Chapter 5

Complete and Early Vitrectomy for Endophthalmitis (CEVE) as Today's Alternative to the Endophthalmitis Vitrectomy Study

5

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Core Messages

- Clinical signs of the disease are sufficient to recognize the condition as endophthalmitis and initiate treatment.
- If the attending ophthalmologist does not have the expertise or equipment and thus cannot offer the optimal treatment option, the patient should immediately be referred to a specialist who is able and willing to perform the most promising therapy.
- It is unacceptable to simply inject intravitreal antibiotics and then claim that everything that possibly could have been done has been done to save your eye, but unfortunately the disease has proven to be too tough to conquer.
- The cell wall of the organism may be toxic, and the bacterium may secrete endo- and exotoxins as well as harmful enzymes. This volatile mixture is rather heavy and tends to "sink" toward the deepest point of the vitreous cavity – the macula.
- Early surgical intervention is advantageous since it allows immediate treatment of all treatable pathologies, it serves as a prophylactic measure, preventing complications that would occur with a prolonged disease process, and it reduces the risk of surgery via improved visibility and decreased tissue fragility.
- An overriding principle of surgery is its step-by-step progression from the corneal epithelium toward the macular surface.
- The authors place the pars plana infusion cannula at the beginning of surgery, but do not open the infusion until the position of the cannula can be verified later during the operation.
- If there is a fibrinous membrane that covers the angle, iris, and the anterior surface of the (intraocular) lens, it is crucial not to leave it behind as the membrane can not only hinder visualization, but lead to postoperative intraocular pressure elevation by blocking the angle.
- Early filling of the anterior chamber with viscoelastics has several advantages.
- The intraocular lens is usually left in place.

Core Messages

- A large capsulectomy with the vitrectomy probe is always necessary to allow the intravitreal infusion fluid to irrigate the capsular bag; it also improves visualization.
- Unfortunately, even preoperative ultrasonography can be of limited value, or can even be misleading with regard to whether the retina is detached or not.
- The posterior vitreous should be detached and removed over retina that is not necrotic.
- Detachment of the hyaloid anterior to the equator should not be aggressively pursued as this increases the risk of iatrogenic retinal tear formation.
- The risk of permanent visual impairment is almost always smaller from a retinal break than from infection-related retinal destruction.
- The authors strongly believe that the primary line of treatment for the vast majority of eyes with endophthalmitis should be vitrectomy, i.e., purely medical treatment is the exception, not the rule.
- It is not a goal to routinely use silicone oil in the management of endophthalmitis; rather, it represents an exception that is reserved for the worst or most difficult cases. Nevertheless, silicone oil has several unique advantages: it does not allow organism growth, it keeps the retina attached, and it maintains clear media, allowing retinal inspection.
- Statistically significantly better anatomical and functional results are achieved with "complete and early vitrectomy" than in either management arm in the Endophthalmitis Vitrectomy Study.

5.1 Introduction and Definitions

5.1.1 Introduction

Endophthalmitis is a severe, purulent intraocular inflammation. Without proper and timely treatment, the infection results in loss of vision, and commonly in the loss of the eye. It is a clinical entity [3]: even if culturing is unsuccessful in identifying the pathogen, the clinical signs of the disease are sufficient to recognize the condition as endophthalmitis and initiate treatment to fight the infection and its consequences.

Regardless of the etiology, both the organism and the inflammatory response it invokes from the body are harmful to the internal structures of the eye. It is therefore necessary to:

- Recognize the condition early;
- Immediately inform the patient about the condition's characteristics, the therapeutic options, and the prognosis;
- Decide, with the patient's consent [11], on the type of therapy to pursue;
- Execute this therapy in the optimal fashion.

