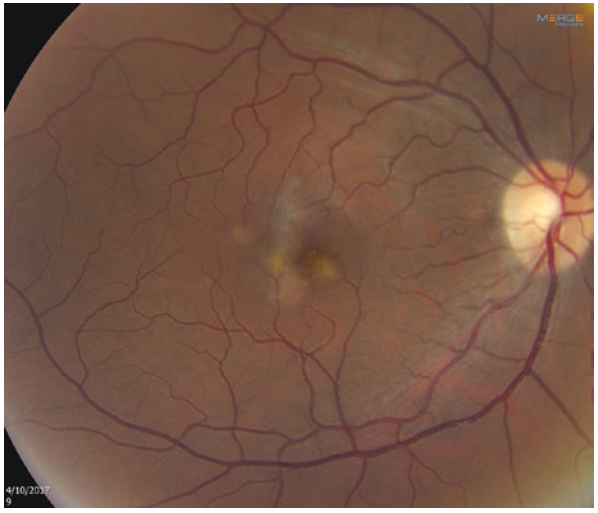

FIGURE 2.5 Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE): A 30-year-old man presented with decreased vision (20/40) and floaters in the right eye for 2 weeks. On ocular examination, anterior segment was unremarkable and fundus picture showed presence of yellowish white exudates adjacent to fovea. After excluding the infectious causes, the patient was started on oral corticosteroids in tapering doses. The visual acuity improved to 20/20 with few RPE changes adjacent to fovea at 2 months

References: Flare-Up of Preexisting Uveitis

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Vitreous Hemorrhage

Chronic long-standing vitreous hemorrhage may present with mild to moderate inflammation of anterior segment and restricted view of the posterior segment (Figs. 2.6, 2.7, and 2.8).

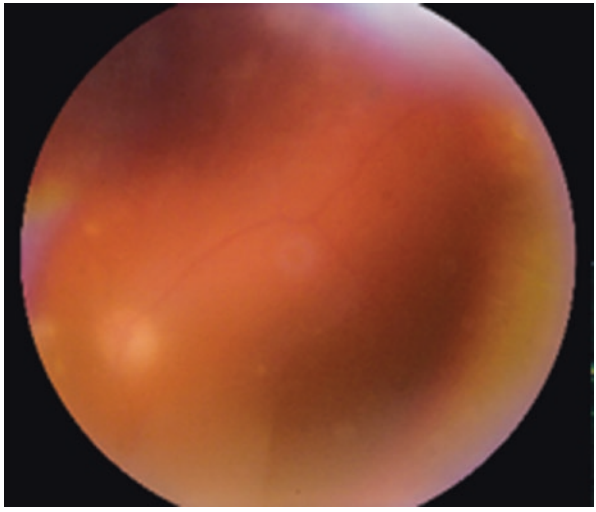

FIGURE 2.6 Vitreous hemorrhage. A 72-year-old man with left eye vitreous hemorrhage. Hazy view of the posterior segment may mimic endophthalmitis

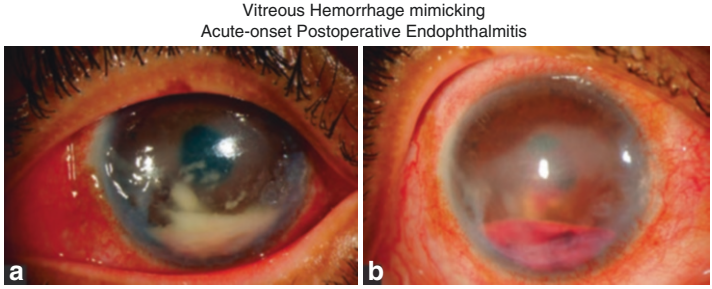

FIGURE 2.7 (**a**) Slit-lamp photograph of hypopyon from old vitreous hemorrhage on the initial examination and (**b**) hypopyon from a combination of old and new vitreous hemorrhage 1 week later

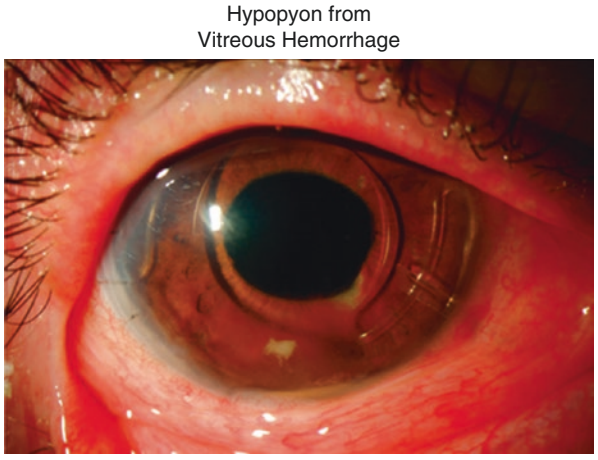

FIGURE 2.8 Slit-lamp photograph of hypopyon and clump of white debris in the anterior chamber on the initial examination

Chronic long-standing vitreous hemorrhage may have an appearance similar to endophthalmitis when the hemorrhage becomes white-gray color after degenerative changes in the hemoglobin content. These clinical features can mimic as endophthalmitis, but the relatively quiet eye can help in excluding endophthalmitis.

Perivasculitis and intraretinal hemorrhage may be early signs of endophthalmitis.

References: Vitreous Hemorrhage

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Retinoblastoma

In children, retinoblastoma may mimic endophthalmitis (Fig. 2.9). It is important to differentiate between endophthalmitis (pseudo-retinoblastoma) and retinoblastoma as the management is entirely different for the two entities. Shields et al. (2013) reported a retrospective series of 604 patients who presented as pseudo-retinoblastomas, and only 2% (10) were due to endogenous endophthalmitis. In a series reported in 1991 by Shield et al., among 500 patients presenting with pseudo-retinoblastoma, endophthalmitis was reported in only two cases (0.4%).

Endophthalmitis usually has prominent inflammation of anterior segment, hypopyon, or synechiae formation. Ultrasonography and CT scan are useful investigations which may show the presence of diffuse faint vitreous echoes in the case of endophthalmitis while mass lesion or dystrophic calcification in case of retinoblastoma.

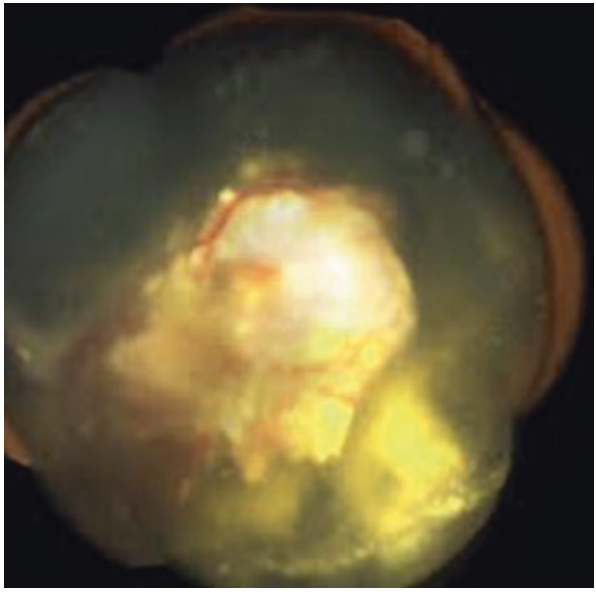

FIGURE 2.9 Retinoblastoma with white calcific deposits on the retina

References: Retinoblastoma

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Uveal Melanoma

Uveal melanoma can mimic uveitis in adults (Fig. 2.9). The disease is vision threatening as well as potentially fatal. Feng et al. (2014) reported the incidence of uveal melanoma about 1200–1500 new cases per year in the United States.

Male sex, age older than 65 years, and delay in presentation are well-known risk factors.

Uveal melanoma cases may present asymptomatically. Rarely, anterior segment inflammation may be the initial presenting feature of uveal melanoma. Mixture of tumor cells, pigment cells, and inflammatory cells are present in the anterior chamber while in immune-mediated anterior uveitis T-cells are present in the anterior chamber.

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Retained Triamcinolone Acetonide

Retained triamcinolone may present with deposits in the anterior chamber also known as pseudoendophthalmitis. These sterile postinjection inflammatory responses are due to the migration of medication to the AC (Figs. 2.10 and 2.11). Rarely true endophthalmitis can occur after triamcinolone intravitreal injection.

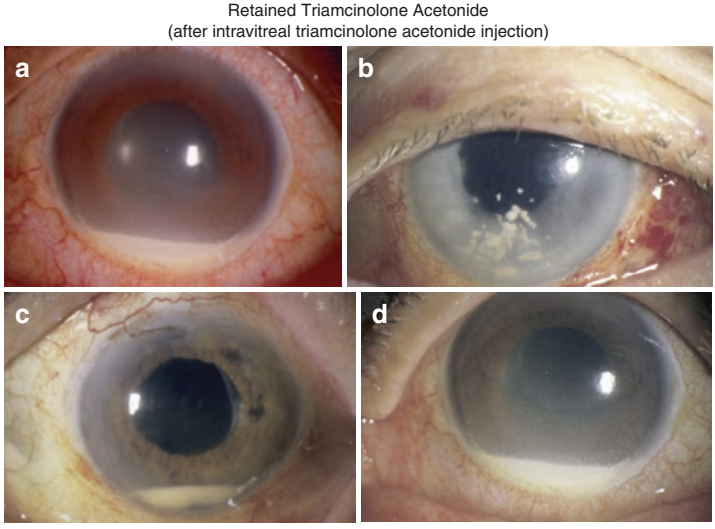

FIGURE 2.10 Patients showing pseudoendophthalmitis after IVTA injection

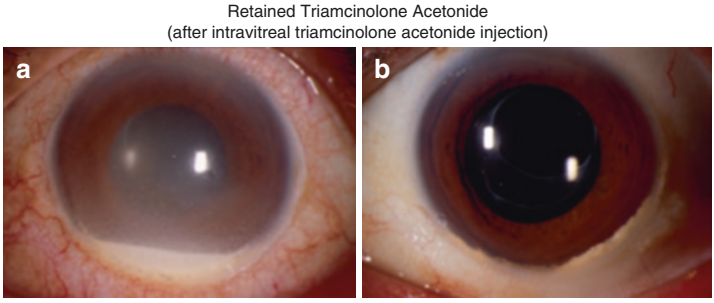

FIGURE 2.11 (**a**) Retained triamcinolone acetonide particles mimicking hypopyon and pseudoendophthalmitis. (**b**) The pseudoendophthalmitis resolved on follow-up

References: Retained Triamcinolone Acetonide Particles

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Viral Retinitis

Viral retinitis including acute retinal necrosis, infectious retinitis caused by cytomegalovirus, herpes simplex, and herpes zoster may have clinical presentation overlapping with endophthalmitis (Fig. 2.12). The patient may present with yellow-white retinitis lesions and/or perivasculitis, with or without retinal hemorrhage. Evaluation of the systemic status of such patients is important as an internist as well as ophthalmologist are essential for the management of these patients.

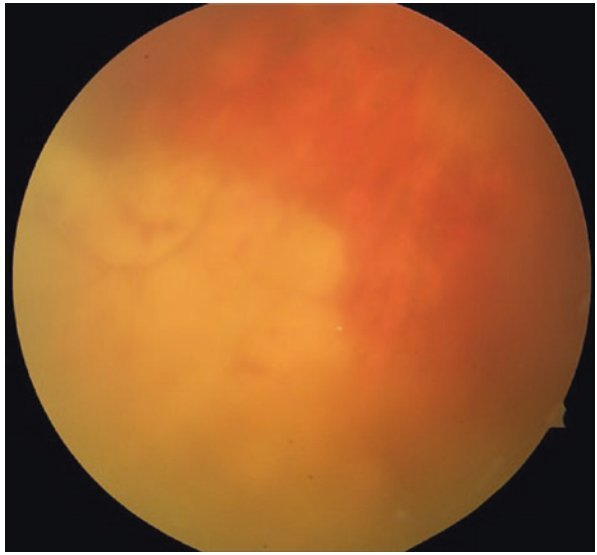

FIGURE 2.12 A 68-year-old man presented with 1-week history of blurred vision in right eye. The patient had positive history of chicken-pox in childhood. His best corrected visual acuity was 20/80 in the right eye and slit lamp examination showed fine keratic precipitates and 2+ cells in the anterior chamber. Fundus picture showed hazy view with white retinitis patch suggestive of acute retinal necrosis

References: Viral Retinitis

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Pseudoendophthalmitis from Intravitreal Injections

A cluster of injection-related sterile intraocular inflammation was reported within the first 3 months after approval of aflibercept (Eylea; Regeneron, Inc., Tarrytown, NY) by the US Food and Drug Administration on November 18, 2011. Figure 2.13 shows a case of pseudoendophthalmitis from intravitreal aflibercept injection.

In 2015, Kim et al. reported sterile inflammation after intravitreal injection of aflibercept in a Korean population. In this retrospective, single-center study, four cases of postinjection sterile inflammation were identified from 723 aflibercept injections in 233 patients. Patients presented 1–13 days after intravitreal aflibercept injection (mean, 5 days). Sterile inflammation after intravitreal aflibercept injection in this case series typically presented without pain, and the visual outcomes were generally favorable. However, 60% (9/15) patients with sterile inflammation after intravitreal aflibercept injection presented with pain among the cases (from February 2012 until the end of March 2012) reported by the Therapeutic Surveillance Subcommittee of the American Society of Retina Specialists. Visual acuity generally recovered to baseline levels with nearly identical mean visual acuities at baseline in these cases.

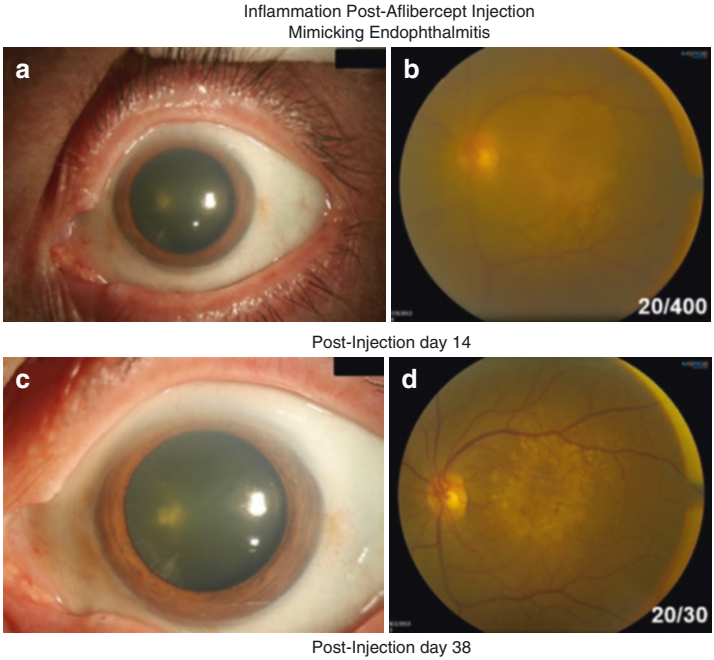

FIGURE 2.13 Post-aflibercept inflammation. A 57-year-old female patient with neovascular age-related macular degeneration (wet-AMD) presented 14 days after intravitreal aflibercept injection with blurred vision (20/400). (**a**) and (**b**) Slit-lamp examination showed quiet conjunctiva, well-dilated pupil, vitritis, and hazy view of the posterior segment. (**c**) and (**d**) At day 38 follow-up, the inflammation and infection resolved with best corrected visual acuity improved to 20/30

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Chapter 3
Diagnosis of Endophthalmitis: Clinical Presentation, Microbiology, and Echography

Clinical Presentations

The diagnosis of endophthalmitis can be made based on clinical examination findings. The patient may present with gradual or sudden onset of symptoms including lid swelling, pain, redness, discharge, and decrease in the vision. Slit-lamp examination may show lid swelling, conjunctival congestion, chemosis, glaucoma implant exposure, corneal edema, epithelial defect, corneal infiltrate, hypopyon, infiltrates/fibrin membrane in the anterior chamber, plaque inside the capsular bag, loss of fundus red reflex, or infiltrates in the vitreous cavity (Figs. 3.1, 3.2, and 3.3).

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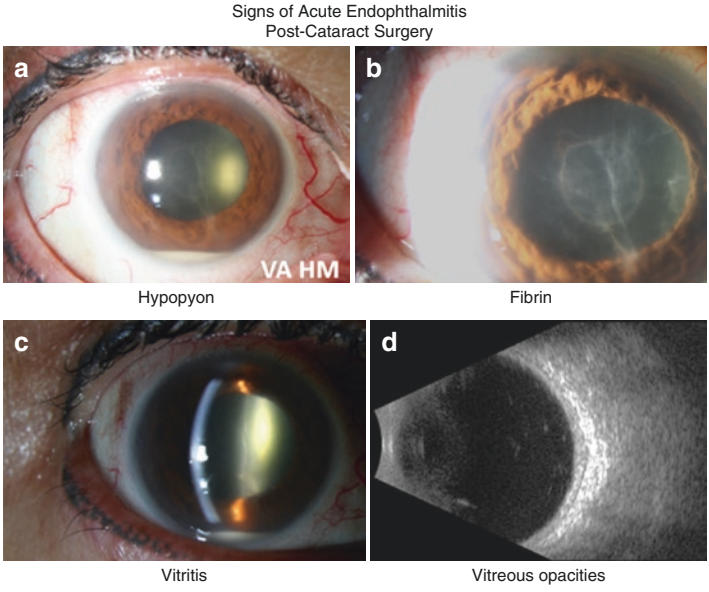

FIGURE 3.1 Acute-onset endophthalmitis. Signs of acute-onset postoperative endophthalmitis following cataract surgery. (**a**) Conjunctival congestion, mild corneal edema, hypopyon, and hand motions (HM) vision on the day of presentation. (**b**) Fibrinous membrane in the anterior chamber and pupillary area. (**c**) Vitritis and hazy view of the posterior segment. (**d**) Ultrasound demonstrates presence of echogenic shadows in the vitreous cavity

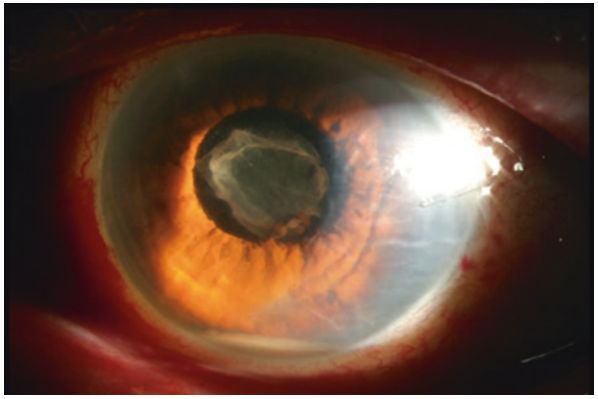

FIGURE 3.2 Acute-onset endophthalmitis. A 73-year-old female patient with acute-onset postoperative endophthalmitis following cataract surgery presented with conjunctival congestion, mild corneal edema, hypopyon, fibrinous membrane in the pupillary area, and hazy view of the posterior segment

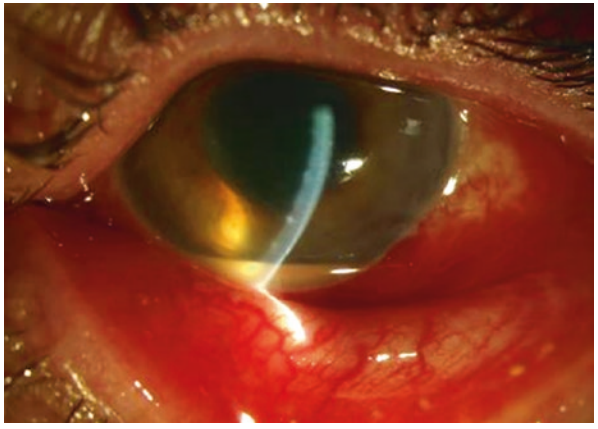

FIGURE 3.3 Acute-onset endophthalmitis. A 69-year-old male patient with acute-onset postoperative endophthalmitis following cataract surgery presented with conjunctival congestion, mild corneal edema, hypopyon, fibrinous reaction in the anterior chamber, and hazy view of the posterior segment

Microbiology

How to Perform TAP and Inject

Treatment of endophthalmitis includes obtaining a vitreous sample for cultures and injection of intravitreal antimicrobials. By obtaining vitreous sample and using it to identify the causative microorganisms, further management of the patient can be planned after the initial empiric treatment.

Traditional approach for vitreous aspiration (TAP) as per Endophthalmitis Vitrectomy Study (EVS): The Endophthalmitis Vitrectomy Study (EVS) provided guidelines for the vitreous tap as well as pars plana vitrectomy (PPV). As per the EVS, 0.2–0.5 mL of vitreous sample was collected by way of the pars plana either by needle aspiration or by vitreous biopsy through a single sclerotomy using a vitrectomy cutter. After the TAP, injections of intravitreal antibiotics were given in separate syringes. If an adequate sample could not be safely obtained, a vitreous biopsy using a vitrectomy instrument was performed. The EVS reported that in a subgroup of patients with presenting visual acuity of hand motions or better, there was no difference in the visual outcome (immediate PPV or TAP). However, in the subgroup of patients with presenting visual acuity of light perception only, visual outcomes were better with immediate PPV compared to TAP.

Current day TAP and inject options (Fig. 3.4)*:* The procedure can be performed in the outpatient clinic under local anesthesia (retro-/peribulbar block). The lids and conjunctiva are prepared with 5% povidone–iodine followed by placement of the speculum. A 23-gauge butterfly needle mounted on 10 cc syringe is inserted through pars plana, and approximately 0.2–0.5 mL of vitreous is aspirated once the needle tip is at the center of the globe. Once the vitreous sample is removed, antimicrobials are injected in to the vitreous cavity. The vitreous sample obtained is sent for the microbiology evaluation including smear and culture. In case of growth on the culture media, antimicrobial susceptibility tests are further performed. A 25G or 27G needle can also be used for vitreous aspiration.

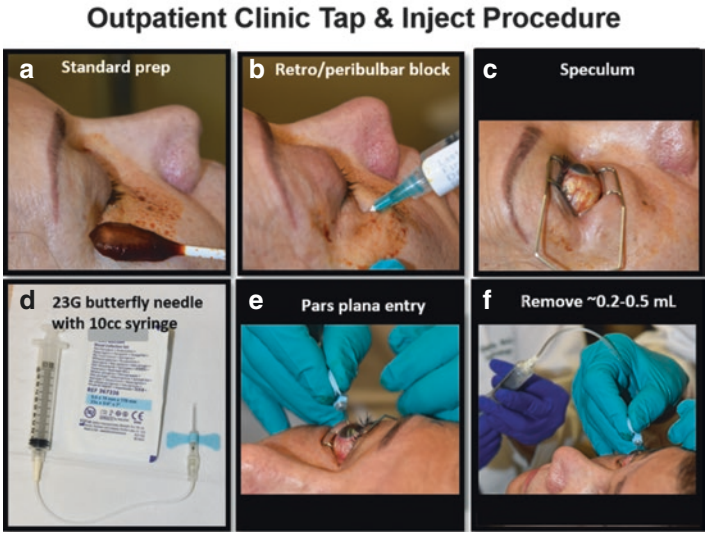

FIGURE 3.4 Vitreous TAP. (**a**) Standard preoperative preparation with povidone–iodine. (**b**) Local anesthesia (retrobulbar or peribulbar block) with lidocaine solution. (**c**) Speculum placement. (**d**) Use 23-gauge butterfly needle on 10 cc syringe for tap. (**e**) Insert 23-gauge butterfly needle on 10 cc syringe through pars plana. (**f**) Tap 0.2-0.5 ml of vitreous by slow suction followed by antibiotic injection through pars plana

Other modifications: A modification of the vitreous TAP procedure has been recently published. In this modified technique under subconjunctival anesthesia, a valved 25-gauge trocar cannula is inserted through pars plana, and subsequent aspiration of exudates/vitreous and antimicrobial injections are performed through the single port. In a prospective, randomized, single-center trial, Vahedi et al. compared comfort and procedural facility using 25-gauge trocar cannula as a port to aspirate vitreous and inject intravitreal antibiotics to treat acute-onset endophthalmitis. Since there were no significant differences in the patient comfort, physician ease-of-use scores, vitreous sample volume, successful vitreous taps, and microbiological yield between the two groups, the study

concluded that 25-gauge trocar technique is a viable option (Fig. 3.5). Comparison of traditional versus 25-gauge trocar cannula-based vitreous TAP is shown in Table 3.1.

Intravitreal antimicrobial injection

Once the vitreous sample is obtained, empiric antimicrobials are injected intravitreally. The selection of antimicrobial agents is important, and the decision should be based on the type of endophthalmitis and suspected microbiological profile. Using 30G needle mounted on 1 cc syringe, antimicrobials are injected intravitreally:

- For presumed bacterial cases: Intravitreal vancomycin and ceftazidime via separate syringes. Intravitreal dexamethasone can be considered.
- For presumed fungal cases: Intravitreal amphotericin B or voriconazole without intravitreal steroids.

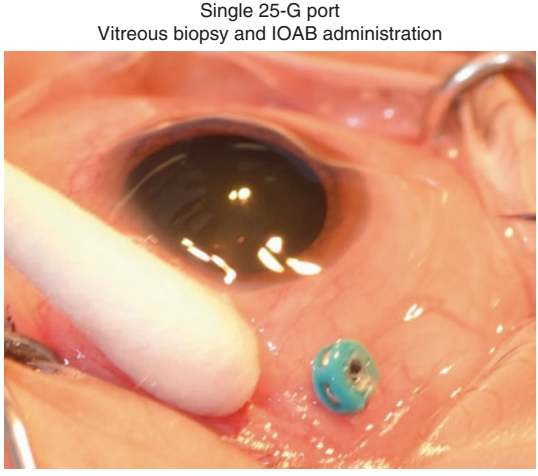

FIGURE 3.5 25-gauge trocar cannula based TAP and inject

Table 3.1 A comparison of the traditional versus 25-gauge trocar cannula-based vitreous TAP

	Standard 23-gauge needle-based TAP and inject	**25-gauge trocar cannula-based TAP and inject**
Instrument cost	Low	Higher
Anesthesia commonly utilized	Retro-/ peribulbar	Subconjunctival
Number of needle entries in the eye	Multiple	One

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Results of AC TAP vs Vitreous TAP

Microbiologic diagnosis of endophthalmitis is made based on the identification of organisms from samples obtained from either anterior chamber fluid or vitreous. Culture positivity rates are reported to be higher with aqueous humor (approximately 22–30% of cases) compared to vitreous (approximately 40–69% of cases).

References: Results of AC TAP Vs. Vitreous TAP

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Culture Media

To detect and identify causative organisms, aqueous and vitreous sample obtained from the biopsy is analyzed as follows:

- Staining of the smear
- Inoculation of culture media

Various stains and culture media used for microbiological diagnosis are discussed and shown in Table 3.2 and Fig. 3.6.

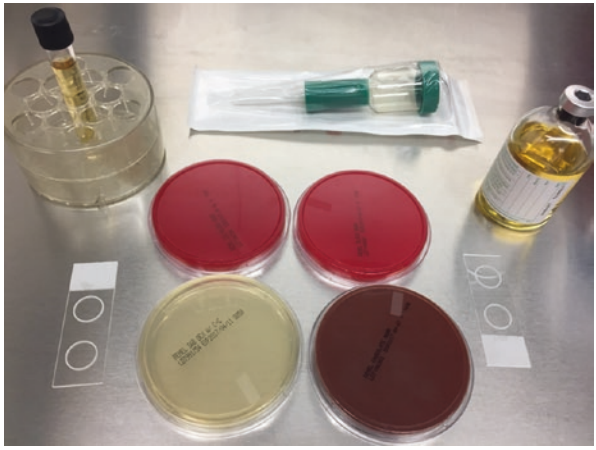

FIGURE 3.6 Culture media to identify causative organisms from aqueous and vitreous samples

TABLE 3.2 Stains and culture media used for microbiological diagnosis

Stains for smears	
Gram stain	Gram-positive organisms versus gram-negative organisms
Acid fast stains	For *Mycobacteria*
Calcofluor white	Fluorescent stain (fungi, microsporidia, and *Acanthamoeba*)

Table 3.2 (continued)

Stains for smears	
Culture media	
Chocolate agar	• Used as an enriched medium for the recovery of fastidious organisms (i.e., *Neisseria gonorrhoeae* and *Haemophilus influenzae*) • Also, is used as a general-purpose medium for the recovery of bacteria, yeasts, and molds from aqueous and vitreous fluids
5% sheep blood agar	• A general-purpose medium for recovery of the most common bacterial and fungal endophthalmitis isolates
Thioglycollate broth	• An all-purpose, enriched medium for the recovery of low numbers of aerobic or anaerobic (including *P. acnes*) organisms form ocular fluids and tissues
Anaerobic blood agar	• An all-purpose medium for the recovery of both anaerobic and facultative anaerobic organisms • Should be included for all chronic endophthalmitis or where *P. acnes* is suspected
Sabouraud agar	• A selective medium used to promote the growth of fungi (yeasts and molds)
Blood culture bottles	• Contain specially prepared for the recovery of both aerobic and anaerobic bacteria and fungi • Undiluted fluids, inoculated in pediatric bottles; diluted samples, inoculated in adult bottles
Lowenstein-Jensen medium	• A selective medium for the recovery of acid-fast organisms (*Mycobacteria, Nocardia*) from aqueous and vitreous fluids

Other Tests: PCR or PNA–FISH

PCR—PCR is an easy, cheap, simple to understand, highly sensitive, reliable technique to repeatedly replicate a focused segment of DNA to produce millions to billions of copies of a specific product for sequencing, cloning, and analysis. One major limitation of PCR is that precise sequence is required in order to generate the primers to allow selective amplification. Also, possibility of error by DNA polymerases and nonspecific binding of primers may result in incorrect interpretation.

PNA–FISH—Molecular techniques are increasingly used to identify pathogens. Fluorescence in situ hybridization (FISH) is a technique whereby DNA probes labeled with fluorophores are attached to a target DNA for identification. The FISH technique has been used for over 20 years for the detection of trisomy in genetics. A new molecular application of fluorescence hybridization can be used to rapidly identify microorganisms (*Staphylococcus*, *Pseudomonas*, *Candida* species) in blood cultures from patients in the intensive care unit with septicemia. FISH has been shown to improve patient outcomes in terms of survival, hospital stay, and total cost.

In ophthalmology, endophthalmitis remains an important cause of ocular morbidity. Changes in prevalence of causative organisms and their antimicrobial susceptibilities over time have been reported. Current methodology of plating and subsequent reading of growth is labor and time intensive. Consequently, there exists a growing need for more rapid and accurate detection of pathogens. If PNA–FISH is proven useful for quick diagnosis of endophthalmitis, it can further be utilized for diagnosis of various other ocular infections.

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Echography

In order to achieve the optimal treatment outcome in cases presenting with endophthalmitis, prompt diagnosis and institution of effective therapy treatment are necessary. Echography is often necessary because of the opaque media preventing detailed visualization of the posterior segment. Echographic features in combination with clinical presentation aid in the diagnosis and influence clinical decision-making. Echographic features including vitreous opacities, vitreous membranes, retinal detachment, subhyaloid opacities, subretinal opacities, choroidal detachment, fundus thickening, and signs of orbital inflammation (Table 3.3) were reported to be associated with endophthalmitis.

In the Endophthalmitis Vitrectomy Study, echography was performed when the ocular media precluded direct visualization of the posterior pole to determine if choroidal detachment, retinal detachment, or both were present.

Initial echographic findings in infectious endophthalmitis are nonspecific with respect to visual prognosis and causative microorganisms (Fig. 3.7). The presence of echographic findings as mentioned above correlates with worse visual prognosis, but there is no correlation with the possible causative organism.

Table 3.3 Differences between infectious and noninfectious ocular inflammation

Clinical features	Infectious	Noninfectious
Pain	Moderate to severe pain	Usually mild pain
Vision loss	Severe	Mild to moderate
Fibrin	Always present	Rare
Hypopyon	Very common	Rare
Vitreous opacity	Usually prominent	Usually mild
Conjunctival vascular congestion	Very common	Often absent
Clinical course	Rapidly progressive	Slow-improvement

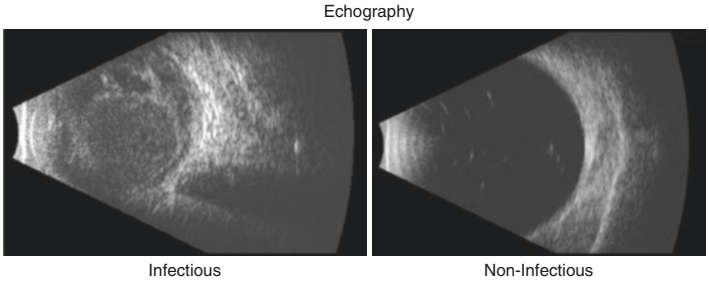

FIGURE. 3.7 Echographic appearance of eye in infectious versus noninfectious ocular inflammation

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Chapter 4
Endophthalmitis Clinical Categories (Incidence Rates, Signs/Symptoms, Risk Factors, Microbiology, Treatment, and Follow-Up)

Postoperative Endophthalmitis: Acute-Onset Postoperative Endophthalmitis Following Cataract Surgery

Acute-onset postoperative endophthalmitis occurs within 6 weeks of cataract surgery or secondary intraocular lens (IOL) implantation.

Incidence

Reported rates vary between about 0.03 and 0.2%.

Signs/Symptoms

The patient presents with lid swelling, pain, redness, discharge, marked decrease in the vision, etc. Slit-lamp examination may show lid swelling, conjunctival congestion, chemosis,

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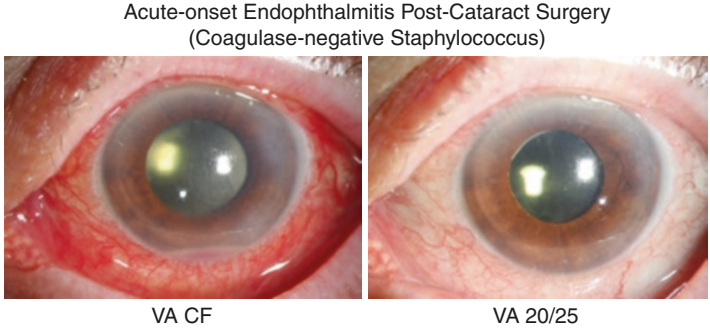

FIGURE 4.1 Acute-onset endophthalmitis. A 78-year-old male patient with acute-onset postoperative endophthalmitis following cataract surgery. (**a**) The patient presented with conjunctival congestion, mild corneal edema, hypopyon, hazy view to the posterior segment, and counting fingers (CF) vision. Patient underwent vitreous tap and intraocular antibiotics (vancomycin and ceftazidime) and was culture positive for coagulase-negative Staphylococcus resistant to all fluoroquinolones. (**b**) At 6-month follow-up, the patient regained best corrected visual acuity of 20/80 with resolution of inflammation. At 2-year follow-up, the patient achieved visual acuity of 20/20

corneal edema, epithelial defect, hypopyon, infiltrates/fibrin membrane in the anterior chamber, loss of red reflex from the retina, and infiltrates in the vitreous cavity (Fig. 4.1).

Risk Factors

- Preoperative:
  - Diabetes mellitus
  - Older age
  - Blepharitis
  - Use of corticosteroids
  - Prosthesis in fellow eye
  - Active systemic infection

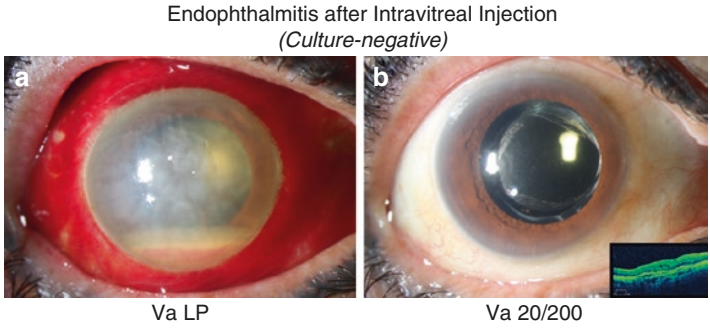

FIGURE 4.2 Acute-onset endophthalmitis. A 69-year-old male patient with acute-onset postoperative endophthalmitis following cataract surgery and anterior chamber intraocular lens implantation following posterior capsular rent. (**a**) The patient presented with conjunctival congestion, corneal edema, hypopyon, fibrinous membrane in the anterior chamber, hazy view of the posterior segment, and hand motions (HM) vision. Patient underwent vitreous tap and intraocular antibiotics. (**b**) At 1-year follow-up, the patient regained best corrected visual acuity of 20/50

- Intraoperative:
  - Failure to use topical povidone–iodine preparation
  - Prolonged surgery
  - Intraoperative complications or Posterior capsular rupture (Fig. 4.2)
- Postoperative:
  - Inpatient status
  - Wound leak (Fig. 4.3)
  - Contaminated eye drops

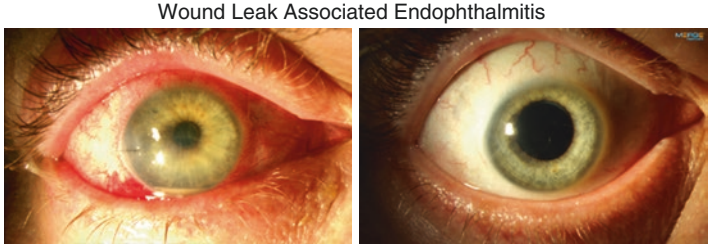

FIGURE 4.3 Wound leak-associated endophthalmitis. A 57-year-old male with acute-onset endophthalmitis after cataract surgery. (**a**) Slit-lamp examination revealed conjunctival congestion, corneal edema, anterior chamber inflammation, hypopyon, and single nylon suture placed temporally with a leaking clear corneal wound. Visual acuity was hand motions (HM). The patient underwent pars plana vitrectomy and additional suture placement onto the leaking wound. (**b**) 2 months after suture removal visual acuity improved to 20/25

Microbial Isolates

Following are the microorganisms most commonly associated with acute-onset postoperative endophthalmitis following cataract surgery (Endophthalmitis Vitrectomy Study data):

- Coagulase-negative *Staphylococci*—70.0%
- *Staphylococcus aureus*—9.9%
- *Streptococcus* species—9.0%
- *Enterococcus* species—2.2%
- Gram-negative bacteria—5.9%
- Other gram-positive bacteria—3.1%

Initial Management of Acute-Onset Postoperative Endophthalmitis

- **Vitreous TAP or pars plana vitrectomy**
- **Injection if intravitreal antimicrobial agents**

Vitreous tap: A small needle is inserted through pars plana into the vitreous, and a sample is withdrawn. The vitreous sample is then sent to the microbiology laboratory for culture and analysis to identify the microorganism and the antibiotic or antifungal medication that it is sensitive to. Following are important considerations while performing vitreous tap:

- *Location*—Clinic lane/minor procedure room/operating room.
- *Anesthesia*—Peribulbar/retrobulbar/topical may be considered.
- *Equipment*—23 gauge, 1 inch needle (butterfly-style needle may be helpful) (Fig. 3.4).
- *Microbiology*—Culture plates or blood culture bottles for specimen (Fig. 3.6).

Pars plana vitrectomy (PPV): Pars plana vitrectomy is a surgical procedure that involves removal of infectious infiltrates and vitreous gel from the eye. A vitreous sample is sent to the microbiology laboratory for culture and analysis (Fig. 4.4). Following are important considerations while performing PPV:

- *Location*—Operating room
- *Anesthesia*—Peribulbar/retrobulbar/topical
- *Equipment*—Transconjunctival small gauge, standard 3 port PPV, or 2 port approach if view is limited

Intravitreal antimicrobials (Fig. 4.5)
For presumed bacterial cases (in separate syringes):

- Vancomycin 1 mg/0.1 mL (for coverage of gram-positive organisms)
- Ceftazidime 2.25 mg/0.1 mL (for coverage of gram-negative organisms)
  - Ceftriaxone 2 mg/0.1 mL may be substituted for ceftazidime if this is more readily available.

- Amikacin 0.4 mg/0.1 mL can be substituted for ceftazidime but has the risks of aminoglycoside macular toxicity.
- Dexamethasone 4 mg/0.1 mL may be considered for acute-onset bacterial cases but should be avoided in suspected fungal endophthalmitis and delayed-onset (chronic) endophthalmitis until the organism is identified.

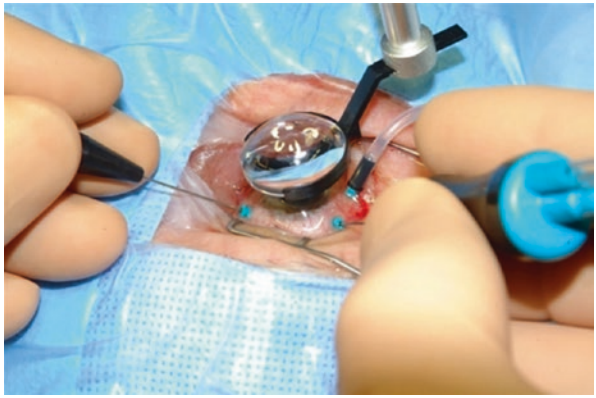

FIGURE 4.4 Pars plana vitrectomy (25 gauge assisted by wide field viewing)

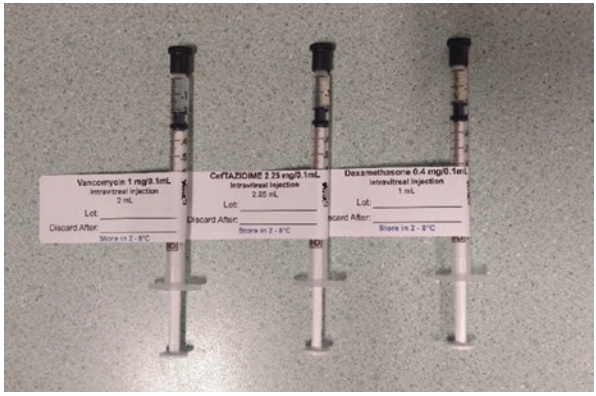

FIGURE 4.5 Intravitreal injections in syringes. Syringes (1 cc) filled with vancomycin (1 mg/0.1 mL), ceftazidime (2.25 mg/0.1 mL), and dexamethasone (0.4 mg/0.1 mL). The reconstituted syringes have a lot number, date of expiration, and storage guidelines (2–8 °C)

For presumed fungal cases:

- Amphotericin B 0.005 mg/0.1 mL
- Voriconazole 0.1 mg/0.2 mL

Follow-Up Management of Acute-Onset Postoperative Endophthalmitis (Fig. 4.6)

First Morning After Initial Treatment

- Topical antimicrobials
  - Consider fortified topical antibiotics if available:
    Vancomycin 25 mg/mL hourly during the day
    Ceftazidime 50 mg/mL hourly during the day
  - Alternatively, commercially available topical antibiotics are used.
  - For fungal cases, topical amphotericin B has poor intraocular penetration and is not used.
- Topical steroids four times daily (not for suspected/proven fungal infection)
- Topical cycloplegics daily

*Topical antibiotics hourly may result in corneal epithelial toxicity as a result of preservatives in commercial preparations. Topical medications are generally not used during night hours while sleeping. Subconjunctival antibiotics at the time of initial treatment provide adequate ocular surface medication for nighttime coverage.

Two to Three Days After Initial Treatment

- If clinically improving—Continue to observe and taper topical steroids over several weeks.
- If clinically worsening:
  - Consider repeat intraocular cultures and/or reinjection of intraocular antibiotics (and possibly intraocular steroids in acute-onset bacterial cases).
  - Consider PPV if not performed initially.

  Change antibiotics if indicated by initial culture results.

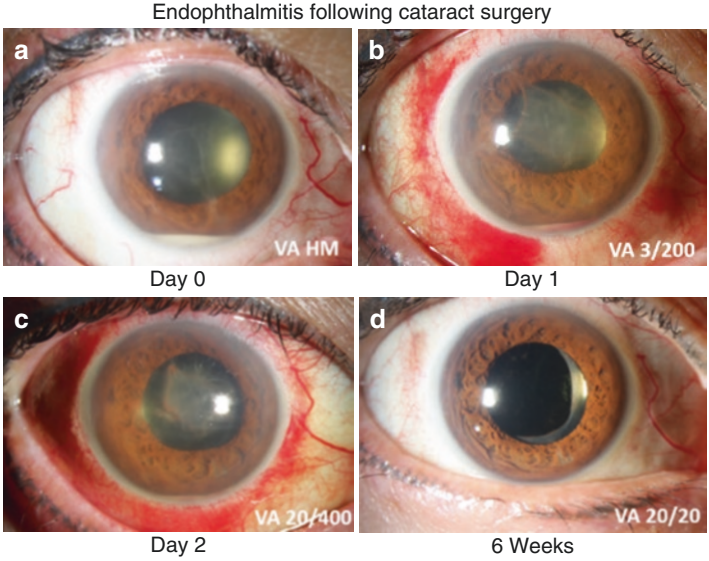

FIGURE 4.6 Follow-up of endophthalmitis. Follow-up course of a patient with acute-onset postoperative endophthalmitis following cataract surgery. (**a**) Conjunctival congestion, mild corneal edema, hypopyon, and hand motions (HM) vision on the day of presentation (**b**) 1 day after vitreous tap and intraocular antibiotics hypopyon reduced, fibrinous membrane contracted in the pupillary zone, and vision improved to 3/200 (**c**) At 2-day follow-up, inflammation reduced further and vision improved to 20/400 (**d**) At 6-week follow-up, the patient regained best corrected visual acuity of 20/20 with resolution of inflammation

References: Acute-Onset Postoperative Endophthalmitis Associated with Cataract Surgery

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Endophthalmitis Vitrectomy Study (EVS)

The Endophthalmitis Vitrectomy Study (EVS) was a randomized clinical trial (RCT) which provides guidelines for the management of postoperative endophthalmitis following cataract surgery or secondary intraocular lens (IOL) implantation (Tables 4.1 and 4.2).