It is also important to remove the ophthalmologist's own ego from the treatment process ("I'm able to handle this situation, I don't need to refer the patient to a colleague") and resist the subconscious reflex to "hide" the patient by relegating him to a remote area of the ward or by sending him home early. If the attending ophthalmologist does not have the expertise or equipment and thus cannot offer the optimal treatment option, the patient should be referred to a specialist who is able and willing to perform the most promising therapy. It is equally unacceptable to simply inject intravitreal antibiotics and then claim that "everything that possibly could have been done has been done to save your eye, but unfortunately the disease has proven to be too tough to conquer."

5.1.2 Definitions

Defining all applicable terms establishes unequivocal communication among opthalmologists, regardless of the individual's place of training or practice. Clarifying certain endophthalmitis-related concepts helps understand the rationale for treatment selection. The definitions and concepts are summarized in Table 5.1.

Table 5.1 Terms and their definitions in the management of endophthalmitis

Term	Definition	Comment
Endophthalmitis	An abscess: intracavital accumulation of purulent material	The eyewall[b] acts like a barrier, a capsule, to effectively shield the purulent process from the rest of the body; this is advantageous because it usually prevents the infection from spreading and thus causing septicemia, but it also concentrates the organism's harmful effects on the tissue it continually bathes: the retina
Early endophthalmitis[a]	An infection with relatively well preserved media clarity, allowing good red reflex, occasionally even observing retinal details	In most cases,[c] the initial signs of endophthalmitis are discrete[d] and the progression is relatively slow. This, however, should not make the ophthalmologist complacent: the infecting organism is rarely known at this point, and the process can rapidly turn for the worst. This is why it is misleading to term an early endophthalmitis "mild"
Advanced endophthalmitis[a]	An infection with severe opacity in the anterior media, typically accompanied by severe vitreous infiltration or true abscess	An (almost) end stage condition, where functional failure is certain and anatomical failure is likely
Anatomical failure[a]	Enucleation, evisceration, or phthisis	The ophthalmologist is either forced to enucleate/eviscerate the eye to cure the infection and prevent its spread, or the infection, even if cured, eventually shuts down aqueous production and the eye becomes phthisical – which can later lead to enucleation or evisceration for cosmetical reasons
Endophthalmitis maculopathy[a]	Macular injury (edema, stress hemorrhage, epimacular proliferation) as a result of the infection	These consequences may result from the organism or the inflammatory reaction of the body; they can cause permanent (i.e., unimproveable) damage or one that requires additional medical therapy or surgery. Even if the therapy results in anatomical success, the functional recovery may not be complete
Macular hypopyon[a]	Accumulation of purulent material in the macular area	The purulent material is heavier than the vitreous/fluid; as most patients spend most of their time in the supine position, the material settles on the lowest point of the eye, typically causing disproportionally more severe damage here

[a]Modified after Morris and Witherspoon who originally introduced the concept [11]

[b]Cornea and sclera

[c]An obvious exception is an infection caused by *Bacillus* sp.

[d]Especially if the infection is restricted to the anterior chamber and the anterior vitreous

5.2 Etiology and Classification

The pathogen may be exogenous or endogenous. Of the former, we distinguish between those caused by trauma or surgery; the latter may follow trabeculectomy or other types of surgery (most commonly cataract extraction). Such postoperative endophthalmitis may be acute (presenting within a few weeks of surgery) or chronic. (This chapter was written on the management of eyes with the same inclusion criteria as those in the Endophthalmitis Vitrectomy Study (EVS): acute postoperative endophthalmitis occurring within 6 weeks of cataract extraction with intraocular lens implantation or of secondary intraocular lens implantation. Treating eyes with endophthalmitis of other etiologies or chronicity requires a somewhat modified strategy, including timing and surgical details. These are not discussed here.)

5.3 Pathophysiology, Organisms, and Diagnostics in Brief

5.3.1 Pathophysiology

The intravitreal organism causes severe inflammation – indeed, some of the most significant visual consequences of the infection, such as cystoid macular edema and epimacular membrane formation, are caused by the body's response, rather than by the organism directly. In addition, the cell wall of the organism may be toxic, and the bacterium may secrete endo- and exotoxins as well as harmful enzymes. These lead to various retinal pathologies, including widespread necrosis. This volatile mixture (inflammatory debris, including organism, white blood cells, humoral agents, etc.) is rather heavy and tends to "sink" toward the deepest point of the vitreous cavity.

5.3.2 Organisms

Table 5.2 lists the most commonly encountered organisms in acute postoperative endophthalmitis. Virulence of the pathogen for the clinician is indicated by how early after surgery the infection presents, how rapidly the disease progresses from early to advanced, and how severe the signs are.

5.3.3 Diagnostics

5.3.3.1 Clinical

Most or all of the following signs/symptoms are present:

- Pain;
- Red ("hot"), inflamed eye, dilated conjunctival and ciliary blood vessels;
- Reduced corneal clarity due to edema;
- Hazy anterior chamber due to fibrin, cells, bacteria, increased protein content, occasionally blood; hypopyon is usually also found (a hypopyon may become invisible simply because the patient is in bed);

Table 5.2 The most common organisms in acute postoperative endophthalmitis[a]

Organism	Comment
Staphylococcus epidermidis	Relatively nonvirulent; by far the most common organism (40–70%), especially in diabetics
Staphylococcus aureus	Quite virulent; 10–20% of those with positive culture
Streptococcus species	Quite virulent; 6–9% of those with positive culture
Gram-negative rods (Proteus, Pseudomonas, Serratia)	Virulent; relatively rare
Bacillus species	Very virulent; extremely rare

[a]Based on an extensive literature survey

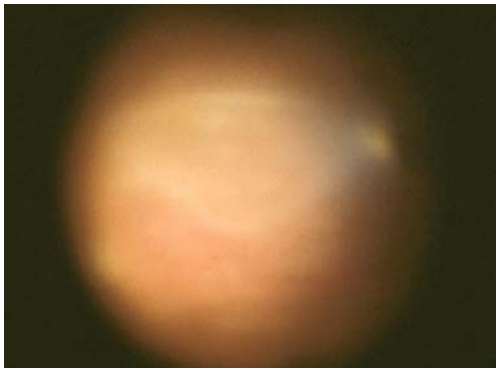

Fig. 5.1 Macular hypopyon. Intraoperative image: accumulation of purulent material over the macula in a patient with postoperative endophthalmitis

- Formation of a fibrinous membrane over the crystalline/intraocular lens and the iris;
- Constricted pupil (which may be masked by dilating drugs prescribed postoperatively);
- Reduced or nonexistent red reflex;
- Vitreous opacity of varying degrees, with foci of pus or abscess/es;
- If the retina can be visualized, endophthalmitis retinopathy: stress hemorrhages, sheathed vessels, necrotic areas, macular swelling, macular hypopyon (Fig. 5.1).

5.3.3.2 Other

Typical appearance on ultrasonography; culture from the anterior chamber and vitreous. These are not discussed in this chapter.

5.4 Principles of Therapy

The intervention aims to:

- Kill the organism;
- Remove the inflammatory debris from the vitreous cavity;
- Block the inflammatory cascade and its effects on the retina;
- Treat the complications of the infection;
- Minimize future complications, whether from the infection or from the treatment itself;
- Intervene as soon as possible. Endophthalmitis is an emergency and must be treated as one. Timing of the intervention is where the surgeon's error (i.e., delay in initiating proper treatment) is most easily controllable.

Summary for the Clinician:

- Without proper and timely treatment, the infection results in loss of vision, and commonly in the loss of the eye.
- The cell wall of the organism may be toxic, and the bacterium may secrete endo- and exotoxins as well as harmful enzymes. These lead to various retinal pathologies, including widespread necrosis.
- Some of the most significant visual consequences of the infection, such as cystoid macular edema and epimacular membrane formation, are caused by the body's response, rather than by the organism directly.
- Virulence of the pathogen for the clinician is indicated by how early after surgery the infection presents, how rapidly the disease progresses from early to advanced, and how severe the signs are.
- The most important signs/symptoms of endophthalmitis are: pain, haze, hypopyon, and endophthalmitis retinopathy.
- Principles of therapy are: killing the organism, removing the inflammatory debris, and to intervene as soon as possible.