The findings of EVS should be interpreted with caution, especially when applying its findings to categories of endophthalmitis other than acute-onset postoperative endophthalmitis

Table 4.1 The Endophthalmitis Vitrectomy Study (EVS): enrollment criteria, exclusion criteria, treatment arms, and results

Endophthalmitis Vitrectomy Study (EVS)
EVS enrollment criteria • Acute-onset postoperative endophthalmitis • Within 6 weeks of cataract surgery or secondary intraocular lens (IOL) implantation • Visual acuity between 20/50 and light perception (LP)
EVS exclusion criteria • Other endophthalmitis etiologies • Presence of cloudy cornea preventing pars plana vitrectomy • Preexisting comorbidities (advanced glaucoma, age related macular degeneration) which could result in <20/200 visual acuity outcomes
Patients were randomized into four treatment arms: • PPV without intravenous antibiotics • PPV with intravenous ceftazidime and amikacin • Vitreous tap (TAP) without intravenous antibiotics • TAP with intravenous ceftazidime and amikacin
EVS results • For patients with presenting visual acuity of – Hand motions (HM) or better: No significant differences in visual outcomes Between PPV and TAP With or without intravenous ceftazidime and amikacin – Light perception (LP): PPV was associated with significantly better visual outcomes Threefold increase in frequency of achieving visual acuity 20/40 or better (33% PPV, 11% TAP) Approximately twofold increase in frequency of achieving visual acuity of 20/100 or better (56% PPV, 30% TAP) Twofold decrease in frequency of sustaining severe visual loss defined as visual acuity worse than 5/200 (20% PPV, 47% TAP) – No significant differences in visual outcomes with or without intravenous ceftazidime and amikacin

Table 4.2 The Endophthalmitis Vitrectomy Study (EVS): patient selection, guidelines, conclusions, and comments

EVS: patient selection, guidelines, conclusions and comments
• Patient selection – EVS selected only patients with acute-onset postoperative endophthalmitis within 6 weeks of cataract surgery of secondary IOL implantation – Other forms of endophthalmitis (post-traumatic/endogenous/bleb-associated endophthalmitis) were not studied in EVS
• Cataract surgery techniques at the time of the EVS – Cataract surgery was predominantly extracapsular cataract extraction or limbal tunnel phacoemulsification – Topical antibiotics gentamicin or polymixin B-trimethoprim were commonly used for cataract surgery – Subconjunctival antibiotics (generally gentamicin) were routinely administered during cataract surgery – 10 EVS patents received antibiotics in the irrigating fluid at the time of the cataract surgery and yet developed endophthalmitis.
• EVS criteria and guidelines for selection of initial treatment – Based on visual acuity at presentation HM or better: TAP without systemic antibiotics LP: PPV is preferable if this is achievable – Initial TAP, followed by close observation and PPV when practicable, may lead to excellent outcomes – The EVS results did not report that PPV was contraindicated in eyes with VA HM or better but initial management with TAP is more time and cost efficient
• EVS-Conclusions and comments – Intravenous ceftazidime and amikacin were not reported to be beneficial in the EVS – Oral gatifloxacin and moxifloxacin may achieve vitreous penetration but their value is uncertain – Oral gatifloxacin is no longer available due to systemic adverse events – Systemic antibiotics may be considered in selected patients with more severe signs and symptoms: Rapid-onset Presenting visual acuity of LP Large hypopyon No red reflex

(continued)

Table 4.2 (continued)

EVS: patient selection, guidelines, conclusions and comments
• The role of systemic steroids – All patients in EVS were treated with prednisone 30 mg twice daily for 5–10 days – The value of this treatment is uncertain – There are significant risks especially in diabetic patients

References: Endophthalmitis Vitrectomy Study

- Results of the Endophthalmitis Vitrectomy Study. A randomized trial of immediate vitrectomy and of intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis. Endophthalmitis Vitrectomy Study Group. Arch Ophthalmol. 1995;113(12):1479–96.
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Chronic/Delayed-Onset Postoperative Endophthalmitis Following Cataract Surgery

Chronic endophthalmitis may occur due to the introduction of low virulence infectious organism at the time of intraocular procedure. This slowly progressive chronic endophthalmitis may become clinically apparent months or years after the procedure.

By contrast, delayed-onset postoperative endophthalmitis results from a weakness in the ocular surface allowing entry of organisms. Examples of delayed-onset endophthalmitis include infection through glaucoma filtering blebs, corneal sutures, or fistulas from previous trauma.

However, these terms are used interchangeably in this chapter.

Incidence

Incidence rates are very low. The rates vary depending upon the predisposing risk factors (e.g. thin bleb, inferior bleb, multiple corneal sutures etc).

Signs/Symptoms

In chronic postoperative endophthalmitis the patient presents with persistent inflammation and mild to moderate decrease in the vision. Slit-lamp examination may show low-grade inflammation not responding to topical antibiotics or steroids, posteriorv capsular plaque, and or cells in the vitreous (Fig. 4.7). With delayed-onset endophthalmitis patients present with acute onset of symptoms with red eye and all features hallmark of acute onset endophthalmitis.

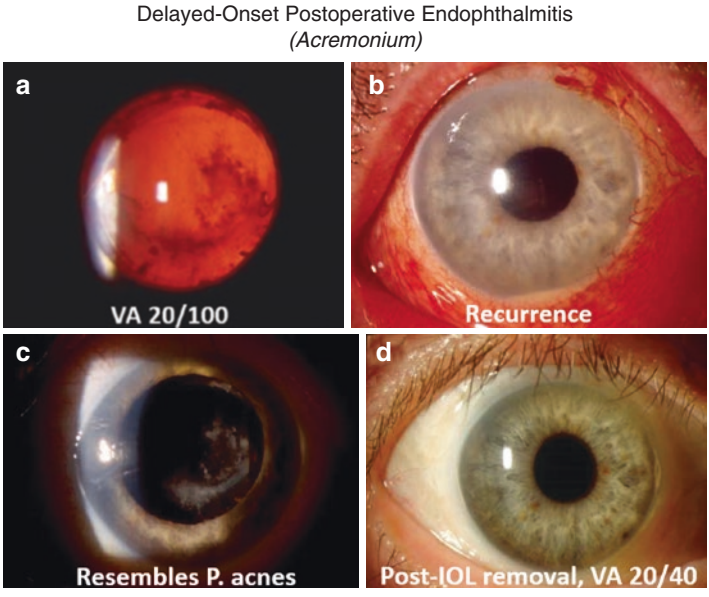

FIGURE 4.7 Chronic/delayed-onset postoperative endophthalmitis. A 70-year-old male patient with delayed-onset postoperative endophthalmitis following cataract surgery. (**a**) The patient presented with low-grade inflammation in the anterior chamber, capsular plaque, and 20/100 visual acuity. (**b** and **c**) Inflammation was recurrent with persisting capsular plaque and low-grade inflammation. Patient underwent pars plana vitrectomy, removal of intraocular lens, capsular bag, and intraocular antibiotics. The vitreous culture was positive for *Acremonium* species. (**d**) At 1-year follow-up, the patient regained best corrected visual acuity of 20/40 with resolution of inflammation

Risk Factors

- Preoperative:
  - Diabetes mellitus
  - Older age
  - Blepharitis
  - Use of corticosteroids
  - Prosthesis in fellow eye
  - Active systemic infection
- Intraoperative:
  - Posterior capsular rupture

Microbial Isolates

Common causative organisms include:

- *Propionibacterium acnes* (Figs. 4.8 and 4.9)
- Coagulase-negative *Staphylococci*
- *Diphtheroid* species
- Fungi (Fig. 4.10)

Initial Management of Delayed-Onset Endophthalmitis

In patients with delayed-onset postoperative endophthalmitis, the microorganisms are usually sequestered in the capsular plaque in these patients. Treatment may involve removal of the capsular plaque along with IOL explantation in addition to pars plana vitrectomy and injection of intravitreal antibiotics.

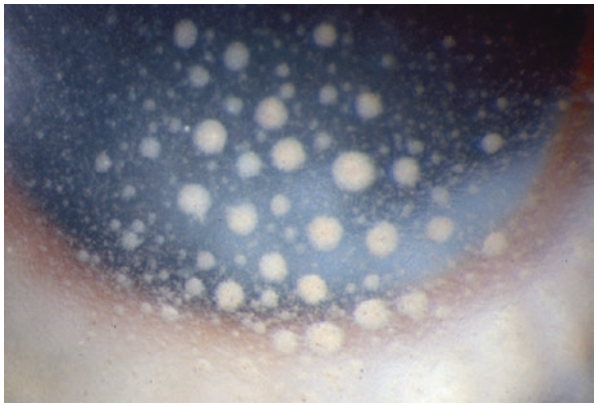

FIGURE 4.8 Chronic/delayed-onset postoperative endophthalmitis. A 69-year-old female patient with delayed-onset postoperative endophthalmitis following cataract surgery. The patient presented with gradual painless decrease in vision, conjunctival congestion, prominent granulomatous keratic precipitates, and 20/400 visual acuity. Patient underwent pars plana vitrectomy and intraocular antibiotics injection in the capsular bag behind the intraocular lens. The vitreous culture was positive for *Propionibacterium acnes*

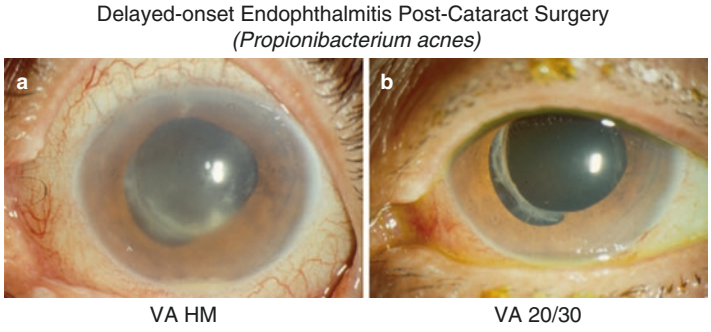

FIGURE 4.9 Chronic/delayed-onset postoperative endophthalmitis. A 69-year-old female patient with delayed-onset postoperative endophthalmitis following cataract surgery. (**a**) The patient presented with gradual painless decrease in vision, conjunctival congestion, mild corneal edema, capsular plaque, and hand motions (HM) vision. Patient underwent pars plana vitrectomy and intraocular antibiotics injection in the capsular bag behind the intraocular lens. The vitreous culture was positive for *Propionibacterium acnes*. (**b**) At 6-month follow-up, the patient regained best corrected visual acuity of 20/30 with resolution of inflammation

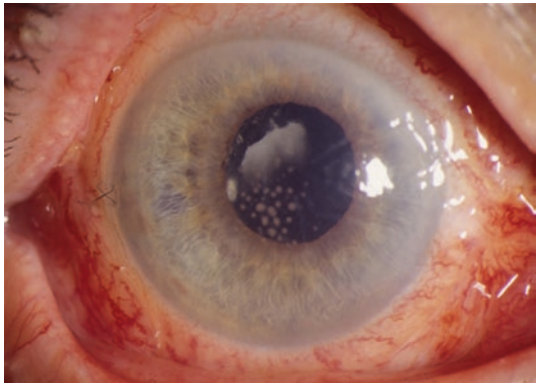

FIGURE 4.10 Chronic/delayed-onset postoperative endophthalmitis. A 72-year-old male patient with delayed-onset postoperative endophthalmitis following cataract surgery with gradual painless decrease in vision, conjunctival congestion, mild corneal edema, and creamy-white-colored plaques over intraocular lens. The vitreous culture was positive for *Candida parapsilosis*

Follow-Up Management in Patients with Delayed-Onset Postoperative Endophthalmitis

First Morning After Initial Treatment

- Topical antimicrobials
  - Consider fortified topical antibiotics if available
    Vancomycin 25 mg/mL hourly during the day and
    Ceftazidime 50 mg/mL hourly during the day
  - Alternatively, commercially available topical antibiotics are used
  - For fungal cases, topical amphotericin B has poor intraocular penetration and is not used
- Topical steroids four times daily (not for suspected/proven fungal infection)
- Topical cycloplegics daily

*Topical antibiotics hourly may result in corneal epithelial toxicity as a result of preservatives in commercial preparations. Topical medications are generally not used during night hours while sleeping. Subconjunctival antibiotics at the time of initial treatment provide adequate ocular surface medication for nighttime coverage.

Two to Three Days After Initial Treatment

- If clinically improving—Continue to observe and taper topical steroids over several weeks
- If clinically worsening:
  - Consider repeat intraocular cultures and/or reinjection of intraocular antibiotics (and possibly intraocular steroids in acute-onset bacterial cases).
  - Consider PPV if not performed initially.

  Change antibiotics if indicated by initial culture results.

References: Delayed-Onset (Chronic) Postoperative Endophthalmitis

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Acute-Onset Endophthalmitis Following PPV

Incidence

Endophthalmitis following pars plana vitrectomy is an uncommon cause of endophthalmitis. The incidence ranges between 0.03 and 0.14% for 20 G PPV.

Signs/Symptoms

Endophthalmitis after pars plana vitrectomy may present as acute or delayed-onset endophthalmitis. These patients usually have a hypopyon and dense vitritis. Some cases, however, may lack vitritis due to the lack of vitreous.

Risk Factors (Table 4.3)

TABLE 4.3 Risk factors associated with endophthalmitis after pars plana vitrectomy

Surgery-related risk factors	Patient-related risk factors
• Inadequate wound closure • Hypotony • Vitreous incarceration • Endotamponade agent (air, gas, or silicone oil) • Subconjunctival and intravitreal injections • Surgeon learning curve (non-beveled sclerotomies)	• Diabetes mellitus or other causes of immune compromise • Trauma or excessive eye rubbing • Noncompliance with treatment

Microbial Isolates

The most common organism causing endophthalmitis after pars plana vitrectomy is coagulase-negative Staphylococci. Other causative organisms include:

- Coagulase-negative Staphylococci
- *Pseudomonas* species
- *Propionibacterium* species
- *Enterococci* species
- *Bacillus* species

Initial Management of Acute-onset Endophthalmitis Following Vitrectomy

Tap and inject is a relatively easy and quick initial approach to manage cases of endophthalmitis occurring after pars plana vitrectomy.

Follow-Up Management in Patients with Acute-onset Endophthalmitis Following Vitrectomy

First Morning After Initial Treatment

- Topical antimicrobials
  - Consider fortified topical antibiotics if available:
    Vancomycin 25 mg/mL hourly during the day
    Ceftazidime 50 mg/mL hourly during the day
  - Alternatively, commercially available topical antibiotics are used.
  - For fungal cases, topical amphotericin B has poor intraocular penetration and is not used.
- Topical steroids four times daily (not for suspected/proven fungal infection)
- Topical cycloplegics daily

* Topical antibiotics hourly may result in corneal epithelial toxicity as a result of preservatives in commercial prepara-

tions. Topical medications are generally not used during night hours while sleeping. Subconjunctival antibiotics at the time of initial treatment provide adequate ocular surface medication for nighttime coverage.

Two to Three Days After Initial Treatment

- If clinically improving—Continue to observe and taper topical steroids over several weeks.
- If clinically worsening:
  - Consider repeat intraocular cultures and/or reinjection of intraocular antibiotics (and possibly intraocular steroids in acute-onset bacterial cases).
  - Consider repeat PPV and injection of antibiotics if no improvement is observed.

  Change antibiotics if indicated by initial culture results.

References: Acute-Onset Endophthalmitis Following Vitrectomy

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Conjunctival Filtering Bleb: Associated Infection and Endophthalmitis

Infection of the conjunctival filtering bleb or associated endophthalmitis may occur months or years following trabeculectomy surgery (Figs. 4.11 and 4.12). However, the presentation of endophthalmitis may be of abrupt and sudden onset.

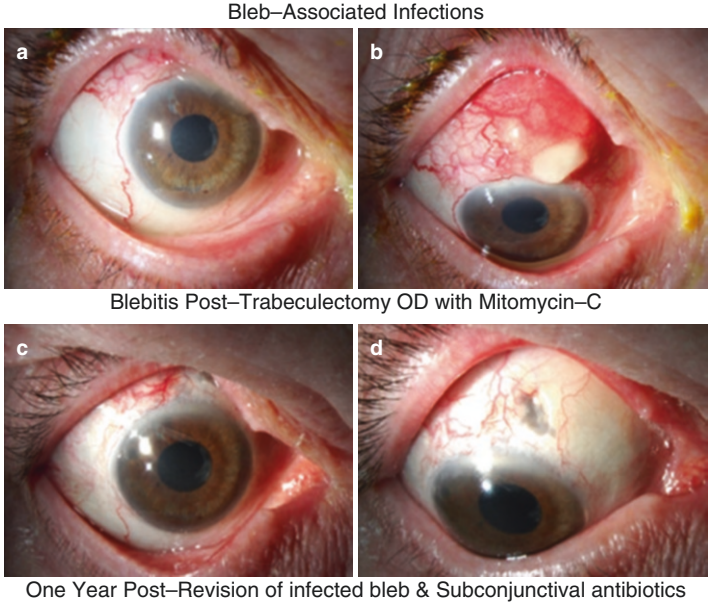

FIGURE 4.11 Blebitis/bleb-associated infections. Follow-up course of a patient (87-year-old female) with bleb-associated infection following trabeculectomy with mitomycin C. (**a** and **b**) Conjunctival congestion, mild corneal edema, and blebitis on the day of presentation (**c** and **d**) 1 year after bleb revision and subconjunctival antibiotics, blebitis resolved. At 2-year follow-up, the visual acuity was 20/60

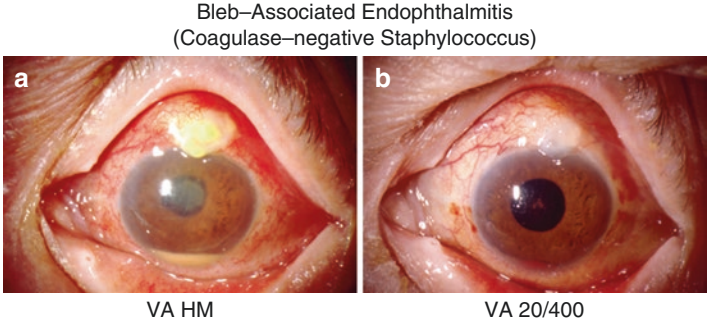

FIGURE 4.12 Bleb-associated endophthalmitis. A 73-year-old male patient with bleb-associated endophthalmitis following trabeculectomy. (**a**) The patient presented with conjunctival congestion, blebitis, mild corneal edema, hypopyon, fibrinous membrane in the anterior chamber and pupillary area, hazy view to the posterior segment, and hand motions (HM) vision. Patient underwent vitreous tap and intraocular antibiotics. The vitreous culture was positive for coagulase-negative Staphylococcus. (**b**) At 6-month follow-up, the patient regained best corrected visual acuity of 20/400 with resolution of endophthalmitis

Incidence

Reported 5-year cumulative incidence: 0.45–1.3%

Signs/Symptoms

The patient may present with lid swelling, pain, redness, discharge, marked decrease in the vision, etc. Slit-lamp examination may show lid swelling, conjunctival congestion, blebitis, conjunctival discharge, corneal edema, hypopyon, infiltrates/fibrin membrane in the anterior chamber, loss of red reflex from the retina, and infiltrates in the vitreous cavity.

Risk Factors

- Preoperative:
  - Younger patient age
  - Blepharitis
  - Axial myopia
- Intraoperative:
  - Use of antimetabolites
  - Inferior trabeculectomy
  - Thin avascular bleb
- Postoperative:
  - Blebitis
  - Late-onset bleb leak
  - Chronic antibiotic use

Microbial Isolates

Common causative organisms include:

- *Streptococcus* species
- *Haemophilus influenza*
- *Staphylococcus* species

Initial Management of Conjunctival Filtering Bleb-Associated Endophthalmitis

The treatment of conjunctival filtering bleb-associated infection or endophthalmitis may include bleb revision and subconjunctival antibiotics in addition to the vitreous tap/pars plana vitrectomy and intravitreal antibiotics injection.

Follow-Up Management in Patients with Conjunctival Filtering Bleb-Associated Infection or Endophthalmitis

First Morning After Initial Treatment

- Topical antimicrobials
  - Consider fortified topical antibiotics if available:
    Vancomycin 25 mg/mL hourly during the day
    Ceftazidime 50 mg/mL hourly during the day
  - Alternatively, commercially available topical antibiotics are used.
  - For fungal cases, topical amphotericin B has poor intraocular penetration and is not used.
- Topical steroids four times daily (not for suspected/proven fungal infection)
- Topical cycloplegics daily

*Topical antibiotics hourly may result in corneal epithelial toxicity as a result of preservatives in commercial preparations. Topical medications are generally not used during night hours while sleeping. Subconjunctival antibiotics at the time of initial treatment provide adequate ocular surface medication for nighttime coverage.

Two to Three Days After Initial Treatment

- If clinically improving (Fig. 4.13)—Continue to observe and taper topical steroids over several weeks.
- If clinically worsening:
  - Consider repeat intraocular cultures and/or reinjection of intraocular antibiotics (and possibly intraocular steroids in acute-onset bacterial cases).
  - Consider PPV if not performed initially.

  Change antibiotics if indicated by initial culture results.

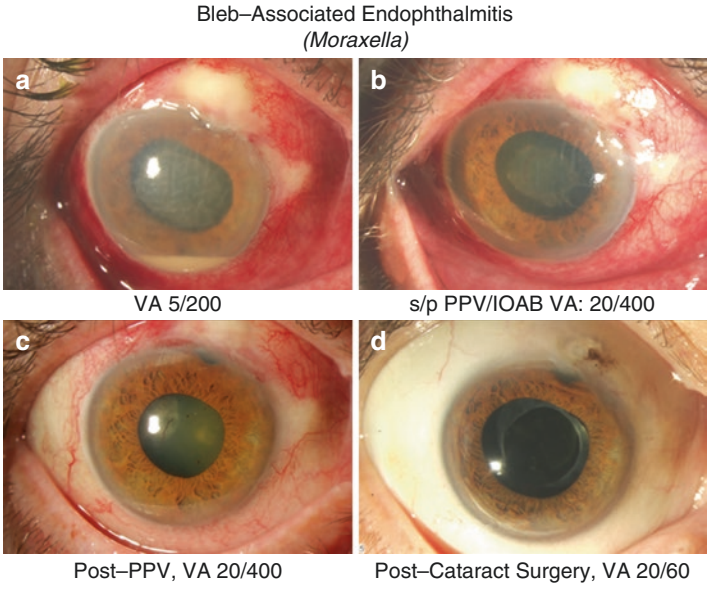

FIGURE 4.13 Bleb-associated endophthalmitis. A 72-year-old female patient with bleb-associated endophthalmitis following trabeculectomy. (**a**) At presentation patient had conjunctival congestion, blebitis, corneal edema, hypopyon, cataract, hazy view to the posterior segment, and 5/200 visual acuity. (**b** and **c**) After pars plana vitrectomy intraocular antibiotics, the visual acuity improved to 20/400 with resolving inflammation and infection. The vitreous culture was positive for *Moraxella* species. (**d**) At 1-year follow-up, the patient regained best corrected visual acuity of 20/60 after subsequent cataract surgery

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Endophthalmitis Associated with Glaucoma Drainage Devices

Glaucoma drainage device associated endophthalmitis may occur months or years following glaucoma drainage device implantation (Fig. 4.14). However, the presentation of endophthalmitis may be of abrupt and sudden onset.

Incidence

Reported rates are approximately 1.7%, but rates are only estimates when considering 5-year follow-up.

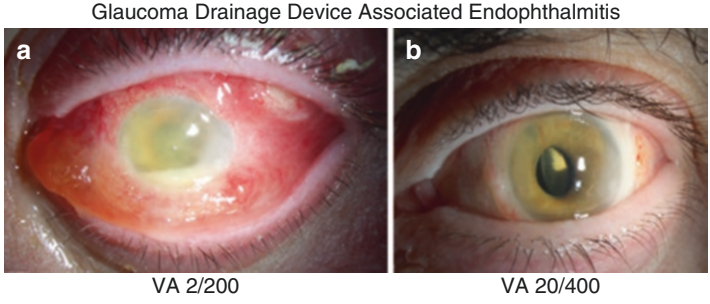

FIGURE 4.14 Glaucoma drainage device-associated endophthalmitis. A 66-year-old female patient with history of prior ocular surgery (retinal detachment and glaucoma drainage implantation). (**a**) The patient presented with lid edema, exposed glaucoma drainage device beneath upper eyelid, conjunctival congestion, severe conjunctival chemosis, corneal edema, hypopyon, fibrinous reaction in the anterior chamber, hazy view to the posterior segment, and 2/200 visual acuity. The patient underwent removal of glaucoma drainage implant, miragel scleral buckle, and subconjunctival and intravitreal vancomycin. In addition, the patient was given oral fluoroquinolones (levofloxacin) and topical vancomycin. The cultures were negative (both intraocular and external). (**b**) At 1-year follow-up, the patient had resolution of endophthalmitis and best corrected visual acuity improved to 20/400

Signs/Symptoms

The patient may present with lid swelling, pain, redness, discharge, marked decrease in the vision, etc. Slit-lamp examination may show lid swelling, conjunctival congestion, exposed tube or implant or device, conjunctival discharge, corneal edema, hypopyon, infiltrates/fibrin membrane in the anterior chamber, loss of red reflex from the retina, and infiltrates in the vitreous cavity.

Risk Factors

- Preoperative: pediatric patients
- Intraoperative: inferior placement
- Postoperative: exposure of device (Fig. 4.15)

Microbiology

Common causative organisms include:

- Coagulase-negative *Staphylococci*
- *Streptococcus* species
- *Staphylococcus* species

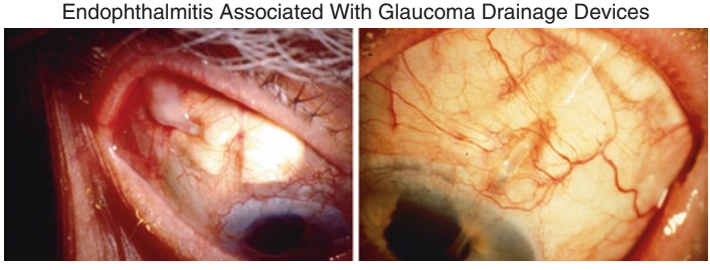

FIGURE 4.15 Glaucoma drainage device-associated endophthalmitis. Patient with exposed glaucoma drainage device leading to endophthalmitis

Initial Management of Glaucoma Drainage Device Associated Endophthalmitis

The treatment of glaucoma drainage device associated endophthalmitis may include removal of the exposed tube/implant/device. When the tube is not exposed then it may be initially retained. Vitreous tap/pars plana vitrectomy and intravitreal antibiotics injection are performed based on clinical features and physician preference.

Follow-Up Management in Patients with Endophthalmitis Associated with Glaucoma Drainage Devices

First Morning After Initial Treatment

- Topical antimicrobials
  - Consider fortified topical antibiotics if available:
    Vancomycin 25 mg/mL hourly during the day
    Ceftazidime 50 mg/mL hourly during the day
  - Alternatively, commercially available topical antibiotics are used.
  - For fungal cases, topical amphotericin B has poor intraocular penetration and is not used.
- Topical steroids four times daily (not for suspected/proven fungal infection)
- Topical cycloplegics daily

*Topical antibiotics hourly may result in corneal epithelial toxicity as a result of preservatives in commercial preparations. Topical medications are generally not used during night hours while sleeping. Subconjunctival antibiotics at the time of initial treatment provide adequate ocular surface medication for nighttime coverage.

Two to Three Days After Initial Treatment

- If clinically improving—Continue to observe and taper topical steroids over several weeks.
- If clinically worsening:
  - Consider repeat intraocular cultures and/or reinjection of intraocular antibiotics (and possibly intraocular steroids in acute-onset bacterial cases).
  - Consider PPV if not performed initially.

  Change antibiotics if indicated by initial culture results.

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Post-Traumatic Endophthalmitis

Open globe injury may lead to post-traumatic endophthalmitis.

Incidence

Reported rates of post-traumatic endophthalmitis are variable, up to 90% in one series but generally less than 10%. Intraocular foreign bodies (IOFBs) have been reported in 10–41% of open globe injuries. In open globe injuries with endophthalmitis on presentation, IOFB may be even more common, up to 53%.

Signs/Symptoms

Patients present with a history of open globe injury and marked loss of vision. Slit-lamp examination may show associated hypopyon, fibrinous membranes in anterior chamber, vitreous infiltrates/opacities, or retained intraocular foreign body (Figs. 4.16 and 4.17).

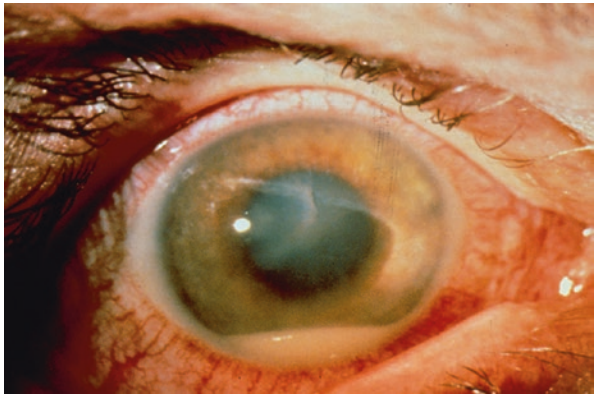


FIGURE 4.16 Slit lamp examination of a patient with open globe injury and post traumatic endophthalmitis showing conjunctival hyperemia, corneal laceration, corneal edema, hypopyon with no view of posterior segment

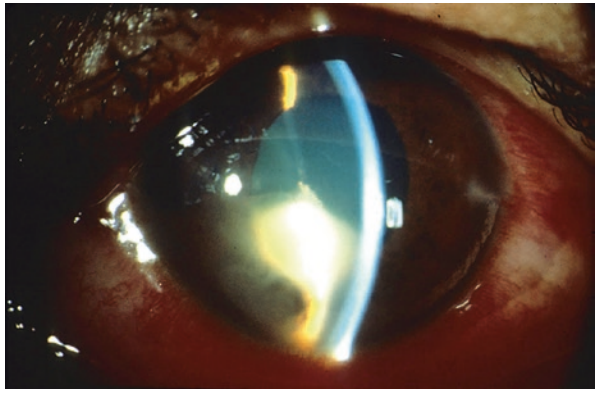


FIGURE 4.17 Slit lamp examination of a patient with open globe injury shows subconjunctival hemorrhage and presence of fibrinous exudates localized in the lens

Risk Factors

- Intraocular foreign body (IOFB) (Fig. 4.18)—Higher risk with vegetable matter
- Delayed presentation after open globe injury
- Contaminated wound
- Traumatic lens rupture
- Cornea wound (Fig. 4.19)

Microbial Isolates

Most common causative organisms include:

- *Bacillus* species (Fig. 4.20)
- *Staphylococcus* species

Initial Management of Post-traumatic Endophthalmitis

- *Pars plana vitrectomy and intravitreal antibiotics*—In patients with post-traumatic endophthalmitis, pars plana

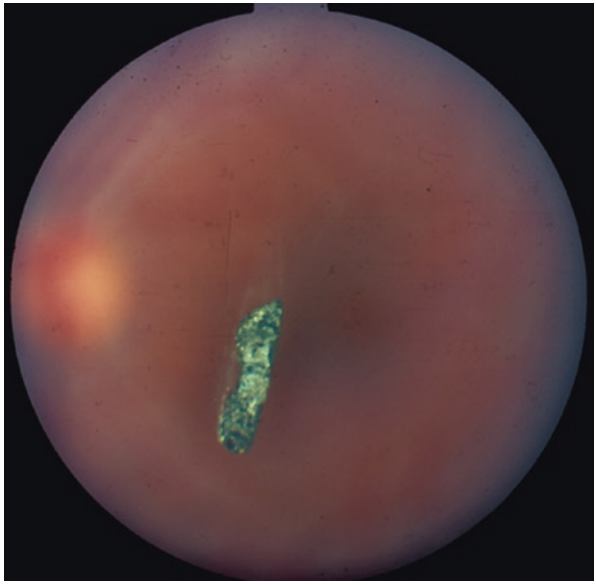


Figure 4.18 Intraocular foreign body (IOFB). A 38-year-old male patient developed post-traumatic endophthalmitis. Fundus photograph shows vitreous hemorrhage, hazy view of the posterior segment, and retained intraocular foreign body (metallic) in the vitreous

vitrectomy with injection of intravitreal antibiotics is generally recommended.

- *Systemic antibiotics in endophthalmitis associated with open globe injury*—In cases of endophthalmitis associated with open globe injury, outcomes data regarding the use or nonuse of systemic antibiotics are limited. Large series of patients with open globe injuries without endophthalmitis at initial presentation, early wound closure and prophylactic use of systemic levofloxacin was associated with a very low endophthalmitis risk (Colyer et al. 2007). Most treating ophthalmologists do utilize systemic antibiotics in such cases.
- *Retained intraocular foreign body*—If the retained intraocular foreign body is organic and source of infection, it should be removed as early as possible. Inert or nonorganic foreign body (metallic or glass) can be removed later when infection and inflammation decrease and the media become clear enough to allow safe removal of the foreign body.

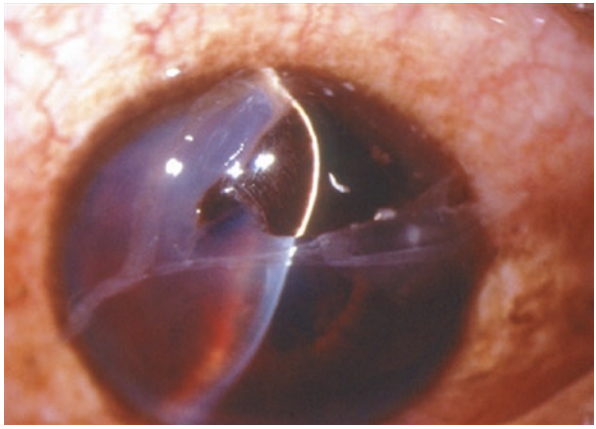


FIGURE 4.19 A 42-year-old male patient with open globe injury. Slit-lamp examination showed conjunctival congestion, corneal laceration with iris tissue prolapse, focal corneal edema, hyphema, and no view of posterior segment

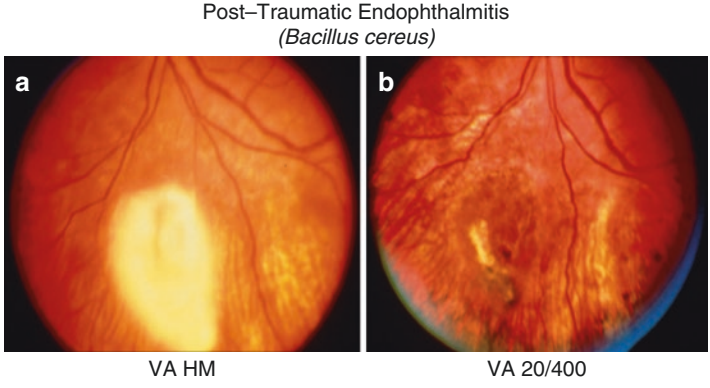


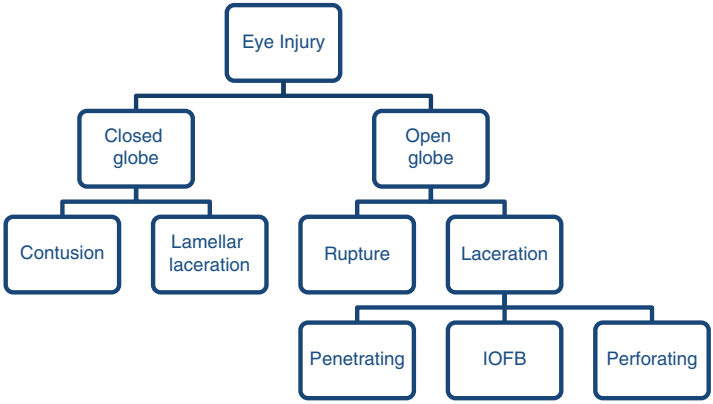
FIGURE 4.20 Post-traumatic endophthalmitis. A 17-year-old male patient with open globe injury and post-traumatic endophthalmitis. (**a**) Fundus photograph shows localized retinal exudates in inferior retina. The vitreous culture was positive for *Bacillus cereus*. (**b**) A 6-month follow-up shows resolved inflammation with residual retinal scarring and vision improved to 20/400

Retained intraocular foreign bodies (IOFBs) have a high risk for endophthalmitis and toxicity. IOFBs have been previously classified according to their location (anterior segment, posterior segment), material characteristics (metallic, magnetic, wood), size, mechanism of injury, setting (work related, battlefield), and duration (acute, long standing). IOFBs can be acute or chronic, obvious, or very subtle and appear anywhere from relatively innocuous to devastating on initial examination.

Endophthalmitis can contribute to additional visual loss beyond the damage of initial open globe injury.

In 1995, a standardized classification of ocular trauma was proposed by ocular trauma experts (Kuhn et al.). Various definitions of the proposed ocular trauma terms are as shown in Table 4.4:

In this classification, ocular trauma system was proposed as follows:



Entry site of the wound (wound's most posterior extent) helps in determining the zone of injury. In 1997, the Ocular Trauma Classification Group (Pieramici et al.) described the zone of injury as follows:

- Zone 1—cornea and limbus
- Zone 2—≤5 mm posterior to the limbus
  Zone 3—greater than 5 mm posterior to the limbus

Table 4.4 Ocular trauma classification terminology

Terms	Definitions
Eyewall	Sclera and cornea
Closed globe injury	The eyewall does not have a full-thickness wound
Open globe injury	The eyewall does have a full-thickness wound
Rupture	Full-thickness wound of the eyewall, caused by a blunt object; the impact results in momentary increase of the IOP and an inside-out injury mechanism
Laceration	Full-thickness wound of the eyewall, usually caused by a sharp object; the wound occurs at the impact site by an outside-in mechanism
Penetrating injury	Single laceration of the eyewall, usually caused by a sharp object
Intraocular foreign body injury	Retained foreign object(s) causing entrance laceration(s)
Perforating injury	Two full-thickness lacerations (entrance + exit) of the eyewall, usually caused by a sharp object or missile

Follow-Up Management in Patients with Post-traumatic Endophthalmitis

First Morning After Initial Treatment

- Topical antimicrobials
  - Consider fortified topical antibiotics if available:
    Vancomycin 25 mg/mL hourly during the day
    Ceftazidime 50 mg/mL hourly during the day
  - Alternatively, commercially available topical antibiotics are used.
  - For fungal cases, topical amphotericin B has poor intraocular penetration and is not used.

- Topical steroids four times daily (not for suspected/proven fungal infection)
- Topical cycloplegics daily

*Topical antibiotics hourly may result in corneal epithelial toxicity as a result of preservatives in commercial preparations. Topical medications are generally not used during night hours while sleeping. Subconjunctival antibiotics at the time of initial treatment provide adequate ocular surface medication for nighttime coverage.

Two to Three Days After Initial Treatment

- If clinically improving—Continue to observe and taper topical steroids over several weeks.
- If clinically worsening:
  - Consider repeat intraocular cultures and/or reinjection of intraocular antibiotics (and possibly intraocular steroids in acute-onset bacterial cases).
  - Consider PPV if not performed initially.

Change antibiotics if indicated by initial culture results.

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Endogenous Fungal Endophthalmitis

Endogenous fungal endophthalmitis is an uncommon disease caused by hematogenous spread of fungi to the posterior segment of the eye. Endogenous endophthalmitis may occur even without obvious systemic infection. *With increasing worldwide prevalence of intravenous drug use, endogenous endophthalmitis remains an important challenge for the ophthalmologists and physicians. Recent opioid crisis in the United States has led to an increase in the numbers of endogenous fungal and bacterial endophthalmitis cases*.

Incidence

Reported rates are 0.05–0.4% among patients with fungemia.

Signs/Symptoms

The patient presents with mild to moderate decrease in the vision in one or both eyes in a delayed-onset manner. The patient may have severe systemic illness. Slit-lamp examination may show a relatively quiet anterior segment. However, the patient may have creamy-white fungal vitreous opacities, focal white raised retinal lesions, retinal infiltrates with retinal vasculitis, or subretinal abscess (Fig. 4.21).

Risk Factors

- Intravenous drug abuse
- Diabetes mellitus
- Immune compromise

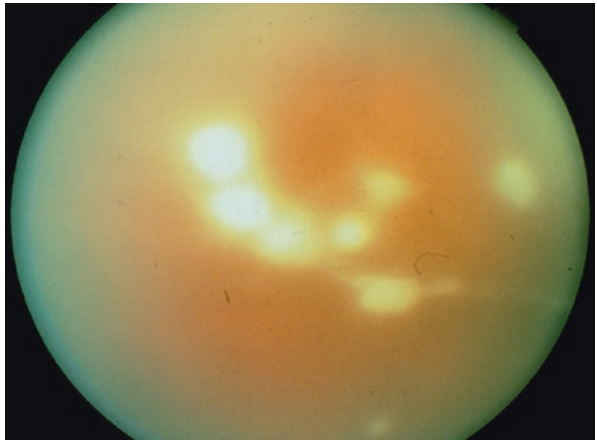

FIGURE 4.21 Endogenous endophthalmitis. A 30-year-old female patient with recent history of abdominal surgery presented with sudden blurring of vision and vitreous floaters. The fundus examination showed the presence of creamy-white opacities in the vitreous with hazy view of the retina

Malignancy

- Longer hospital stays/prolonged intravenous antibiotic administration

Microbial Isolates

Common causative organisms include:

- *Candida* species (Figs. 4.22, 4.23, 4.24, and 4.25)
- *Aspergillus* species

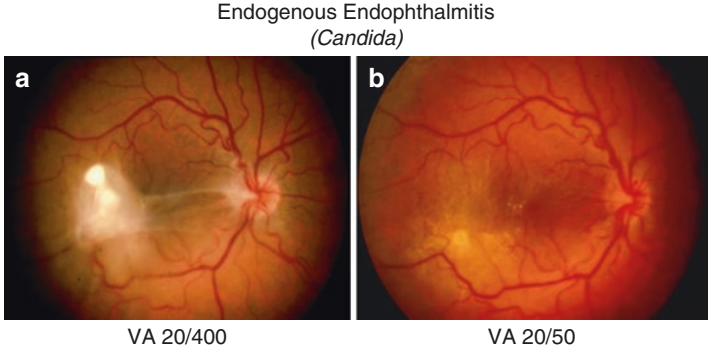

FIGURE 4.22 Endogenous endophthalmitis. (**a**) A 60-year-old female patient with breast cancer (on chemotherapy and radiotherapy) presented with sudden blurring of vision, vitreous floaters, and 20/400 visual acuity. The fundus examination showed a white patch of retinitis and overlying vitreous inflammation at the posterior pole. The patient underwent pars plana vitrectomy and intraocular injection of amphotericin B. The vitreous culture was positive for *Candida* species. (**b**) At 6-month follow-up, the inflammation and infection resolved with residual scarring at the posterior pole. The best corrected visual acuity improving to 20/50

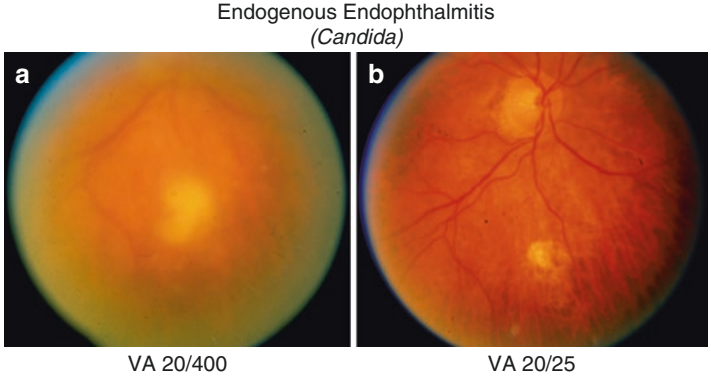

FIGURE 4.23 Endogenous endophthalmitis. A 60-year-old female patient presented with sudden blurring of vision, vitreous floaters, and 20/400 visual acuity. (**a**) The fundus examination showed vitreous haze with a white patch of retinitis in the inferior retina. The patient underwent pars plana vitrectomy and intraocular injection of amphotericin B. The vitreous culture was positive for *Candida* species. (**b**) At 6-month follow-up, the inflammation and infection resolved with residual scarring. The best corrected visual acuity improving to 20/25

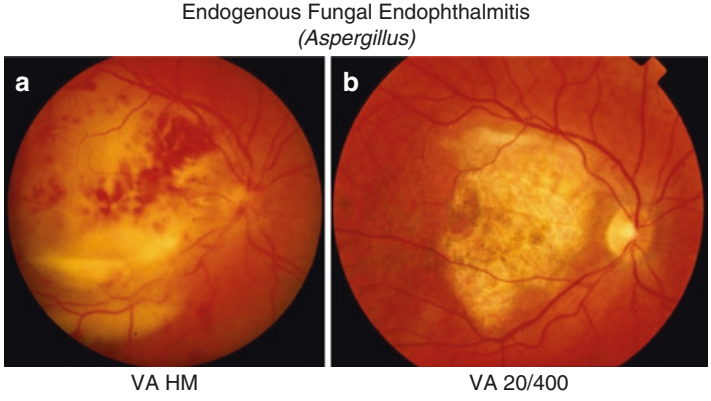

Figure 4.24 Endogenous endophthalmitis. A 67-year-old female patient presented with sudden blurring of vision, vitreous floaters, and hand motions (HM) vision. (**a**) The fundus examination showed a creamy-white patch of retinitis at the posterior pole. The patient underwent pars plana vitrectomy and intraocular injection of amphotericin B. The vitreous culture was positive for *Aspergillus* species. (**b**) At 1-year follow-up, the inflammation and infection resolved with residual scarring at the posterior pole. The best corrected visual acuity improved to 20/400

Initial Management of Endogenous Fungal Endophthalmitis

Patient with suspected endogenous fungal endophthalmitis should undergo systemic investigations (including blood culture, urine culture, peripheral blood count, throat swab, vaginal swabs) after consulting with other medical specialists. In patients with endogenous fungal endophthalmitis, systemic antifungals are considered. Intravitreal antifungal injections are usually employed and pars plana vitrectomy can be considered.