5.5 The EVS

5.5.1 Study Design

Conducted between January 1990 and January 1994, the EVS [4] was a prospective, randomized, multicenter trial on 420 eyes to determine whether it is necessary in acute postoperative endophthalmitis to use systemic antibiotics or perform routine immediate vitrectomy (Table 5.3).

Table 5.3 Design of the Endophthalmitis Vitrectomy Study (EVS)

	Vitrectomy	No vitrectomy
Intravenous antibiotics	106[a]	100[a]
No intravenous antibiotics	112[a]	102[a]

[a]Number of eyes in each group; total: 420 eyes

5.5.2 Results

Statistical analysis of the EVS findings led the study authors to the following conclusions:

- Systemic antibiotics do not improve the outcome;
- Vitrectomy is indicated only in eyes with light perception vision.

5.5.3 Consequences of the EVS Recommendations

Vitrectomy for endophthalmitis was becoming increasingly popular [3] when the publication of the EVS in 1995 dramatically and abruptly changed the treatment philosophy. As advocated by the EVS, vitrectomy is now reserved for the most severe cases, and this vitrectomy is limited to the anterior vitreous. (Systemic antibiotics are still used by many ophthalmologists.) The following quote is a typical example: "If a vitrectomy is indicated (e.g., a patient with visual acuity of light perception…), a core vitrectomy should be performed, and no attempt should be made to excise the cortical…vitreous" [6]. This management approach is now typical even in countries where the ophthalmologist's decisions can still be made based on purely medical, rather than on medicolegal or insurance company-forced reasoning.

5.6 Rationale for Performing Complete and Early Vitrectomy for Endophthalmitis

The following presents a systematic, logic- and experience-based (re)consideration of the advantages of a surgical approach to eyes with endophthalmitis [7].

5.6.1 Why Perform Vitrectomy?

Surgery has several advantages over conservative therapy. Vitrectomy:

- Increases retinal oxygenization [13];
- Provides a large specimen for diagnostic evaluation;
- Allows definite treatment at a time when the organism (and its virulence) is still unknown (i.e., antibiotic selection is based on statistical probability, not on case-specific information);
- Dramatically reduces the inflammatory debris load in the vitreous cavity, thereby lessening its harmful effect on the retina and other intraocular tissues;
- Reduces the incidence and severity of macular complications;
- Allows direct inspection of the retina by removing the nontransparent medium, thereby permitting timely treatment of coexisting or developing pathologies;
- Increases the access to the retina of intravitreally administered pharmacological agents;
- Reduces the duration of the disease, thus accelerating visual rehabilitation;
- Reduces the incidence and severity of retinal, especially macular, complications.

5.6.2 Why Perform Early Vitrectomy?

As mentioned earlier, endophthalmitis is a process that progressively destroys the intraocular tissues it bathes. Early surgical intervention is advantageous since it:

- Allows immediate treatment of all treatable pathologies;
- Serves as a prophylactic measure, preventing complications that would occur with a prolonged disease process;

- Reduces the risk of surgery via improved visibility (as the disease progresses, the corneal transparency decreases due to increasing edema) and decreased tissue fragility (the less severe the existing pathology, the less likely that iatrogenic complications will occur).

5.6.3 Why Perform Complete Vitrectomy?

The inflammatory debris, as mentioned earlier, is heavy, and typically settles over the posterior pole since most patients spend most of their days lying in bed.