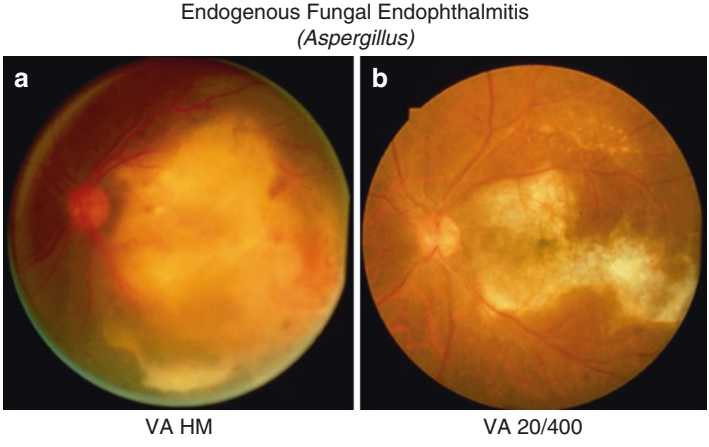

FIGURE 4.25 Endogenous endophthalmitis. A 77-year-old male patient presented with sudden blurring of vision, vitreous floaters, and hand motions (HM) vision. (**a**) The fundus examination showed a yellow-white patch of retinitis and subretinal exudates at the posterior pole. The patient underwent pars plana vitrectomy and intraocular injection of amphotericin B. The vitreous culture was positive for *Aspergillus* species. (**b**) At 1-year follow-up, the inflammation and infection resolved with residual scarring at the posterior pole. The best corrected visual acuity improved to 20/400

Follow-Up Management in Patients with Endogenous Fungal Endophthalmitis

First Morning After Initial Treatment

- Topical antimicrobials
  - Topical natamycin.
  - Topical amphotericin B has poor intraocular penetration and is not used.
- Topical cycloplegics daily.

Two to Three Days After Initial Treatment

- If clinically improving—Continue oral antifungal agents as indicated.
- If clinically worsening:
  - Consider repeat intraocular cultures and/or reinjection of intraocular antifungals.
  - Consider PPV if not performed initially.

Change antifungals if indicated by initial culture results.

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Endogenous Fungal Endophthalmitis

Endogenous bacterial endophthalmitis is an uncommon disease caused by hematogenous spread of bacteria to the posterior segment of the eye. Endogenous endophthalmitis may occur even without obvious systemic infection.

Incidence

Reported rates are about 0.04% among patients with bacteremia.

Signs/Symptoms

The patient presents with mild to moderate decrease in the vision in one or both eyes. The patient may have severe systemic illness. Slit-lamp examination may show conjunctival congestion, corneal edema, hypopyon, fibrinous membrane in the anterior chamber, and vitreous infiltrates.

Risk Factors

- Diabetes mellitus
- Immune compromise

Malignancy

- Longer hospital stays/prolonged intravenous antibiotic administration

Microbial Isolates

Common causative organisms include:

- *Staphylococcus aureus* (Fig. 4.26)
- Gram-negative bacteria

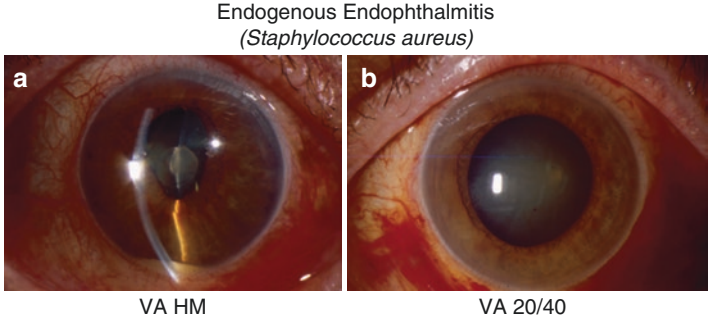

FIGURE 4.26 Endogenous endophthalmitis. (**a**) A 60-year-old female patient with uncontrolled diabetes mellitus presented with sudden blurring of vision, vitreous floaters, and hand motions (HM) vision. The fundus examination showed hyperemic disc and the presence of subretinal exudates at the posterior pole. The patient underwent vitreous tap and intraocular antibiotics. The vitreous culture was positive for *Staphylococcus aureus*. (**b**) At 1-month follow-up, the inflammation and infection started resolving with best corrected visual acuity improving to 20/40

Initial Management of Endogenous Bacterial Endophthalmitis

Patient with suspected endogenous bacterial endophthalmitis should undergo systemic investigations (including blood culture, urine culture, peripheral blood count, throat swab, vaginal swabs) to look for the source of infection. In patients with endogenous bacterial endophthalmitis, systemic antibiotics are considered after consultation with an infectious disease or internal medicine specialist. Intravitreal antibiotic injections are usually employed and pars plana vitrectomy can be considered.

Follow-Up Management in Patients with Endogenous Bacterial Endophthalmitis

First Morning After Initial Treatment

- Topical antimicrobials
  - Consider fortified topical antibiotics if available:
    Vancomycin 25 mg/mL hourly during the day
    Ceftazidime 50 mg/mL hourly during the day
  - Alternatively, commercially available topical antibiotics are used.
- Topical steroids four times daily (not for suspected/proven fungal infection)
- Topical cycloplegics daily

*Topical antibiotics hourly may result in corneal epithelial toxicity as a result of preservatives in commercial preparations. Topical medications are generally not used during night hours while sleeping. Subconjunctival antibiotics at the time of initial treatment provide adequate ocular surface medication for nighttime coverage.

Two to Three Days After Initial Treatment

- If clinically improving—Continue to observe and taper topical steroids over several weeks.
- If clinically worsening:
  - Consider repeat intraocular cultures and/or reinjection of intraocular antibiotics (and possibly intraocular steroids in acute-onset bacterial cases).
  - Consider PPV if not performed initially.

Change antibiotics if indicated by initial culture results.

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Endophthalmitis Associated with Keratitis

Endophthalmitis associated with keratitis is usually seen in chronic, large, deep corneal ulcers nonresponsive to topical antimicrobial therapy.

Incidence

Generally considered rare

Signs/Symptoms

The patient presents with a chronic, large-sized corneal ulcer involving deeper layers of the cornea. These corneal infections are nonresponsive to antimicrobial therapy. Slit-lamp examination may show corneal ulcer, hypopyon, infiltrates in anterior chamber, or vitreous. These cases are difficult to manage.

Risk Factors for Keratitis that May Lead to Endophthalmitis

- Topical steroid use
- Contact lens misuse
- Systemic immunosuppression
- Diabetes mellitus

Microbial Isolates

Common causative organisms include:

- *Pseudomonas aeruginosa*
- *Staphylococcus* species
- Fungal species (Fig. 4.27)

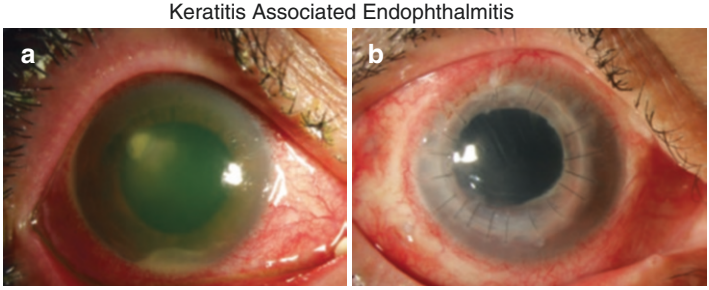

FIGURE 4.27 Keratitis-associated endophthalmitis. A 54-year-old woman with corneal ulcer with a history of soft contact lens use. (**a**) Slit-lamp examination revealed conjunctival congestion, corneal edema, corneal infiltrate, and anterior chamber inflammation with hypopyon. The culture from corneal infiltrates was positive for *Fusarium* species. The patient underwent penetrating keratoplasty, pars plana vitrectomy, lensectomy, and intravitreal voriconazole. (**b**) A 3-week follow-up exam showed clear corneal graft with resolution of the hypopyon and anterior chamber inflammation

Initial Management of Endophthalmitis Associated with Keratitis

In patients with endophthalmitis associated with keratitis, the corneal scraping or biopsy may reveal the causative organism and help in guiding the management. The management may involve therapeutic keratoplasty in addition to the pars plana vitrectomy and injection of intravitreal antibiotics. It is always better to perform keratoplasty in a quiet eye with no inflammation. In cases of recalcitrant and fulminant keratitis, the infected cornea can be removed as part of treatment of endophthalmitis.

Follow-Up Management in Patients with Endophthalmitis Associated with Keratitis

First Morning After Initial Treatment

- Topical antimicrobials
  - Consider fortified topical antibiotics if available:
    Vancomycin 25 mg/mL hourly during the day
    Ceftazidime 50 mg/mL hourly during the day
  - Alternatively, commercially available topical antibiotics are used.
  - For fungal cases, topical amphotericin B has poor intraocular penetration and is not used.
- Topical steroids four times daily (not for suspected/proven fungal infection)
- Topical cycloplegics daily

*Topical antibiotics hourly may result in corneal epithelial toxicity as a result of preservatives in commercial preparations. Topical medications are generally not used during night hours while sleeping. Subconjunctival antibiotics at the time of initial treatment provide adequate ocular surface medication for nighttime coverage.

Two to Three Days After Initial Treatment

- If clinically improving—Continue to observe and taper topical steroids over several weeks.
- If clinically worsening:
  - Consider repeat intraocular cultures and/or reinjection of intraocular antibiotics (and possibly intraocular steroids in acute-onset bacterial cases).
  - Consider PPV if not performed initially.

Change antibiotics if indicated by initial culture results.

References: Endophthalmitis Associated with Keratitis

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Endophthalmitis Associated with Intravitreal Injection

Endophthalmitis can occur following intravitreal anti-VEGF therapy for the treatment of age-related macular degeneration (AMD), diabetic macular edema (DME), or retinal vascular diseases.

Incidence

Reported rates are 0.016–0.053% per injection for anti-vascular endothelial growth factor (VEGF) agents. Many patients receive a series of injections, so the per-patient rate is generally higher. Probably the rates are higher for intravitreal corticosteroids.

*The per-injection rate of clinically suspected endophthalmitis incidence rate after anti-VEGF injections at the Bascom Palmer Eye Institute (BPEI) between 2006 and 2016 was 0.014% (23/159,066). The incidence rates of post-intravitreal injection endophthalmitis among the three intravitreal anti-VEGF agents were: bevacizumab 10/79,105 (0.013%), ranibizumab 6/36,791 (0.016%) and aflibercept 7/42,478 (0.016%). Treatment outcomes were variable but were generally better in the culture-negative cases. Visual acuity outcomes were the worst in *Streptococcus* cases referred during an outbreak of contaminated bevacizumab.

Signs/Symptoms

The patient presents with vision loss, pain, redness, discharge generally within a few days of the intravitreal injection. Slit-lamp examination may show lid edema, discharge, conjunctival congestion, chemosis, corneal edema, hypopyon, fibrinous infiltrates in the anterior chamber, or vitreous (Fig. 4.28). However, it is important to differentiate post-intravitreal injection endophthalmitis from noninfectious postinjection inflammation (Table 4.5 and also see section "Pseudoendophthalmitis with intravitreal anti-VEGFs")

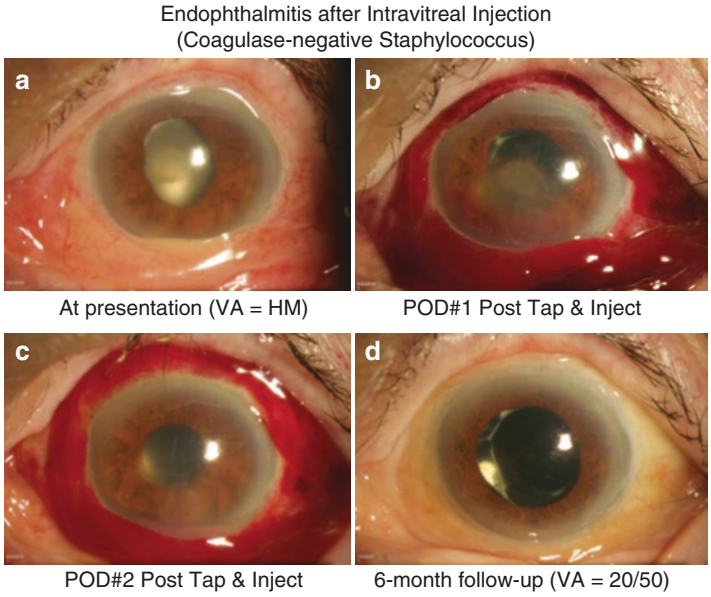

FIGURE 4.28 Follow-up course post-tap and inject for endophthalmitis. (**a**) Post-intravitreal injection endophthalmitis with conjunctival congestion, chemosis, hypopyon, fibrinous membrane in anterior chamber, and hand motions (HM) vision. (**b** and **c**) Day 1 after intravitreal injection of antibiotics showing retracting fibrinous membrane in the anterior chamber. (**d**) At 6-month follow-up inflammation and infection resolved. The visual acuity improved to 20/50

Risk Factors

- Nonuse of povidone–iodine
- (Possible) exposure to oral flora during injection
- Topical antibiotics do not reduce rates of endophthalmitis associated with intravitreal injection

Table 4.5 Differentiating features between post-intravitreal injection endophthalmitis and noninfectious postinjection inflammation (pseudoendophthalmitis)

More common features	Infectious	Noninfectious
Pain	Moderate to severe pain	Usually mild pain
Vision loss	Severe	Mild to moderate
Fibrin	Always present	Rare
Hypopyon	Very common	Rare
Vitreous opacity	Usually prominent	Usually mild
Conjunctival vascular congestion	Very common	Often absent

Microbial Isolates

Common causative organisms include:

- *Staphylococcus* species
- *Streptococcus* species (Fig. 4.29)

Initial Management of Endophthalmitis Associated with Intravitreal Injection

The treatment includes vitreous tap or pars plana vitrectomy with intravitreal antimicrobials.

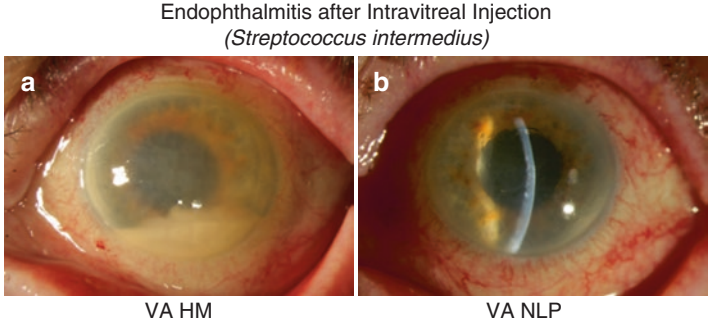

FIGURE 4.29 Post-intravitreal injection endophthalmitis. An 80-year-old male patient with neovascular age-related macular degeneration (AMD) presented 2 days after intravitreal ranibizumab injection with sudden painful decrease in vision. (**a**) The patient presented with conjunctival congestion, corneal edema, hypopyon, fibrinous reaction in the anterior chamber, hazy view of the posterior segment, and hand motions (HM) vision. The patient underwent vitreous tap and intraocular injection. (**b**) At 3-month follow-up, the inflammation and infection persisted and visual acuity deteriorated to no light perception (NLP). The patient underwent evisceration and the specimen culture was positive for *Streptococcus intermedius*

Follow-Up Management in Patients with Endophthalmitis Associated with Intravitreal Injection

First Morning After Initial Treatment

- Topical antimicrobials
  - Consider fortified topical antibiotics if available:
    Vancomycin 25 mg/mL hourly during the day
    Ceftazidime 50 mg/mL hourly during the day
  - Alternatively, commercially available topical antibiotics are used.
  - For fungal cases, topical amphotericin B has poor intraocular penetration and is not used.
- Topical steroids four times daily (not for suspected/proven fungal infection)
- Topical cycloplegics daily

*Topical antibiotics hourly may result in corneal epithelial toxicity as a result of preservatives in commercial preparations. Topical medications are generally not used during night hours while sleeping. Subconjunctival antibiotics at the time of initial treatment provide adequate ocular surface medication for nighttime coverage.

Two to Three Days After Initial Treatment

- If clinically improving—Continue to observe and taper topical steroids over several weeks.
- If clinically worsening:
  - Consider repeat intraocular cultures and/or reinjection of intraocular antibiotics (and possibly intraocular steroids in acute-onset bacterial cases).
  - Consider PPV if not performed initially.

Change antibiotics if indicated by initial culture results.

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Chapter 5
Antimicrobial Treatment: Routes/Dosages/Preparation/ Adverse Effects, Antimicrobial Resistance, and Alternatives

Antimicrobial Routes

- **Intravitreal antimicrobials:**
  For presu-med bacterial cases (in separate syringes):
  - Vancomycin 1 mg/0.1 mL (for coverage of gram-positive organisms)
  - Ceftazidime 2.25 mg/0.1 mL (for coverage of gram-negative organisms)

  For presumed fungal cases:
  - Amphotericin B 0.005 mg/0.1 mL
  - Voriconazole 0.1 mg/0.2 mL

  For presumed bacterial cases: Vancomycin and ceftazidime in separate syringes
  For presumed fungal cases: Amphotericin B or voriconazole without intravitreal steroids
  - Amikacin may be substituted for ceftazidime (EVS proven efficacy).
  - Ceftriaxone (2 mg/0.1 mL) may be substituted for ceftazidime if more readily available.

H.W. Flynn Jr. et al., *Endophthalmitis in Clinical Practice*,
In Clinical Practice,
https://doi.org/10.1007/978-3-319-66351-7_5

  - Dexamethasone 4 mg/0.1 mL may be considered for acute-onset bacterial cases but should be avoided in suspected fungal endophthalmitis and delayed-onset (chronic) endophthalmitis until the organism is identified.

- **Periocular/subconjunctival antimicrobials and steroids:** Periocular antibiotics may be helpful in bleb-related endophthalmitis.

- **Systemic antimicrobials:**
  - For endogenous fungal endophthalmitis
    Voriconazole 200 mg PO bid for 2–4 weeks
    Fluconazole 200 mg PO bid for 2–4 weeks
    Itraconazole 200 mg PO bid for 2–4 weeks
    Ketoconazole 200 mg PO bid for 2–4 weeks
    Amphotericin B 0.25–1.0 mg/kg IV every 6 hours as tolerated
  - For endogenous bacterial endophthalmitis
    Vancomycin 1 g IV bid plus ceftazidime 1 g IV bid
    Systemic fluoroquinolones for susceptible organisms

- **Topical antimicrobials:**
  - Antibiotic topical therapy:
    Fortified vancomycin: 25 mg/mL (2.5%) or 50 mg/mL (5%)
    Fortified ceftazidime: 50 mg/mL (5%)
    Fortified cefazolin: 50 mg/mL (5%)
    Fortified gentamicin: 14 mg/mL (1.4%)
    Fortified tobramycin: 14 mg/mL (1.4%)
    Fortified amikacin: 8 mg/mL (2.5%)
    Fortified linezolid: 2 mg/mL (0.2%)
    Fortified imipenem–cilastin: 10 mg/mL (1%)
  - Antifungals eye drops:
    Fortified amphotericin B: 1.5 mg/mL (0.15%)
    Fortified voriconazole: 10 mg/mL (1%)
    Itraconazole

- **Intrastromal antimicrobials:**
  - Amphotericin B: 5–10 μg/0.1 mL
  - Voriconazole: 50 μg/0.1 mL

Antimicrobial Dosages (Table 5.1)

Table 5.1 Commonly used antimicrobial agents and recommended doses

		Intravitreal	Subconjunctival	Topical (mg/mL)	Intravenous/oral
Antibiotics	Vancomycin	1 mg/0.1 mL	25 mg/0.25 mL	25	1 g IV bid
	Ceftazidime	2.25 mg/0.1 mL	100 mg/0.5 mL	50	1 g IV bid
	Amikacin	0.4 mg/0.1 mL	25 mg/0.5 mL	8	–
Antifungal	Amphotericin B	0.005 mg/0.1 mL	–	1.5 (0.15%)	0.25–1.0 mg/kg IV every 6 h
	Voriconazole	0.05 mg/0.1 mL	–	10 (1%)	200 mg PO

Preparation of Antimicrobials

Preparation of Intravitreal Antimicrobials (Table 5.2)

They are prepared in a volume of 10 mL or greater and labeled in a sealed sterile vial. The treating physician will then withdraw the appropriate dose in a tuberculin syringe for injection.

Table 5.2 Preparation of intravitreal antimicrobial agents

Intravitreal antimicrobials
Vancomycin (1 mg/0.1 mL) • Start with vancomycin 500 mg vial (powder). • Add 10 mL of 0.9% sodium chloride for injection, USP (no preservatives) or balanced salt solution (BSS). • Inject 2 mL of the above solution into a sterile empty vial. • Add 8 mL of 0.9% sodium chloride for injection, USP (no preservatives) or BSS. • Seal this vial.
Ceftazidime (2.25 mg/0.1 mL) • Start with ceftazidime 500 mg vial (powder). • Add 10 mL of 0.9% sodium chloride for injection, USP (no preservatives) or BSS. • Inject 1 mL of the above solution into a sterile empty vial. • Add 1.2 mL of 0.9% sodium chloride for injection, USP (no preservatives) or BSS. • Seal this vial.
Amikacin (0.4 mg/0.1 mL) • Start with amikacin 500 mg/2 mL (solution). • Inject 0.16 mL of this solution into a sterile empty vial. • Add 9.84 mL of 0.9% sodium chloride for injection, USP (no preservatives). • Seal this vial.

Table 5.2 (continued)

Intravitreal antimicrobials
Amphotericin B (0.005 mg/0.1 mL) • Start with amphotericin B 50 mg vial. • Add 10 mL sterile water for injection, USP (no preservatives). • Inject 0.1 mL of the above solution into a sterile empty vial. • Add 9.9 mL of sterile water for injection, USP (no preservatives) to the above solution. • Seal this vial.
Voriconazole (0.05 mg/0.1 mL) • Start with voriconazole 200 mg vial and reconstitute with 19 mL of sterile water for injection, USP (no preservatives). • Withdraw 1 mL of this solution and dilute with 19 mL of sterile water for injection, USP (no preservatives). • Transfer this solution into two sterile empty vials. • Seal these vials.

Preparation of Subconjunctival Antibiotics (Table 5.3)

TABLE 5.3 Preparation of subconjunctival antibiotics

Antibiotic	Amount in package	Volume added (mL)	Volume for injection (mL)	Final dose
Vancomycin	500 mg	5	0.25	25 mg/0.25 mL
Ceftazidime	500 mg	2.5	0.5	100 mg/0.5 mL
Cefazolin	500 mg	2.5	0.5	100 mg/0.5 mL
Amikacin	100 mg/2 mL	0	0.5	25 mg/0.5 mL
Gentamycin	80 mg/2 mL	0	0.5	20 mg/0.5 mL
Tobramycin	80 mg/2 mL	0	0.5	20 mg/0.5 mL
Clindamycin	600 mg/4 mL	0	0.33	50 mg/0.33 mL
Methicillin	1 g	5	0.5	100 mg/0.5 mL
Cephalothin	1 g	5	0.5	100 mg/0.5 mL
Ampicillin	1 g	5	0.5	100 mg/0.5 mL

Preparation of Fortified Topical Antimicrobials (Table 5.4)

Table 5.4 Preparation of fortified topical antimicrobial agents

Vancomycin (25 mg/mL)
- Start with vancomycin 500 mg vial (powder).
- Add 20 mL of 0.9% sodium chloride for injection, USP (no preservatives) or artificial tears.
- Refrigerate and shake well before instillation.

Ceftazidime (50 mg/mL)
- Start with ceftazidime 500 mg vial (powder).
- Add 9.2 mL of artificial tears.
- Take 5 mL of this solution, and dilute with 5 mL of artificial tears.
- Refrigerate and shake well before instillation.

Cefazolin (50 mg/mL)
- Start with ceftazidime 500 mg vial (powder).
- Reconstitute with 2 mL sterile water.
- Add 8 mL of artificial tears to reconstituted solution.
- Refrigerate and shake well before instillation.