If vitrectomy is not complete (see the instructions in the "Methods" section of the EVS ["If there was no posterior vitreous separation, no attempt was made to induce a vitreous detachment, and the posterior cortical vitreous was not aggressively removed. It was a goal of surgery to remove at least 50% of the vitreous gel in eyes with no vitreous separation."] [4]), the part that is not removed is obviously the posterior half. Only by detaching the posterior hyaloid does the surgeon gain access to the "naked" retinal surface, allowing complete removal of the pus and debris that have accumulated there (macular hypopyon). (Contrary to popular belief, the posterior vitreous cortex remains attached to the retina in the majority of cases. What appears in many eyes as vitreous detachment is often vitreoschisis; no current preoperative evaluation method allows absolute determination with regard to whether a posterior vitreous detachment exists). Complete vitrectomy, however, implies detachment and removal of the vitreous posteriorly, not in the periphery, where the surgeon must be more conservative (see below).

- Conclusions from the EVS: systemic antibiotics do not improve the outcome; vitrectomy is indicated only in eyes with light perception vision.
- Consequences of the EVS: if a vitrectomy is indicated a core vitrectomy should be performed, and no attempt should be made to excise the cortical vitreous.
- Complete and early vitrectomy for endophthalmitis, on the other hand, dramatically reduces the inflammatory debris load in the vitreous cavity and provides a large specimen for diagnostic evaluation.
- Complete and early vitrectomy for endophthalmitis allows definite treatment, reduces the incidence and severity of retinal, especially macular, complications. Early vitrectomy reduces the risk of surgery via improved visibility and decreased tissue fragility.
- Only a complete vitrectomy allows detachment of the posterior hyaloid and complete removal of the pus and debris.

5.7 Complete and Early Vitrectomy for Endophthalmitis: Surgical Steps

Cases in which the eye is still phakic are included. It must be emphasized that what is described here presents the desired, optimal case. The surgeon must be ready to accept compromises if visibility is too poor to allow fine intravitreal maneuvers or if the retina is too necrotic to permit manipulations such as posterior vitreous detachment. An overriding principle of surgery is its step-by-step progression from the corneal epithelium toward the macular surface. No step described here should be skipped as this may result in surgical compromises that may not otherwise have been necessary and that can impair the functional outcome.

The benefits of a wide-angle viewing system cannot be overemphasized. It makes otherwise difficult surgery much easier to perform, and dramatically increases safety and efficacy.

5.7.1 Initial Steps

Prepare the eye as for any intraocular surgery; be especially careful if the fellow eye had surgery recently. Make sure that if no "septic" operating room is available for the surgery, a proper protocol is in place to clean/sterilize the operating room afterward. The authors perform most of their surgery under local anesthesia. Prepare your diagnostic kit in time so that culturing is efficient in terms of sterility, media availability, delivery to the lab, and processing in the lab. Make sure that no undue pressure is exerted on the eye when

placing the lid speculum (or retracting sutures if necessary): the eye is "hot" and the intraocular pressure may be high, therefore the risk of intraoperative hemorrhage [8] is not negligible. The authors place the pars plana infusion cannula at the beginning of surgery, but do not open the infusion until the cannula's position can be verified later during the operation. (The initial tool for providing intraocular infusion is typically an anterior chamber maintainer.)

5.7.2 Cornea

As the epithelium is always edematous, its removal is necessary in virtually every case, even in diabetics. Scraping the epithelium dramatically increases visibility of the deeper structures and thus increases the safety and scope of surgery. Do not remove the epithelium in the limbus (removing the stem cells interferes with re-epithelialization) and be careful not to damage Bowman's membrane. If the stroma also has significant edema, the surgeon may try to press a dry sponge against it, or use topical high-concentration glucose. It is uncommon, though, for stromal edema to significantly impair visibility. Descemet's folds may also be a problem, see below. If visibility through the cornea remains compromised despite all efforts, there are several options:

- Vitrectomy may be delayed until topical corticosteroids are successful in improving media clarity. This must be weighed against the damage inflicted by the ongoing disease process.
- Vitrectomy may be performed in a limited fashion, consistent with safety [10]. ("proportional pars plana vitrectomy" [PPPV], a term coined by R. Morris [10]). This must be weighed against the damage inflicted by the ongoing disease process.
- An endoscope may be utilized [2]. This requires not only availability of the equipment, but also considerable experience on the surgeon's part.
- A temporary keratoprosthesis (TKP) can be placed [12], followed by implantation of a donor cornea at the conclusion of surgery (Fig. 5.2). If no donor cornea is available, even the original corneal button may be temporarily reused. Use of a TKP requires availability of the device and expertise in its use as well as extensive knowledge of postoperative handling of the transplant.

5.7.3 Anterior Chamber

There are several instruments/techniques to rid the anterior chamber of *loose debris*: with an irrigation–aspiration cannula; via irrigation and then aspiration through a single paracentesis; using an anterior chamber maintainer while aspirating through a separate paracentesis, etc. The vitrectomy probe is usually preferred by the authors since this also allows cutting if some formidable material is engaged. It is mandatory to always have some type of irrigation in place before aspirating, even if the material to be removed is apparently of insignificant volume: collapse of the anterior chamber – a sudden drop in the intraocular pressure – risks severe hemorrhage. The angle is typically also full of debris and should be thoroughly irrigated. The material ultimately removed is usually much more voluminous than presumed.

There is almost always a fibrinous membrane that covers the angle, iris, and the anterior surface of the (intraocular) lens. The membrane may be relatively thin, barely visible until engaged,

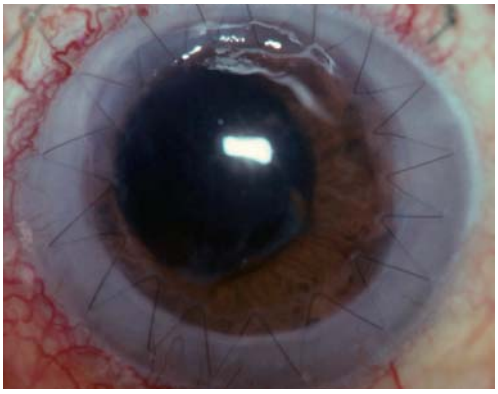

Fig. 5.2 Corneal transplantation after complete and early vitrectomy for endophthalmitis (CEVE). Five weeks afterward, a temporary keratoprosthesis (TKP) was necessary to allow treatment of endophthalmitis with severe retinal complications. The corneal graft is clear with no signs of rejection

but can also be fairly substantial. It is rather elastic and very sticky (adhesion) – but also strong (cohesion). Once grabbed by a vacuum (cannula, vitrectomy probe) or forceps, it is usually possible to remove it in its entirety and in one piece. It is crucial not to leave it behind as the membrane can not only hinder visualization, but lead to postoperative intraocular pressure elevation by blocking the angle. The membrane occasionally reoccurs during surgery, especially in children, requiring repeat removal.

Early filling of the anterior chamber with viscoelastics has several advantages. It:

- Prevents reaccumulation of the inflammatory debris;
- Reduces the risk of bleeding;
- Pushes/keeps out of the visual axis any fresh blood or other debris;
- Keeps the anterior chamber formed;
- Keeps the pupil dilated;
- Reduces Descemet's folds.

5.7.4 Pupil

A large pupillary opening greatly enhances visibility of the posterior segment. If dilating agents – including intracameral adrenalin – are insufficient and neither do viscoelastics help, iris retractors should be used.

5.7.5 (Intraocular) Lens

The crystalline lens is usually left in place. If its anterior surface is "dirty" and cannot be displaced with viscoelastics, and it impairs posterior segment manipulations, the lens should be sacrificed. Whether lensectomy or phacoemulsification is performed is an individual decision. (It is the surgeon's decision as to whether any of the lens capsules is retained; the focus should be on saving the eye, not "the bag for optimal subsequent placement of an intraocular lens.") The rule is: saving the lens or any of its capsules should not compromise curing the infection or its consequences.

The intraocular lens is usually left in place. If its anterior surface is "dirty" it should be wiped clean with a sponge, a small piece of cotton held in intravitreal forceps, or some other tool (for instance, a Tano membrane scraper).