Amikacin (8 mg/mL)
- Start with amikacin 500 mg/2 mL (solution).
- Add 0.48 mL of this solution to 15 mL of sterile water (preservative free).
- Refrigerate and shake well before instillation.

Fortified gentamicin eye drops: 14 mg/mL (1.4%)
- Add 2 mL/80 mg of parenteral gentamicin to commercial gentamicin ophthalmic solution 0.3% 5 mL (15 mg/5 mL).
- Shelf life: 1 week in refrigerator at 4 °C and 4 days in room temperature.

Fortified tobramycin: 14 mg/mL (1.4%)
- Add 2 mL/80 mg of parenteral tobramycin to commercially available tobramycin eye drops 0.3% 5 mL (15 mg/5 mL).
- Shelf life: 1 week in refrigerator at 4 °C and 4 days in room temperature.

(continued)

Table 5.4 (continued)

Topical linezolid 2 mg/mL (0.2%)
- Can use directly from parenteral linezolid (Lancure/Adlid/Rapidline) available as 200 mg/100 mL (2 mg/mL) IV infusion

Topical imipenem–cilastin eye drops 1%
- To parenteral imipenem (500 mg)–cilastin (500 mg), add 10 mL sterile water to create a solution of strength 50 mg/mL.
- Take 1 mL of this solution and add 4 mL sterile water to make topical imipenem 1%–1 mg/mL.
- Storage—in amber colored bottles.
- Stability—3 days at 2–8 °C.

Topical amphotericin B 0.15%
- Add 10 mL distilled or sterile water to parenteral 50 mg of amphotericin B powder for injection.
- Draw 3 mL of this and add to 7 mL of artificial tears eye drops.
- Storage: Refrigerate at 4 °C.
- Shelf life: 7 days in refrigerator at 4 °C and 4 days at room temperature.

Topical voriconazole eye drops 1%
- Mix 20 mL Ringer's Lactate to 200 mg voriconazole lyophilized powder.
- Stability: 30 days at 4 °C or room temperature.

Adverse Effects of Antimicrobials

Adverse effects of intravitreal antimicrobials

- Intravitreal aminoglycoside—Risk of macular infarction (Fig. 5.1)
- Intravitreal vancomycin—Hemorrhagic occlusive retinal vasculitis (HORV Fig. 5.2)
- Intravitreal amphotericin B—Risk of retinal damage
- Intravitreal fluoroquinolones—Risk of retinal/systemic toxicity

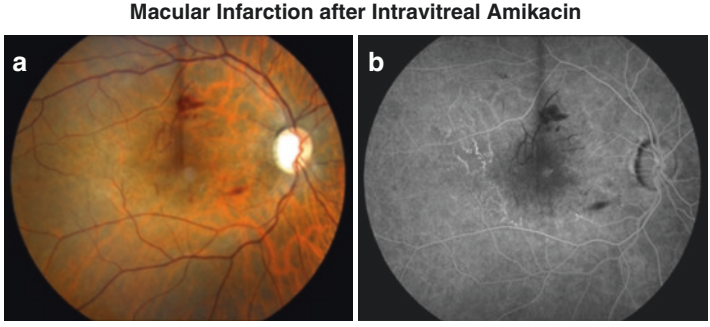

FIGURE 5.1 Macular infarction after intravitreal amikacin. Retinal toxicity with intravitreal amikacin (**a**). Fundus photo showing retinal hemorrhages at the posterior pole. (**b**) Fundus fluorescein angiography demonstrates lack of perfusion at the posterior pole with ischemic macula and patches of hypofluorescence in the area of retinal hemorrhages

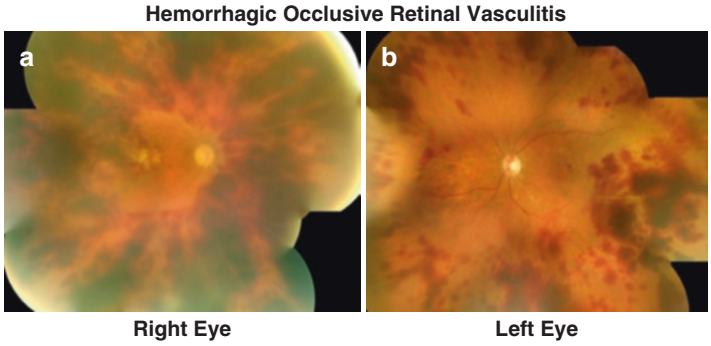

FIGURE 5.2 Hemorrhagic occlusive retinal vasculitis (HORV) in both eyes developing within 1 week of cataract surgery in right eye with intracameral vancomycin. The fundus pictures show multiple retinal hemorrhages and retinal vasculitis

Adverse effects of systemic antimicrobials

- Systemic fluoroquinolones—Disabling and potentially permanent serious side effects involving the tendons, muscles, joints, nerves, and central nervous system. As per May 10, 2017, the US Food and Drug Administration (FDA) currently does not support that fluoroquinolones results in retinal detachment or aortic aneurysm/dissection.
- Systemic amphotericin B—Nephrotoxicity, nausea, vomiting, rigors, fever, hypertension or hypotension, and hypoxia.
- Systemic voriconazole—Generally well tolerated, reversible disturbance of vision (altered color discrimination, blurred vision, the appearance of bright spots and wavy lines, and photophobia), fever, nausea, skin rash, vomiting, and chills.

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Antimicrobial Resistance and Alternatives

Antimicrobial resistance (Fig. 3.2): Emergence of resistance to commonly used antimicrobial agents is a great challenge in health care. The overuse of antibiotics in hospitals and outpatient clinics, widespread agricultural use of antibiotics, and intrinsic genetic factors may all contribute to increasing antimicrobial resistance.

Antimicrobial Resistance Data from EVS

- 100% of gram-positive isolates susceptible to vancomycin.
- 89.5% of gram-negative isolates susceptible to both amikacin and ceftazidime. Among gram-negative isolates, 2/19 (one *Pseudomonas vesicularis* and one *Flavobacterium*, not speciated) were resistant to both amikacin and ceftazidime.

Recent Data on Antimicrobial Resistance

- In the Centers for Disease Control and Prevention (CDC) guidelines for appropriate use of vancomycin and the report by the Rockefeller University Workshop published in 1994, the prophylactic use of vancomycin was discouraged in view of the risk of increasing the prevalence of vancomycin-resistant *Enterococci* (VRE) and methicillin-resistant *Staphylococcus aureus* (MRSA).
- In 2016, Relhan et al. reviewed 27 cases of gram-positive endophthalmitis with reduced vancomycin susceptibility or vancomycin resistance.
- Another review by Dave et al. reported 11 cases of gram-negative endophthalmitis with ceftazidime resistance.
- These 11 cases of endophthalmitis caused by ceftazidime-resistant gram-negative organisms were reported from a single center in India. These cases were subsequently managed with intravitreal imipenem.

Alternative intravitreal agents: Following antimicrobial options are available in cases of resistance (Tables 5.5, 5.6, and 5.7):

(Tables adapted from Relhan N, Pathengay A, Schwartz SG, Flynn HW Jr. Emerging Worldwide Antimicrobial Resistance, the Need for Antibiotic Stewardship and Alternative Intravitreal Agents for the Treatment of Endophthalmitis. Retina. 2017 May;37(5):811–818.)

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Table 5.5 Alternative intravitreal antimicrobial agents for gram-positive organisms

Name of drugs	Class of drugs	Mechanism of action	Intravitreal dose
Linezolid (Zyvox®)	Oxazolindinone (fermentation byproduct of *Streptomyces roseosporus*)	Inhibits initiation of protein synthesis by binding 23S rRNA of the 50S subunit of bacterial ribosome	300 μg/0.1 mL (rabbits and case series in humans)
Quinupristin/dalfopristin (Synercid®)	Streptogramin (isolated from *Streptomyces pristinaespiralis*)	Inhibits bacterial protein synthesis by interfering with function of 23S RNA (quinupristin/dalfopristin, 3:7)	0.4 mg/0.1 mL (rabbits and case reports in humans)
Daptomycin (Cubicin®)	Cyclic lipoglycopeptide	Terminates bacterial DNA, RNA, and protein synthesis and cell death by forming transmembrane channels in cell membrane and depolarization of membrane potential	200 μg/0.1 mL (case report in humans)
Tigecycline (Tygacil®)	Glycylcycline (a derivative of minocycline)	Inhibits bacterial protein synthesis by irreversibly binding to 30 S ribosomal unit	0.5–1 mg/0.1 mL (rabbits)

Table 5.6 Alternative intravitreal antimicrobial agents for gram-negative organisms

Name of drugs	Class of drugs	Mechanism of action	Intravitreal dose
Imipenem (Primaxin®)	Carbapenem	Interrupts cell-wall synthesis of various GPO and GNO and is a strong inhibitor of β-lactamases from some GNO that are resistant to most β-lactam antibiotics	50 μg/0.1 m (case series in humans)
Ciprofloxacin (Cipro®)	Fluoroquinolones	Inhibition of the enzymes topoisomerase II (DNA gyrase) and topoisomerase IV, which are required for bacterial DNA replication, transcription, repair, and recombination	0.1 mg/0.1 mL
Levofloxacin (Levaquin®)	Fluoroquinolones	Same as above	0.1 mL of 0.5% ophthalmic solution (rabbits)
Moxifloxacin (Avelox®)	Fluoroquinolones	Same as above	0.2 mg/0.1 mL (case report in humans)

Table 5.7 Alternative intravitreal antimicrobial agents for fungal organisms

Name of drugs	Class of drugs	Mechanism of action	Intravitreal dose
Miconazole	Azole	Effects on respiration and cell permeability. It inhibits the growth of several species of *Candida*	25 μg/0.1 mL (case series in humans)
Caspofungin (Cancidas®)	Echinocandin	Blocks the synthesis of β(1,3)-d-glucan of the fungal cell wall, by noncompetitive inhibition of the enzyme β(1,3)-d-glucan synthase. β(1,3)-d-Glucan is an essential component of the cell wall of numerous fungal species	50 μg/0.1 mL (rabbits and mice)
Micafungin (Mycamine®)	Echinocandin	It inhibits an enzyme essential for fungal cell-wall synthesis	0.025 mg/0.1 mL (rabbits)

Chapter 6
Endophthalmitis Prophylaxis

Antisepsis

This is the prevention of infection by inhibiting or arresting the growth and multiplication of germs (infectious agents) which is usually achieved by povidone-iodine, hydrogen peroxide, chlorhexidine, or polyhexanide application on the skin (Fig. 6.1).

Povidone-iodine antisepsis is the only clinical practice achieving class 1 evidence for effectiveness to prevent endophthalmitis in the setting of intraocular surgery. Povidone-iodine is a low-cost antiseptic agent with no antibiotic resistance and is rapidly bactericidal and used worldwide. In 2013, a prospective randomized study (Friedman et al.) of patients undergoing intravitreal injections reported that the use of 5% povidone-iodine leads to significant reduction in bacterial colonies, and exposure of 30 seconds appeared to be an adequate time to decrease conjunctival bacterial counts. Modjtahedi et al. (2016) retrospectively analyzed cases of endophthalmitis occurring in patients with self-reported iodine allergy who underwent intravitreal injections without povidone-iodine antisepsis. The study concluded that avoiding povidone-iodine owing to self-reported iodine "allergy" risks substantial ocular morbidity.

Chlorhexidine gluconate is a bisguanide germicide available for preoperative antisepsis. Concentrations of 0.1–4% to

H.W. Flynn Jr. et al., *Endophthalmitis in Clinical Practice*,
In Clinical Practice,
https://doi.org/10.1007/978-3-319-66351-7_6

Preoperative Povidone-Iodine Antisepsis

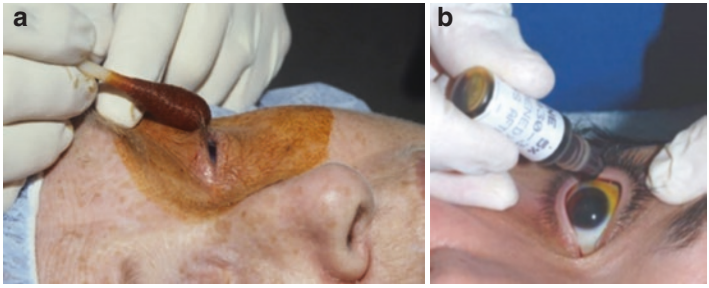

FIGURE 6.1 Preoperative povidone-iodine antisepsis. (**a**) Skin antisepsis with povidone-iodine. (**b**) Conjunctival antisepsis with 5% povidone-iodine drops

be highly active against a variety of gram-positive and gram-negative bacterial pathogens as noted in in vitro experiments. Chlorhexidine concentration of 2.0 and 4.0% in the external irrigating fluid has been shown to slow the corneal epithelial healing rate. Prolonged corneal contact with chlorhexidine may cause irreversible corneal endothelial damage.

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Topical Antibiotics

Topical antibiotics are utilized for endophthalmitis prophylaxis in two settings:

- Preoperative topical antibiotics
- Postoperative topical antibiotics

Preoperative topical antibiotics—A review by Packer et al. (2011) discussed the roles of surgical technique and topical antibiotic prophylaxis in prevention of endophthalmitis. The optimal timing and frequency of topical antibiotic prophylaxis as per this review has been the subject of debate. According to the European Society of Cataract & Refractive Surgeons (ESCRS) guidelines and several national European recommendations (Sweden, Denmark, France), the preoperative use of topical antibiotics is not justified when intracameral antibiotics are used. Generally, preoperative topical antibiotics are more commonly used for prophylaxis in the United States.

Postoperative topical antibiotics—A review by Kuklo et al. (2017) reported wide variations in the prophylaxis practices around the world. As per this review, there is no consensus on the use of prophylactic perioperative antibiotics to prevent endophthalmitis after cataract surgery. Another systematic review and meta-analysis of randomized controlled trials and observational studies performed by Huang et al. (2016) failed to show any evidence to support the use of postoperative topical antibiotics to prevent endophthalmitis after ocular surgery. However, postoperative topical antibiotics are a common standard in the United States to prevent endophthalmitis after ocular surgery.

Topical Antibiotics: Literature

Following are the few selected studies regarding the role of topical antibiotics in specific case scenarios:

- **Cataract Surgery**
  - *Allen HF and Mangiaracine AB* (*1974*): In a series of 36,000 cataract operations, the low rate of infection (0.086% 31/36,000 cataract surgeries) was reported to be achieved by following three principles: (1) meticulous aseptic technique, (2) minimally traumatic surgery, and (3) preoperative antibiotic prophylaxis using a combination of chloramphenicol-polymyxin B sulfate drops and erythromycin ointment.
  - *Jabbarvand* et al. (*2016*)*:* This retrospective, single-center, cross-sectional descriptive study evaluated patients who underwent cataract surgery in an eye hospital in Iran from 2006 through 2014. An incidence of endophthalmitis was reported to be 0.023% (112/480,104 operations). This series demonstrated 40–50% reduced odds of endophthalmitis with short-term treatment with topical or systemic preoperative antibiotics or postoperative subconjunctival injection compared with no prophylaxis.

- **Intravitreal Injections**
  - *Kim SJ* et al. (*2010*): This prospective, observational study of 48 eyes (24 patients) demonstrated substantial levels of resistance to third- and fourth-generation fluoroquinolones and multidrug resistance among coagulase-negative Staphylococcus isolated from patients undergoing multiple intravitreal injections for choroidal neovascularization.
  - *Kim SJ* et al. (*2011*): In this prospective, randomized, controlled, clinical trial of 48 eyes (24 patients) undergoing unilateral intravitreal injections for choroidal neovascularization, it was concluded that repeated exposure of surface ocular flora to ophthalmic antibiotics selects for resistant strains.
  - *Cheung CSY* et al. (*2012*): Retrospective, comparative case series reported the effect of different antibiotic prophylaxis strategies on the incidence of endophthalmitis after intravitreal injections of anti-vascular endothelial growth factors and triamcinolone acetonide. In this study, the rate of endophthalmitis after intravitreal injection was greater with the use of postoperative

topical antibiotics (given for 5 days after injection) compared with no antibiotics.

Category	Rates of endophthalmitis, n/N (%)
• No antibiotics	• 2/5266 (0.04%)
• With antibiotics	• 7/10,629 (0.07%)

– *Yannuzzi* et al. *(OSLI-Retina 2017)*: This is a retrospective case series (2006 and 2016) of 38 patients with endophthalmitis associated with intravitreal injection of anti-VEGF agents [27 (71%) referred and 11 (29%) in-house patients]. At the Bascom Palmer Eye Institute, topical antibiotics were not used before, during, or after intravitreal injections after 2008. The rates of post-injection endophthalmitis during the time period when no topical antibiotics were used (2015 to 2016) were approximately 1 in 20,000 compared to the time period when topical antibiotics were utilized (2006 to 2007) which were approximately 1 in 4,000 injections performed. This implies that topical antibiotics are not essential to prevent postintravitreal injection endophthalmitis.

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Intracameral Antibiotics

Please see next section for more information on intracameral antibiotics.

Systemic Antibiotics

Preoperative or postoperative systemic antibiotics may be utilized in some cases to prevent postoperative endophthalmitis.

- Sharma et al. (2015) showed that oral antibiotics achieve low intraocular concentrations as compared to topical antibiotics in patients undergoing cataract surgery. The role of oral antibiotics in preventing postoperative endophthalmitis after cataract surgery remains unknown.
- However, in patients presenting with open globe injury, systemic antibiotics (preoperative/intraoperative/postoperative) are utilized. Prophylactic systemic antibiotics are considered as follows in cases of open globe injury:
  - Vancomycin 1 g IV bid plus ceftazidime 1 g IV bid prior to surgery
  - Levofloxacin 500–750 mg PO prior to surgery

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Endophthalmitis Prophylaxis for Specific Case Scenarios

- **Endophthalmitis prophylaxis for cataract surgery**
- **Endophthalmitis prophylaxis for intravitreal injections**
- **Endophthalmitis prophylaxis for open globe injuries**

Endophthalmitis Prophylaxis for Cataract Surgery

- **Preoperative povidone-iodine antisepsis** is the only technique to achieve level II evidence in the reduction of endophthalmitis rates (Fig. 2.9)
  - 5% povidone-iodine to ocular surface in holding room prior to surgery
  - 10% povidone-iodine to lids and lashes immediately before surgery
  - Drape to cover eyelashes and lid margins
- **Preoperative and postoperative topical antibiotics** are widely used but there is relatively little evidence to support their efficacy in actually reducing endophthalmitis rates.
- **Intracameral antibiotics**
  - The European Society of Cataract & Refractive Surgeons (ESCRS) randomized clinical trial—Randomized patients to topical levofloxacin, intracameral cefuroxime, both, or neither. Approximate fivefold reduction in endophthalmitis rates associated with intracameral cefuroxime (about 0.2–0.04%).
- Criticisms of the ESCRS study:
  - Relatively high rates of endophthalmitis in eyes not treated with intracameral cefuroxime (about 0.2%)
  - Multiple surgical techniques allowed

Use of topical levofloxacin, rather than fourth-generation fluoroquinolones

– Many retrospective series have documented a decreased rate of endophthalmitis associated with intracameral antibiotics. These studies generally compare patients from an earlier time frame (operated without intracameral antibiotics) to patients from a later time frame (operated with intracameral antibiotics). Criticisms of these cohort studies:

  Endophthalmitis rates may decrease over time for many reasons other than the use of intracameral antibiotics
  – Multiple surgeons
  – Different patients
  – Different techniques
  – Different equipment
  – Unknown factors

Current status of intracameral antibiotics—The use of intracameral antibiotics during cataract surgery is controversial. Three antibiotics for intracameral use during cataract surgery have been primarily reported. These are vancomycin, cefuroxime, and moxifloxacin. All three antibiotics have limitations and risks that must be considered.

- **Vancomycin**, a glycopeptide antibiotic, is usually effective against most gram-positive organisms (*Streptococcus*, *Staphylococcus*, and *Bacillus* species). Vancomycin is associated with hemorrhagic occlusive retinal vasculitis (HORV), a poorly understood and potentially devastating complication.
- **Cefuroxime** is a second-generation cephalosporin antibiotic and has broad spectrum activity against the beta-lactamase-positive pathogens. It is effective against various organisms, such as S*taphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *E. coli*, *N. gonorrhea*, and many others. Intracameral cefuroxime has been

studied in a RCT, but a prepackaged formulation indicated for intracameral use (Aprokam, Thea Pharmaceuticals, Clermont-Ferrand, France) is unavailable in many nations, including the United States, India, and Japan. This has been associated with risks of dilution error, and infection during reconstitution.

- **Moxifloxacin** is a fourth-generation synthetic fluoroquinolone antibacterial agent and is used as an off label intracameral antibiotic. This is increasingly used as the drug is readily available. It is active against a broad spectrum of bacteria including *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*. *Klebsiella* spp., *Moraxella catarrhalis*, *Enterobacter* spp., *Mycobacterium* spp., *Bacillus anthracis*, etc. The paper by Stringham et al. (JAMA 2017) highlights the increasing trend of fluoroquinolone non-susceptibilities among coagulase-negative Staphylococcus isolates causing endophthalmitis reviewed over the past 22 years at the Bascom Palmer Eye Institute, Miami. This study reported that among coagulase-negative Staphylococcus isolates, non-susceptibility to fluoroquinolones increased over time.

The risks of compounding errors, contamination, storage, and transport of the drug are important concerns. Cakir et al. (2009) reported a case series of *Fusarium* endophthalmitis in eight patients in whom compounded intracameral cefuroxime was used. There is a potential risk for toxic anterior segment syndrome (TASS) and corneal endothelial toxicity with all intracameral agents.

Aside from toxicity, there are concerns about fluoroquinolone antimicrobial efficacy. Coagulase-negative Staphylococcus (CoNS) is the most common cause of post-cataract surgery endophthalmitis. In the United States, fluoroquinolone (including moxifloxacin) resistance rates among CoNS endophthalmitis isolates have been reported as high as 40–60%. All intracameral antibiotics are associated with increased costs (moxifloxacin costs average retail price ranges from $175 to $22 per vial in the US) as well as increased risks of emergence of drug resistance. The risk of

post-cataract surgery endophthalmitis in the United States without the use of intracameral antibiotics is about 0.02–0.1%. Even using a 0.1% incidence rate for calculations, it would require intracameral injection in 999 cases in order to prevent one case of endophthalmitis. These 999 patients would be exposed to increased costs in addition to risks of dilution errors, TASS, and corneal endothelial toxicity.

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Endophthalmitis Prophylaxis For Intravitreal Injections

The community standard for endophthalmitis prophylaxis during intravitreal injections continues to evolve, but there appears to be a shift toward focusing on antisepsis and away from the use of peri-intravitreal injection antibiotics. Table 6.1 provides the updated guidelines of an expert panel.

Table 6.1 Guidelines of expert panel on intravitreal injection technique and monitoring

Injection technique	2004	2014
Pupillary dilation	Necessary	No consensus
Sterile drape	No	No
Gloves (universal precautions)	Yes	Yes, but many do not use gloves
Speculum use	Recommended	No consensus
Povidone-iodine: prep	Yes, lids, lashes, and ocular surface	Yes, last drop applied to ocular surface (+/− lids)
Povidone-iodine: allergy	Rare (consider skin test)	Rare (use focal application)
Pre-, peri-, or post-, injection antibiotics	Considered but no consensus	No, 100% agreement
Needle size	27 g or smaller	30 g or smaller
Masks or minimize speaking	Not addressed	Yes
Monitor IOP	Yes	Yes
AC paracentesis	Generally, avoid	Generally, avoid
Post-inject call to patient	Call within 1 week	Tailored to individual patient

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Endophthalmitis Prophylaxis for Open Globe Injuries

- Prophylactic Intravitreal Antibiotics
  - Zone 1 open globe injury—May be considered depending upon nature of injury
  - Zone 2 or 3 open globe injury—Intravitreal antibiotics are more often considered
- Prophylactic Systemic Antibiotics Guidelines:
  - Vancomycin 1 g IV bid plus ceftazidime 1 g IV bid prior to surgery or
  - Levofloxacin 500–750 mg PO prior to surgery

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Chapter 7
Retinal Detachment (RD) and Endophthalmitis

In patients with endophthalmitis, the occurrence of rhegmatogenous retinal detachment (RD) is uncommon and is generally associated with poor visual outcomes. Management of such patients can pose a surgical challenge. While managing the endophthalmitis, RD can be identified at the time of presentation, during vitrectomy or in the postoperative time period. Indirect ophthalmoscopy, echography or direct visualization under microscope may confirm the diagnosis.

- Frequency
- Visual outcomes
- Presentation
- Risk factors associated with poor visual outcomes

Frequency: Retinal Detachment in Endophthalmitis

- In the Endophthalmitis Vitrectomy Study (EVS), patients with RD at initial diagnosis of endophthalmitis were excluded. However, 35/420 (8.3%) patients overall developed RD during follow-up.
- The rates of RD among group of patients undergoing vitrectomy, needle vitreous aspiration, and mechanical vitreous biopsy were 7.8, 11, and 8%, respectively.

H.W. Flynn Jr. et al., *Endophthalmitis in Clinical Practice*,
In Clinical Practice,
https://doi.org/10.1007/978-3-319-66351-7_7

Visual Outcomes: Retinal Detachment in Endophthalmitis

- In the EVS patients with available data, final visual acuity 20/40 or better was reported in 8/30 (27%) patients with RD compared to 201/364 (55%) patients without RD.
- The overall visual outcomes in this subgroup of the EVS were reported to be poor with more than half (16/30) patients with RD achieving visual acuity worse than 5/200 despite a high anatomic success rate of 78% (18/23).

Presentation: Retinal Detachment in Endophthalmitis

- Patients with endophthalmitis and concurrent RD
- Patients with endophthalmitis and delayed-onset RD

In the setting of endophthalmitis, RD developing after vitrectomy surgery has been reported to range from 4.6 to 16% (1, 5–7) (compared to 5% in vitrectomy performed for non-endophthalmitis cases 1, 5, 6).

Risk Factors Associated with Poor Visual Outcomes in Eyes with RD and Endophthalmitis

RD associated with endophthalmitis is associated with generally poor anatomic and visual outcomes. Following are the risk factors associated with poor visual outcomes:

- Infection with more virulent organisms
- Open globe injuries
- Retained intraocular foreign body

Role of Silicone Oil in Endophthalmitis Patients

Silicone oil may be utilized in cases with endophthalmitis. Silicone oil is reported to have antimicrobial properties as well as stabilizes the eye and may even help in maintaining the integrity of eyeball (prevent need for evisceration/enucleation).

Antimicrobial Properties of Silicone Oil

- **Ozdamar et al. (In 1999)**—This experimental study showed antimicrobial activity of silicone oil against endophthalmitis-causing agents in vitro. In this study, the antimicrobial activity of silicone oil (1300 centistokes) was demonstrated against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, *Candida albicans*, and *Aspergillus* spp. However, in one report by Arici et al. (2016), anaerobic bacteria such as *Propionibacterium acnes* were reported to be resistant to silicone oil.

Literature: Silicone Oil in Endophthalmitis and Rhegmatogenous Retinal Detachment

- **Nagpal et al. (2012)**—This is a prospective, randomized, interventional, comparative study comprising 129 eyes with endophthalmitis (postsurgical and traumatic) that underwent PPV. Anatomic and visual outcomes among following groups were compared:
  - Group 1 (pars plana vitrectomy alone $n = 65$ eyes)
  - Group 2 (pars plana vitrectomy with silicone oil injection, $n = 64$ eyes)

In this study, group undergoing pars plana vitrectomy (PPV) with silicone oil injection resulted in significantly better anatomic outcomes and significantly less need for additional surgery as compared with PPV alone.

- **Dave et al. (2017)**—Anatomic and functional treatment outcomes of 93 patients with endophthalmitis and concurrent or delayed-onset retinal detachment are reported (Figs. 7.1 and 7.2). RD was diagnosed at presentation in 20/93 (21.5%) patients (concurrent group—group 1) and during follow-up in remaining 73/93 (78.5%) patients (delayed-onset group—group 2). In group 1, the initial treatment consisted of vitrectomy, intravitreal antibiotics, and silicone oil injection in 19/20 patients. In group 2, patients did not receive silicone oil during initial treatment but underwent silicone oil injection during subsequent surgery for repair of retinal detachment.
  - Group 1 (concurrent group)—Rates of complete retinal reattachment and visual acuity ≥20/400 were 73.7 and 30.0%, respectively.
  - Group 2 (delayed-onset group)—Rates of complete retinal reattachment and visual acuity ≥20/400 were 98.5 and 39.7%, respectively.

The median visual acuity at last follow-up in 44 eyes undergoing silicone oil removal was 20/100 (logMAR 0.7) while in the remaining 49 eyes which did not undergo silicone oil removal was 20/2000 (logMAR 2.0). Although 53/93 (57%) eyes in this series had final vision as only light perception or no light perception, none of the eyes are needed to be eviscerated or enucleated. In these endophthalmitis patients with concurrent or delayed-onset retinal detachment, the use of silicone oil can be a useful adjunct.

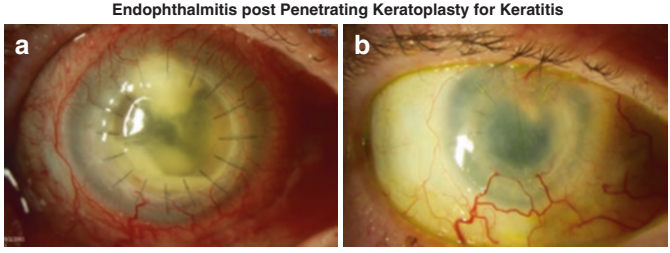

FIGURE 7.1 (**a**) Post-intravitreal injection endophthalmitis following penetrating keratoplasty. (**b**) Eye underwent pars plana vitrectomy fluid-air exchange, injection of intravitreal voriconazole and amphotericin-B and silicone oil injection which lead to resolution of infection and inflammation

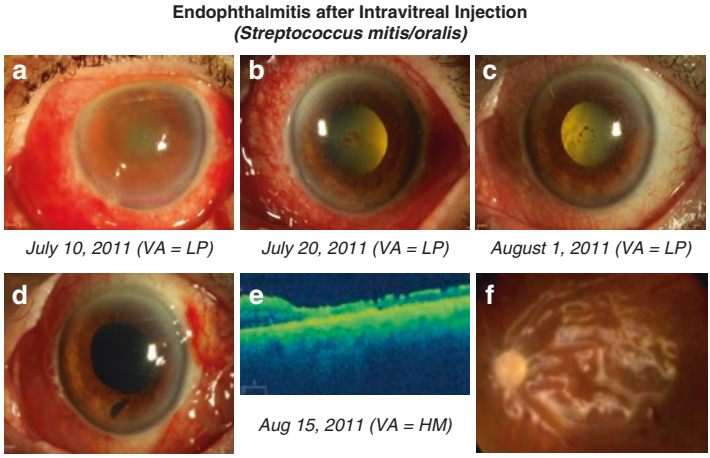

FIGURE 7.2 Post-intravitreal injection endophthalmitis—80-year-old male patient with neovascular age-related macular degeneration (AMD) presented 2 days after intravitreal ranibizumab injection with sudden painful decrease in vision (Steers et al., 2002). (**a**) Slit-lamp examination showed conjunctival congestion, corneal edema, hypopyon, fibrinous reaction in the anterior chamber, hazy view of the posterior segment, and light perception (LP) vision. The patient underwent vitreous tap and intraocular antibiotic injection. The vitreous culture was positive for *Streptococcus mitis*/*Streptococcus oralis*. (**b**, **c**) Inflammation reduced but vitreous exudates persisted. (**d**–**f**) Six days after pars plana vitrectomy, lensectomy, and silicone oil injection showing resolving inflammation, retinal thinning on OCT, pale optic disc, and attached retina in silicone oil filled eye

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Chapter 8
Antibiotic Stewardship

In order to address emerging antimicrobial resistance (Fig. 8.1), the US Centers for Disease Control and Prevention (CDC) recommends antibiotic stewardship programs to optimize antibiotic selection and reduce the inappropriate use of broad-spectrum antibiotics. The new medication management standards (MM.09.01.01) for hospitals, critical access hospitals, and nursing care centers became effective January 1, 2017 and are available online at https://www.jointcommission.org/assets/1/6/New_Antimicrobial_Stewardship_Standard.pdf. This new antimicrobial stewardship standard includes elements of leadership commitment (accountability documents, budget plans, performance improvement plans, strategic plans, use of electronic health records), education of staff and patients, multidisciplinary teams, analysis of individual medical center data, and application of these results towards improvement in treatment outcomes.

In ophthalmology, antimicrobial use is mostly prophylactic, with little peer-reviewed evidence to support its use. With regard to elective intraocular procedures, antisepsis, rather than antibiotics, may be more important. In cataract surgery, there is no worldwide consensus regarding antibiotic prophylaxis in general and intracameral antibiotics in particular. Intracameral antibiotics are used more commonly in Europe than in the US. Prophylactic antibiotics are associated with increased costs, risks to the individual patient (dilution errors,

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In Clinical Practice,
https://doi.org/10.1007/978-3-319-66351-7_8

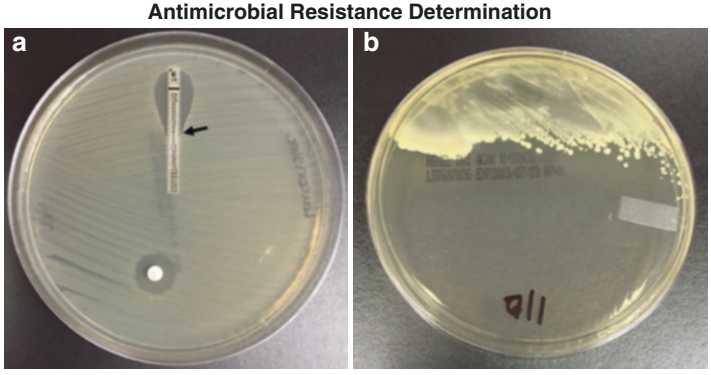

FIGURE 8.1 Antimicrobial resistance determination. (**a**) E-test showing *Leuconostoc* species with minimum inhibitory concentration (MIC) levels of 4 μg/mL (*black Arrow*) to vancomycin E-test strip, indicating intermediate resistance to vancomycin. (**b**) Lower part of the culture plate shows clear zone around vancomycin disc (30 μg). Growth of *Leuconostoc* species over brain–heart infusion (BHI) agar containing vancomycin (6 μg/mL) indicating reduced vancomycin susceptibility

contamination during compounding, toxic anterior segment syndrome (TASS), corneal endothelial toxicity, HORV, toxic effects on the retina, and others), and risks to society as a whole by contributing to emerging antimicrobial resistance. Antibiotic stewardship programs are hospital-based programs which can optimize the treatment of infections, reduce adverse events associated with antibiotic use, and help to mitigate these concerns.

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Chapter 9
Outcomes (Anatomic and Functional) and Treatment-Related Complications

Treatment outcomes are highly variable and are related to the infecting organism as well as the time to diagnosis and treatment. Prompt treatment is more important than any other consideration, including the decision between TAP and PPV. Treatment outcomes may be substantially worse in certain categories of endophthalmitis, such as post-traumatic and post-PPV, due to preexisting or concomitant posterior segment disease.

Treatment Outcomes of Acute-Onset Postoperative Endophthalmitis Following Cataract Surgery

Treatment outcomes are discussed as reported by following studies:

(a) The EVS
(b) Lalwani et al. (Ophthalmology, 1998)
(c) Yannuzzi et al. (AJO 2017)

H.W. Flynn Jr. et al., *Endophthalmitis in Clinical Practice*, In Clinical Practice,
https://doi.org/10.1007/978-3-319-66351-7_9

Outcomes as Reported by the EVS

The multicenter, randomized clinical trial enrolled 420 patients with clinical evidence of endophthalmitis within 6 weeks of cataract surgery or secondary intraocular lens (IOL) implantation. The EVS determined the roles of immediate pars plana vitrectomy and systemic antibiotic treatment in the management of acute-onset postoperative endophthalmitis. Reported outcomes were as follows:

- 53% of patients had final visual acuity of 20/40 or better
- 15% of patients had final visual acuity of 20/200 or worse
- Coagulase-negative Staphylococci associated with best outcomes

Lalwani et al. 2008

Retrospective case series of 73 eyes of 73 patients, with endophthalmitis treated at a single medical center between January 1, 1996, and December 31, 2005, for clinically diagnosed, culture-positive endophthalmitis occurring within 6 weeks of clear corneal cataract surgery. Reported outcomes were as follows:

- Hypopyon was present in 60 of 73 (82.2%) eyes. The initial treatment included intravitreal vancomycin, ceftazidime, and dexamethasone. A vitreous tap and intravitreal injection were performed in 54 of 73 (74.0%) eyes and pars plana vitrectomy in 19 of 73 (26.0%) eyes.
- Coagulase-negative Staphylococcus was isolated in 50 of 73 (68.4%) eyes. Other isolates included *Staphylococcus aureus* in 5/73 (6.8%) and *Streptococcus* species in 6 of 73 (8.2%).
- A visual acuity of 20/40 or better was achieved in 36 of 73 patients (49.3%) at final follow-up.
- The features and outcomes of endophthalmitis associated with clear corneal cataract surgery were similar to those reported in the EVS, which are associated with scleral incisions, but time to diagnosis was later with clear corneal incisions.

Yannuzzi et al. 2016

Retrospective case series of 63 eyes of 63 patients (clinical and microbiology records) with culture-positive endophthalmitis occurring within 6 weeks of clear corneal cataract surgery who presented to a tertiary referral center between 2006 and 2015 were analyzed. Reported outcomes were as follows:

- Coagulase-negative Staphylococcus was isolated in 39 of 63 (62%) eyes, *Staphylococcus aureus* in 7 of 63 (11%) eyes, and *Streptococcus* species in 7 of 63 (11%) eyes.
- A VA of 20/40 or better was achieved in 24 of 63 (38%) eyes.
- A number of isolates were resistant to cephalosporins and fluoroquinolones.

Comparison of Yannuzzi et al. *(2016) vs. Lalwani* et al. *(2008)*. Both studies were reported from the same medical center

- The number of patients presenting with 5/200 or better was similar in both studies, but mean time to presentation was reported to be shorter in Yannuzzi et al. (8 vs. 13 days).
- The overall distribution of organisms was similar between the two studies with coagulase-negative Staphylococcus comprising most cases.
- While 19 (26%) of 73 eyes were treated with PPV as the initial treatment in Lalwani et al., only 6 (10%) of 73 eyes were treated with PPV as the initial treatment in Yannuzzi et al. ($p = 0.013$).
- Final visual outcomes were slightly more favorable in Lalwani et al. with a larger proportion of patients achieving 20/40 and 20/100 or better, although these differences were not statistically significant ($p = 0.189$ and $p = 0.058$, respectively). There was, however, a statistically significant difference in the percentage of eyes ending with 5/200 or better (63 of 73 eyes, 86%, in Lalwani et al. vs. 45 of 63 eyes, 71%, in Yannuzzi et al. ($p = 0.032$).
- Of the eyes with coagulase-negative Staphylococcus, 31 (62%) of 52 eyes achieved 20/40 or better in Lalwani et al. in comparison to 20 (51%) of 39 in Yannuzzi et al. $p = 0.310$.

- Both patients treated with tap and inject as the initial treatment and those treated with PPV and inject as the upfront treatment in Yannuzzi et al. study fared slightly worse than Lalwani et al. with fewer achieving 20/40 or 20/100 or better.

References: Treatment Outcomes Acute-Onset Endophthalmitis

- Results of the Endophthalmitis Vitrectomy Study. A randomized trial of immediate vitrectomy and of intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis. Endophthalmitis Vitrectomy Study Group. Arch Ophthalmol. 1995;113(12):1479–96.
- Lalwani GA, Flynn HW, Jr., Scott IU, Quinn CM, Berrocal AM, Davis JL, et al. Acute-onset endophthalmitis after clear corneal cataract surgery (1996–2005). Clinical features, causative organisms, and visual acuity outcomes. Ophthalmology. 2008;115(3):473–6.
- Sridhar J, Yonekawa Y, Kuriyan AE, Joseph A, Thomas BJ, Liang MC, et al. Microbiologic spectrum and visual outcomes of acute-onset endophthalmitis undergoing therapeutic pars plana vitrectomy. Retina. 2017;37(7):1246–51.
- Thomas BJ, Mehta N, Yonekawa Y, Sridhar J, Kuriyan AE, Relhan N, et al. Pars plana vitrectomy for late vitreoretinal sequelae of infectious endophthalmitis: surgical management and outcomes. Retina. 2017;37(4):651–6.
- Yannuzzi NA, Si N, Relhan N, Kuriyan AE, Albini TA, Berrocal AM, et al. Endophthalmitis after clear corneal cataract surgery: outcomes over two decades. Am J Ophthalmol. 2017;174:155–9.

Treatment Outcomes of Delayed-Onset Postoperative Endophthalmitis Following Cataract Surgery

Visual outcomes are discussed as reported by following two studies:

(a) Clarke et al. (1999)
(b) Shirodkar et al. (2012)

Clark et al.

Clark et al. (1999) report the treatment strategies and visual acuity outcomes of chronic postoperative endophthalmitis caused by *Propionibacterium acnes*. In this retrospective non-comparative case series of 36 patients treated at two institutions from 1974 to 1996, the mean follow-up after the last treatment was 2.9 years. Patients underwent three different initial treatment strategies:

1. Intraocular antibiotic injection alone (IOAB; $n = 12$)
2. Pars plana vitrectomy and IOAB injection (PPV; $n = 10$)
3. PPV with subtotal capsulectomy and IOAB injection (PPV-PC; $n = 14$)

- The number of patients with recurrent or persistent inflammation after one of the three initial treatment strategies was as follows: (1) IOAB alone, 12 (100%); (2) PPV, 5 (50%); and (3) PPV-PC, 2 (14%).
- None of the patients that underwent subsequent PPV, total capsular bag removal, IOAB injection, and either intraocular lens (IOL) exchange or removal had persistent or recurrent intraocular inflammation.
- Overall, final visual acuity was 20/40 or better in 18 patients (50%), and a total of 28 patients (78%) retained 20/400 or better vision.

  – In this series of chronic *P. acnes* endophthalmitis, initial treatment with IOAB injection alone or vitrectomy without capsulectomy was associated with high rates of recurrent or persistent intraocular inflammation.

  - Pars plana vitrectomy, partial capsulectomy, and IOAB injection without IOL exchange were usually successful on long-term follow-up.
  - In patients with recurrent intraocular inflammation, pars plana vitrectomy, total capsular bag removal, IOAB injection, and IOL exchange or removal were a uniformly successful strategy.

The study recommended that in contrast to other types of postoperative endophthalmitis, IOL exchange can be considered in these patients after total capsular bag removal.

Shirodkar et al. (2012)

Shirodkar et al. (2012) reported a large retrospective consecutive case series of 118 patients with delayed-onset and acute-onset endophthalmitis (culture-proven) after cataract surgery, who were treated at the Bascom Palmer Eye Institute between January 2000 and December 2009. The study results were as follows (Table 9.1):

Visual Outcome

- Patients with delayed-onset endophthalmitis generally presented with better initial visual acuities, had a lower frequency of hypopyon, and had better visual outcomes compared to acute-onset patients.

Microbiology

- In delayed-onset endophthalmitis group—*Propionibacterium acnes* was the most common organism cultured and was associated with the best visual acuity outcomes.
- In the acute-onset endophthalmitis group, Coagulase-negative Staphylococcus was the most common organism cultured and was associated with the best visual acuity outcomes.

Table 9.1 Results of retrospective case series by Shirodkar et al. 2012

	Acute-onset endophthalmitis (≤6 weeks after surgery)	**Delayed-onset endophthalmitis (>6 weeks after surgery)**
Number of cases	92	26
Presenting visual acuity 5/200 or worse	89%	31%
Hypopyon	80%	46%
Most frequent isolate	Coagulase-negative Staphylococcus (57/92)	*Propionibacterium acnes* (11/26)
Visual outcome of 20/100 or better in patients with most frequent isolate	56%	91%
Intraocular lens removed or exchange	–	19 of 26 cases (73%) Of these 19 cases, 13 achieved a visual outcome of 20/100 or better

References: Treatment Outcomes Delayed-Onset Endophthalmitis

- Clark WL, Kaiser PK, Flynn HW, Belfort A, Miller D, Meisler DM. Treatment strategies and visual acuity outcomes in chronic postoperative Propionibacterium acnes endophthalmitis. Ophthalmology. 1999;106(9):1665–70.
- Shirodkar AR, Pathengay A, Flynn HW, Jr., Albini TA, Berrocal AM, Davis JL, et al. Delayed- versus acute-onset endophthalmitis after cataract surgery. Am J Ophthalmol. 2012;153(3):391–8 e2.

Treatment Outcomes of Endophthalmitis After Pars Plana Vitrectomy

Visual outcomes after treatment of post-PPV endophthalmitis are generally worse than after cataract surgery. Underlying retinal pathology could be the reason for poor visual potential. A review by Dave et al. of various series on endophthalmitis post vitrectomy is shown in Table 9.2.

Table 9.2 Review of literature on various series on endophthalmitis post pars plana vitrectomy

Paper	Diagnosis at time of PPV	Year	Cases	Visual outcome at last visit
Cohen et al.	ERM, MH, PDR	1995	18/12,216	3 EV, 6 NLP, 1 HM, 1 LP, 2 20/400, 1 20/50, 1 20/30, 1 20/25 and 2 20/20
Aaberg et al.	–	1998	3/6557	All eyes NLP
Eifrig et al.	PDR, macular pucker, recurrent RD	2004	6/15,326	3 NLP, 1 LP, 1 2/200 and 1 20/200
Joondeph et al.	VH, MH, ERM, RD	2005	5/10,397	2 NLP, 1 HM, 1 20/200 and 1 20/50
Shaikh et al.	ERM	2007	2/129	One 20/400, one 20/40
Scott et al.	ERM, PDR, CRVO, disc pit	2008	13/7682	1 LP, 1 HM, 1 20/400, 1 5/200, 2 20/150, 1 20/100, 2 20/20, 2 20/40, 2 20/30
Shimada et al.	ERM	2008	2/6935	Both cases NLP

Table 9.2 (continued)

Paper	Diagnosis at time of PPV	Year	Cases	Visual outcome at last visit
Chen et al.	VH, TRD with VH	2009	2/3477	One 20/200, one 20/125
Mollan et al.	MH, PDR	2009	2/5278	One 1/60, one 6/12
Scott et al.	RD, MH, ERM	2011	3/8554	One HM, one 20/100, one 20/40
Mutoh et al.	CME, ERM	2012	4/502	One 20/30, one 20/100, one 20/20, one 20/25

Abbreviations: *PPV*, pars plana vitrectomy; *NLP*, no light perception; *LP*, light perception; *HM*, hand motion vision; *ERM*, epiretinal membrane; *RD*, retinal detachment; *VH*, vitreous hemorrhage; *CRVO*, central retinal vein occlusion; *PDR*, proliferative diabetic retinopathy; *CME*, cystoid macular edema; *MH*, macular hole; *TRD*, traction retinal detachment; *EV*, eviscerated

References: Treatment Outcomes of Endophthalmitis after Pars Plana Vitrectomy

- Dave VP, Pathengay A, Schwartz SG, Flynn HW, Jr. Endophthalmitis following pars plana vitrectomy: a literature review of incidence, causative organisms, and treatment outcomes. Clin Ophthalmol. 2014;8:2183–8.