5.7.6 Posterior Lens Capsule

A large capsulectomy with the vitrectomy probe is always necessary to allow the intravitreal infusion fluid to irrigate the capsular bag (irrigation through the pars plana/posterior capsulectomy with antibiotic solution using a syringe may also have to be performed); it also improves visualization. (The bag, and the intraocular lens, must be removed if the endophthalmitis is chronic.) Occasionally, the posterior surface of the intraocular lens must also be wiped clean.

5.7.7 Vitrectomy

There is a considerable future for 23- and even 25-gauge systems; however, a smaller gauge and the lack of having to suture the sclerotomies is no justification for incomplete vitreous removal. The sequence of vitreous removal is primarily determined by the clarity of the vitreous. A relatively transparent vitreous allows posterio-anterior vitrectomy [9], which the authors prefer: the posterior vitreous is detached first, followed by vitreous removal that is progressively anterior in its direction. If the vitreous is moderately hazy, removal should start behind the lens and advance carefully, slowly, toward the retina. Once the posterior pole is reached and the hyaloid is detached there, vitrectomy is completed by moving the probe anteriorly. If the vitreous is very hazy, surgery becomes extremely difficult. There are several vitreous layers present, which are shaped (like onion peel). There may be streaks of blood among the layers, giving the appearance of a detached retina; conversely, the retina may be necrotic and not bleed when cut into. (Such a condition represents one of the most challenging indications for vitrectomy. Even for experienced surgeons, distinguishing between white vitreous layers with streaks of hemorrhage and a white, necrotic retina without patent blood vessels may be extremely difficult.) A less experienced or careful surgeon may remove large chunks of the retina before realizing what he has "bitten into."

Unfortunately, even preoperative ultrasonography can be of no value, or even be misleading, with regard to whether or not the retina is detached (Fig. 5.3).

The least risky technique in such eyes is to "dig" a vertical "well" nasally (rather than, as first instinct would suggest, carefully peeling the onion layers by moving the vitrectomy probe in horizontal sweeps); the surgeon may create a small retinal break, but once the vitrectomy probe is behind the retina, the anatomical situation becomes much clearer. It is helpful to use the vitrectomy probe and the flute needle alternately: the latter can vacuum the typical grayish fluid that otherwise blocks the surgeon's view. Once the cleavage plane between vitreous and retina has been found, heavy liquids, among other tools, can be used to separate the retina from the vitreous. Vitreous separation and removal is usually possible even if the retina is already detached (Fig. 5.4).

Unless the vitreous is very hazy, the posterior hyaloid is rather easy to identify since it is somewhat opaque, not transparent as usual. Occasionally, colonies of bacteria may be present on it surface (appearing as multiple white [yellowish] dots), also helping identification. If the surgeon is in doubt, a single drop of filtered triamcinolone helps identify it. The hyaloid is carefully lifted; if the retina is necrotic and would also detach, the vitreous is only trimmed over this area (Fig. 5.5). The posterior vitreous, however, should be detached and removed over retina that is not necrotic. The retinal appearance instantly changes to a clear image once the vitreous "veil" has been lifted. The central vitreous must be completely removed to minimize the bacterial load ("reservoir") inside the eye.

Detachment of the hyaloid anterior to the equator should not be aggressively pursued as this increases the risk of iatrogenic retinal tear formation. Only trimming is recommended in the periphery to reduce the incidence of iatrogenic retinal injury. Careful trimming is sufficient to reduce the volume of the infected medium while keeping the retinal injury risk at an acceptably low level. (In other words: posterior vitreous removal in complete and early vitrec-