Treatment Outcomes of Endophthalmitis Following Glaucoma Surgery

- Conjunctival filtering bleb-associated infection and endophthalmitis
- Endophthalmitis associated with glaucoma drainage devices

Conjunctival filtering bleb-associated infection and endophthalmitis:

Leng et al. (2011)

Leng et al. (2011) reported the clinical features, organisms, and outcomes of 71 eyes from 68 patients with delayed-onset bleb-associated endophthalmitis. In this retrospective consecutive case series, patients who were treated for delayed-onset bleb-associated endophthalmitis between January 1, 1996, and July 1, 2008, at a single institution were included. Infections within 1 month of glaucoma filtering surgery, inadvertent filtering blebs after cataract surgery, and patients with glaucoma drainage devices were excluded. The study results were as follows:

- An adjunctive antifibrotic agent was used in 48 eyes (68%).
- The mean time between surgery and endophthalmitis was 4.8 years (range, 0.1–16; standard deviation, 3.6).
- The average follow-up time after initial treatment was 37 months (range 1–144; standard deviation, 41).
- At presentation, 17 eyes (24%) had a bleb leak.
- Fifty-seven eyes (83%) were culture positive.
- The most common causative organisms were *Streptococcus* species in 20 eyes (30%), gram-negative organisms in 19 eyes (28%), and coagulase-negative Staphylococcus in 12 eyes (18%).
- All gram-positive isolates were sensitive to vancomycin.

- Nine eyes (13%) eventually underwent evisceration or enucleation secondary to pain and/or poor vision.
- The main outcome measure was best-corrected visual acuity at the last follow-up examination.
- Final visual acuities in the initial tap/inject group (n = 45) versus the initial vitrectomy group (n = 24) were as follows: 20/40 or better (29% vs. 4.2%), 20/50 to 20/400 (36% vs. 29%), and worse than 5/200 (36% vs. 62%).
  - *Streptococcus* species and gram-negative organisms were the most common causative isolates identified in this case series of delayed-onset bleb-associated endophthalmitis.
  - Despite treatment of the infection, visual outcomes were generally poor.

References: Treatment Outcomes of Endophthalmitis Following Glaucoma Surgery

- Leng T, Miller D, Flynn HW, Jr., Jacobs DJ, Gedde SJ. Delayed-onset bleb-associated endophthalmitis (1996–2008): causative organisms and visual acuity outcomes. Retina. 2011;31(2):344–52.
- Song A, Scott IU, Flynn HW, Jr., Budenz DL. Delayed-onset bleb-associated endophthalmitis: clinical features and visual acuity outcomes. Ophthalmology. 2002;109(5):985–91.

Endophthalmitis associated with glaucoma drainage devices:

Medina et al. (2016)

Medina et al. (2016) reported the clinical features, organisms, and treatment outcomes in patients with endophthalmitis associated with glaucoma drainage implants. In this

retrospective noncomparative case series of 13 patients, exposure occurred in eight eyes, including exposure of the tube in four eyes, exposure of the patch graft in three eyes, and exposure of the plate in one eye. In the remaining five eyes, either recent implant placement or conjunctival revision occurred.

- Intravitreal antibiotics were administered in all eyes, with the exception of one eye (primary evisceration).
- Removal of the implant was performed in six eyes and evisceration or enucleation was performed in three eyes.
- Median preinfection visual acuity was 20/80 (range, 20/30 to hand motion).
- Visual acuity at last follow-up was no light perception (five eyes), light perception (two eyes), hand motion (one eye), and better than or equal to 20/200 (five eyes).
  - Clinical features associated with endophthalmitis include implant exposure and a history of recent surgery.
  - The most common organism was *Staphylococcus epidermidis* (five eyes).
  - In some patients, successful treatment could be achieved even without removal of implant.
  - Visual outcomes were generally poor.

References: Treatment Outcomes of Endophthalmitis Associated with Glaucoma Drainage Devices

- Medina CA, Butler MR, Deobhakta AA, Banitt MR, Albini TA, Smiddy WE, et al. Endophthalmitis associated with glaucoma drainage implants. Ophthalmic Surg Lasers Imaging Retina. 2016;47(6):563–9.
- Tai AX, Song JC. Surgical outcomes of Baerveldt implants in pediatric glaucoma patients. J AAPOS. 2014;18(6):550–3.

Treatment Outcomes of Post-Traumatic Endophthalmitis

Outcomes of post-traumatic endophthalmitis are highly variable depending upon the causative organism, associated globe injuries, presence of intraocular foreign bodies, delayed presentation after injury, and type of injury (gunshot wound/infected wound/clean wound). Retained intraocular foreign bodies (IOFBs) are associated with endophthalmitis in approximately 7–13% of cases:

(a) Colyer et al. (Ophthalmology 2007)
(b) Mieler et al. (Ophthalmology 1990)
(c) Banker et al. (OSLI Retina, 2017)

Colyer et al. (Ophthalmology 2007)

The study by Colyer et al reported the long-term follow-up results of intraocular foreign body (IOFB) removal at Walter Reed Army Medical Center during Operation Iraqi Freedom and Operation Enduring Freedom from February 2003 through November 2005. This study also looked at the prognostic factors for visual outcome in this patient population. In this retrospective, noncomparative, interventional case series, 79 eyes of 70 United States military soldiers deployed in support of operations Iraqi Freedom and Enduring Freedom sustained IOFB injuries and subsequently were treated at the Walter Reed Army Medical Center with a minimum of 6 months of follow-up were analyzed.

- Final visual acuity, rate of proliferative vitreoretinopathy, rate of endophthalmitis were the primary outcome measures.
- Average patient age was 27 years, with an average of 331 days of postoperative follow-up.
- Average IOFB size was 3.7 mm (range, 0.1–20 mm).
- Median time to IOFB removal was 21 days (mean, 38 days; range, 2-661 days).

- Mean preoperative visual acuity was 20/400 (1.36 logarithm of mean angle of resolution [logMAR] units) and mean final visual acuity was 20/120 (0.75 logMAR).
- There were no cases of endophthalmitis (0/79 eyes; 95% confidence interval, 0%-3.1%), siderosis bulbi, or sympathetic ophthalmia.
- Timing of vitrectomy did not correlate with visual outcome.
- The most common systemic antibiotic administered was levofloxacin, whereas the most common topical antibiotic administered was moxifloxacin.
- Delayed IOFB removal with a combination of systemic and topical antibiotic coverage can result in good visual outcome without an apparent increased risk of endophthalmitis or other deleterious side effects.

Mieler et al. (Ophthalmology 1990)

Mieler et al. reviewed retained IOFBs presenting to The Medical College of Wisconsin between July 1986 and June 1989. A total of 27 cases were evaluated and surgically treated. All eyes presenting within 24 hours of injury underwent immediate surgery (average, 4.5 h after presentation).

- None of the 27 cases presented with or developed clinical signs of endophthalmitis, yet bacterial cultures of the removed intraocular material were positive in seven cases (foreign body in five cases, the aqueous fluid and the vitreous fluid in one case each).
- Of the seven eyes with positive intraocular cultures, all had pars plana vitrectomy removal of the IOFB, and three of these eyes received intravitreal antibiotics at the time of surgery over concern of a high risk of infection. Two of these eyes eventually grew out the *Bacillus* sp. Even after the positive cultures, no signs of clinical infection developed in any of the eyes.
- All eyes received subconjunctival antibiotics and postoperative topical and systemic antibiotics.
- All seven eyes retained excellent visual acuity of 20/70 or better at an average of 10 months' follow-up.
- Follow-up ranged from 1 to 31 months.

Banker et al. (OSLI Retina, 2017)

Banker et al. reported the visual and anatomical outcomes and microbiologic spectrum of culture-positive endophthalmitis in open globe injuries with or without intraocular foreign bodies (IOFBs). In this retrospective, interventional case series 718 patients with open globe injury treated at a University Referral Center between 2004 and 2015 were included.

- Culture-positive cases of endophthalmitis after open globe repair occurred in 2.1% (n = 15/718) of eyes; two eyes had evidence of endophthalmitis on presentation.
- The most common organism was *Staphylococcus* sp. (5/17).
- An IOFB was present in 6.8% (n = 49/718) of eyes.
- All eyes received prophylactic intravitreal antimicrobials.
- In eyes with IOFB, the rate of culture-positive endophthalmitis after initial globe repair in eyes with IOFB was 8.1% (n = 4/49) vs. 1.6% (n = 11/669) in eyes without IOFB ($p < 0.01$).
- Culture-positive endophthalmitis was identified after open globe injuries more often in eyes with a concurrent IOFB.

References: Treatment Outcomes of Endophthalmitis Associated with Open Globe Injuries

- Banker TP, McClellan AJ, Wilson DW BS, Juan FM, Kuriyan AE, Relhan N, Chen FV, Albini TA, Berrocal AM, Sridhar J, Gregori NZ, Townsend JH, Flynn HW Jr. Culture-positive endophthalmitis after open globe injuries with and without retained intraocular foreign bodies. OSLI Retina 2017 Aug 1;48(8):632–7.
- Colyer MH, Weber ED, Weichel ED, Dick JS, Bower KS, Ward TP, Haller JA. Delayed intraocular foreign body removal without endophthalmitis during Operations Iraqi Freedom and Enduring Freedom. Ophthalmology. 2007;114(8):1439–47.
- Mieler WF, Ellis MK, Williams DF, Han DP. Retained Intraocular Fore ign Bodies and Endonhthalmltls. Ophthalmology. 1990;97(11):1532–8.

Treatment Outcomes of Endogenous Endophthalmitis

Outcomes of endogenous endophthalmitis as reported by following studies are discussed:

(a) Schiedler et al. (2004)
(b) Lingappan et al. (2012)
(c) Sridhar et al. (2016)

Schiedler et al. (2004)

Schiedler et al. reported the clinical features and visual acuity outcomes associated with endogenous endophthalmitis. In this retrospective, observational case series of 21 eyes of 21 patients treated at the Bascom Palmer Eye Institute for culture-proven endogenous endophthalmitis between 1996 and 2002 were reviewed.

- Compared with published series of postoperative or post-traumatic endophthalmitis, patients with endogenous endophthalmitis were more likely to have fungal isolates with a predominance of *Candida albicans*.
- Endogenous endophthalmitis was generally associated with high mortality and poor visual acuity outcomes, particularly when caused by more virulent species such as *Aspergillus*.

Lingappan et al. (2012)

Lingappan et al. reported the causative organisms, management strategies, and visual outcomes in endogenous fungal endophthalmitis. In this observational case series of 65 eyes of 51 patients with culture-positive endogenous fungal endophthalmitis between January 1, 1990, and July 1, 2009 were analyzed (mean follow-up of 18 months).

- Yeasts were the most common causative organism in 38 (75%) patients compared with molds in 13 (25%) patients.
- Visual acuity of 20/200 or better was present in 28 (56%) eyes with yeasts and in 5 (33%) eyes with molds at the last follow-up.
  - Endogenous fungal endophthalmitis was generally associated with poor visual acuity outcomes, especially when caused by molds.
  - Retinal detachment was reported in 26% (17/65) eyes during follow-up.

Sridhar et al. (2013)

Sridhar et al. reported risk factors, clinical features, and treatment outcomes in patients with endogenous fungal endophthalmitis with yeast and mold infections. In this retrospective consecutive case series, 67 eyes of 53 patients were identified, 51 eyes of 39 patients had positive cultures for yeast, and 16 eyes of 14 patients had positive cultures for molds.

Patients with molds as a causative organism (compared to those patients with yeast as a causative organism):

- Had significantly shorter duration of symptoms prior to diagnosis (molds 3.8 days, yeast 21.0 days, $p = 0.002$).
- Were more likely to be receiving iatrogenic immunosuppression (molds 57.1%, yeast 7.7%, $p = 0.001$).
- Have a history of whole-organ transplantation (molds 35.7%, yeast 2.6%, $p = 0.001$).
- Were more likely to have hypopyon at the time of diagnosis (molds 37.5%, yeast 6.0%, $p = 0.001$).
- Had significantly worse visual acuity at the time of diagnosis (logMAR visual acuity molds 1.80, yeast 1.15, $p = 0.008$) and at final visit (logMAR visual acuity molds 1.97, yeast 1.05, $p = 0.005$).
- There was no significant difference in the rate of retinal detachment between the two groups (mold 12.5%, yeast 30.6%, $p = 0.201$).

- Patients with cultures positive for mold were significantly more likely to undergo enucleation (molds 25.0%, yeast 0%, $p < 0.001$).
  - Outcomes—While endogenous fungal endophthalmitis is generally associated with poor visual acuity outcomes, infection with mold species was associated with worse visual acuity on presentation and on final follow-up than infection with yeast species. Enucleation rates were much higher in mold cases.

References: Treatment Outcomes of Endogenous Endophthalmitis

- Lingappan A, Wykoff CC, Albini TA, Miller D, Pathengay A, Davis JL, et al. Endogenous fungal endophthalmitis: causative organisms, management strategies, and visual acuity outcomes. Am J Ophthalmol. 2012;153(1):162–6 e1.
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- Sridhar J, Flynn HW, Jr., Kuriyan AE, Miller D, Albini T. Endogenous fungal endophthalmitis: risk factors, clinical features, and treatment outcomes in mold and yeast infections. J Ophthalmic Inflamm Infect. 2013;3(1):60.

Treatment Outcomes of Endophthalmitis Associated with Intravitreal Injection

Outcomes of endophthalmitis associated with intravitreal injections as reported by following studies are discussed:

(a) Goldberg et al. (Ophthalmology 2013)
(b) Gregori et al. (Retina 2015)
(c) Yannuzzi et al. (In Press - OSLI-Retina)

Goldberg et al. (Ophthalmology 2013)

Goldberg et al. reported the 1-year clinical outcomes of an outbreak of *Streptococcus* endophthalmitis after intravitreal injection of bevacizumab, in this retrospective consecutive case series of 12 eyes of 12 patients who developed endophthalmitis after receiving intravitreal bevacizumab prepared by a single compounding pharmacy:

- All patients received initial vitreous tap and injection, and eight patients (67%) subsequently underwent pars plana vitrectomy (PPV).
- After 12-month follow-up, outcomes have been poor. Seven patients (58%) required evisceration or enucleation, and only one patient regained preinjection visual acuity.
- Molecular testing using real-time polymerase chain reaction, partial sequencing of the groEL gene, and multilocus sequencing of seven housekeeping genes confirmed the presence of a common strain of *Streptococcus mitis*/*Streptococcus oralis* in vitreous specimens and seven unused syringes prepared by the compounding pharmacy at the same time.
- An FDA investigation of the compounding pharmacy noted deviations from standard sterile technique, inconsistent documentation, and inadequate testing of equipment required for safe preparation of medications.
  - In this outbreak of endophthalmitis, outcomes have been generally poor, and PPV did not improve visual results at 1-year follow-up.

Gregori et al. (Retina 2015)

Gregori et al. reported the outcomes of infectious endophthalmitis after intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) agents from January 1, 2005, through December 31, 2014.

- In this study, population-based rate of endophthalmitis after anti-VEGF injections from 2011 to 2013 was 391/740,757 (0.053%).
- The Bascom Palmer Eye Institute's rate was 20/121,285 (0.016%) during the study period: eight after bevacizumab (0.012%), six after ranibizumab (0.018%), and six after aflibercept (0.031%) injection.
- Nine cases (45%) were culture positive: *Streptococcus* species (5), coagulase-negative Staphylococcus (3), and non-anthracis *Bacillus* (1).
- Final visual acuity varied from 20/25 to no light perception.
- Treatment outcomes were variable but generally fared better in the culture-negative cases.

Yannuzzi et al. (OSLI-Retina 2017)

Yannuzzi et al. reported the treatment outcomes in patients with endophthalmitis (between 2006 and 2016) associated with intravitreal injection of anti-VEGF agents, in this retrospective case series of 38 eyes of 38 patients including 27 (71%) referred and 11 (29%) in-house patients:

- The per-injection rate of all clinically suspected endophthalmitis was 0.014% (23/159,066).
- The most common isolates were coagulase-negative Staphylococcus and *Streptococcus*.
- A VA of 5/200 or better was achieved in 21/38 (55%) eyes overall and 2/14 (14%) eyes infected with *Streptococcus*.
- The rate of in-house post-intravitreal injection endophthalmitis was low.
  - Outcomes were generally poor and the worst in *Streptococcus* cases.

References: Treatment Outcomes of Endophthalmitis Associated with Intravitreal Injections

- Goldberg RA, Flynn HW, Jr., Miller D, Gonzalez S, Isom RF. Streptococcus endophthalmitis outbreak after intravitreal injection of bevacizumab: one-year outcomes and investigative results. Ophthalmology. 2013;120(7):1448–53.
- Gregori NZ, Flynn HW, Jr., Schwartz SG, Rosenfeld PJ, Vaziri K, Moshfeghi AA, et al. Current infectious endophthalmitis rates after intravitreal injections of anti-vascular endothelial growth factor agents and outcomes of treatment. Ophthalmic Surg Lasers Imaging Retina. 2015;46(6):643–8.
- Yannuzzi NA, Gregori NZ, Rosenfeld PJ, Relhan N, Patel NA, Si N, Miller D, Dubovy SR, Smiddy WE, Schwartz SG, Flynn HW Jr. Endophthalmitis associated with intravitreal injections of anti-vascular endothelial growth factor agents at a tertiary referral center (in-house and referred cases). (In Press – OSLI-Retina).

Complications Associated with Endophthalmitis Prophylaxis/Treatment

- Complications associated with prophylaxis
  - Hemorrhagic occlusive retinal vasculitis (Fig. 9.1)—Poorly understood entity. May occur following intracameral or intravitreal injection of vancomycin. Appears to represent a delayed-onset hypersensitivity to vancomycin. May respond to intravitreal corticosteroids
  - Toxic anterior segment syndrome (TASS)
- Complications associated with treatment
  - Mechanical complications related to the ophthalmic intervention (TAP or PPV)
  - Damage to crystalline lens (in phakic eyes)
  - Peripheral retinal tears or retinal detachment
  - Wound leak
  - Elevated intraocular pressure
  - Toxicity of antimicrobials

    Macular infarction (Fig. 9.2): Associated with aminoglycosides with no known treatment (gentamicin appears to be more toxic than amikacin)
    Optic atrophy

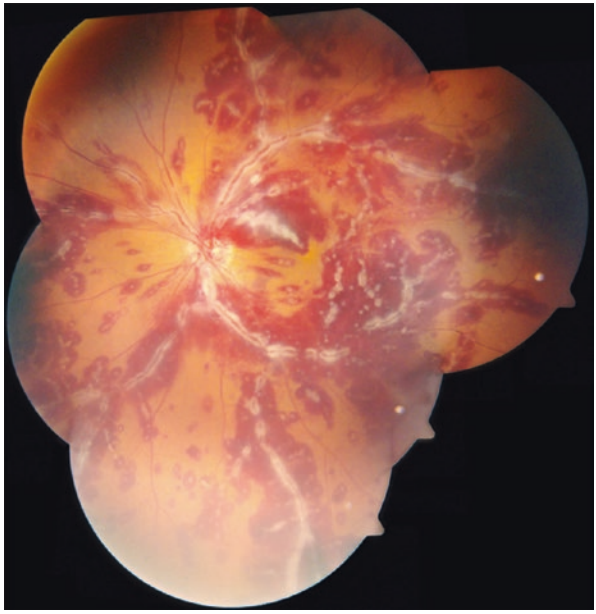

FIGURE 9.1 Hemorrhagic Occlusive Retinal Vasculitis (HORV)

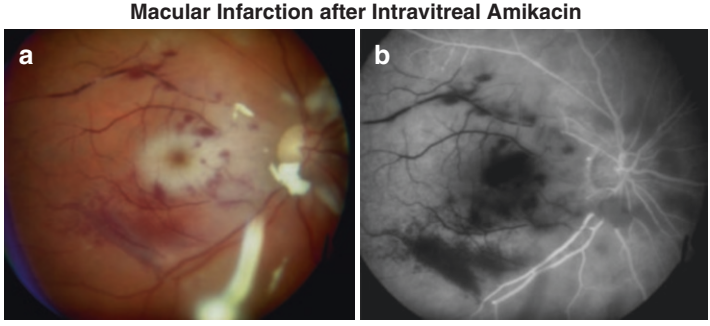

FIGURE 9.2 Macular infarction after intravitreal amikacin. Retinal toxicity with intravitreal amikacin. (**a**) Fundus photo showing multiple retinal hemorrhages, white appearance of macula, and multiple cotton wool spots surrounding disc. (**b**) Fundus fluorescein angiography demonstrates lack of perfusion at the posterior pole with ischemic macula and patches of hypofluorescence in the area of retinal hemorrhages and cotton wool spots

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Chapter 10
Endophthalmitis: Miscellaneous Categories

- Endophthalmitis after vitrectomy for floaters
- Endophthalmitis after scleral buckling
- Endophthalmitis after corneal suture removal
- Endophthalmitis after using infected eye drops
- Endophthalmitis after refractive surgery procedures (Fig. 10.1)
- Endophthalmitis after pterygium surgery

In cases of endophthalmitis in phakic eyes, it is not necessary to do lensectomy. Endophthalmitis may occur in phakic eyes, but patients with uninvolved crystalline lens can be

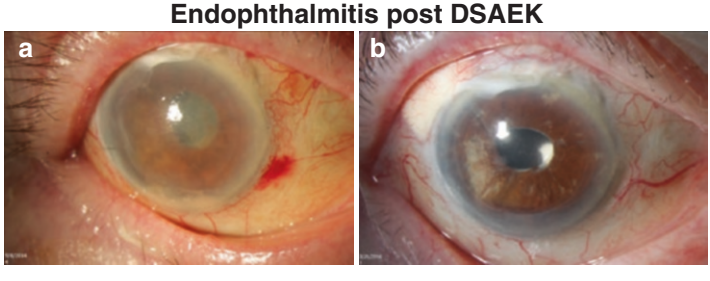

Fig. 10.1 (**a**) Endophthalmitis after refractive surgery procedures presenting with hazy Descemet graft, corneal edema, and hypopyon. (**b**) Two-year follow-up shows resolution of infection after initial management with pars plana vitrectomy with intraocular antibiotics

H.W. Flynn Jr. et al., *Endophthalmitis in Clinical Practice*,
In Clinical Practice,
https://doi.org/10.1007/978-3-319-66351-7_10

managed without lensectomy, and subsequent cataract surgery can be performed with IOL after infection is cured.

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Index

H.W. Flynn Jr. et al., *Endophthalmitis in Clinical Practice*, In Clinical Practice,
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