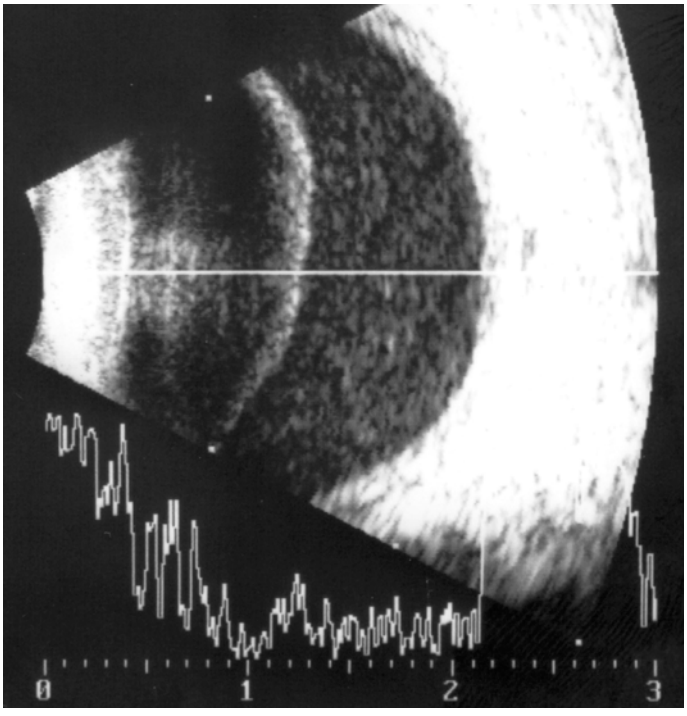

Fig. 5.3 Ultrasound imaging of an eye with hazy vitreous due to endophthalmitis. The preoperative image suggests posterior vitreous detachment with subhyaloid infiltration. During surgery, however, a nondetached vitreous was found with a complete retinal detachment and a subretinal fluid rich in protein and cellular elements

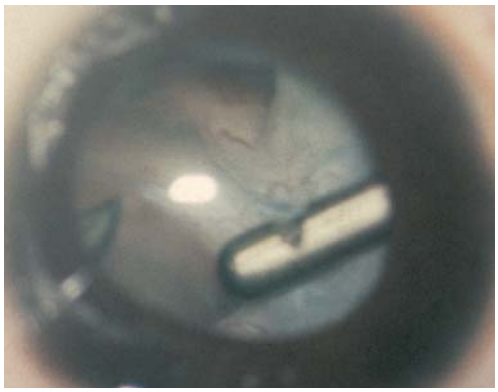

Fig. 5.4 Complete and early vitrectomy for endophthalmitis in an eye with detached retina. If the retina is detached, separation and then removal of the still attached vitreous requires careful manipulation with the vitrectomy probe, occasionally also requiring the use of other tools (see the text for more details)

tomy for endophthalmitis (CEVE) is just the opposite of what the EVS recommended; there is similarity between the CEVE and EVS regarding peripheral vitrectomy.)

5.7.8 When to Stop Vitreous Removal?

This is an important question that only experience can answer in each individual case. The surgeon faces two, antagonistic treatment goals:

- Curing the infection requires as complete a vitrectomy as possible;
- Vitreous removal should be performed without creating iatrogenic retinal damage.

This conflict is not an easy one to resolve. As a general rule, the primary goal is to cure the infection. If a retinal break is created, however, this does not represent a death sentence for the eye (an ongoing infection may be). The risk of permanent visual impairment is almost always smaller from a retinal break than from infection-related retinal destruction. Treatment of a retinal break or detachment is a routine procedure for the vitreoretinal surgeon (see below).

5.7.9 Retina

The macular surface should always be vacuumed, even if there is no apparent pus accumulation on it. The silicone-tipped flute needle is used with passive, not active, suction. Even if larger pus fragments are present, these tend to break up and can easily exit the eye through the needle. Alternatively, the vitrectomy probe's aspiration is utilized once the sticky material has been mobilized from the macular surface. It is rarely necessary to meticulously vacuum the retinal surface elsewhere.

If areas of necrosis are encountered, these may be surrounded by rows of laser treatment, once the vitreous is trimmed/removed. (Laser treatment presumes a healthy retina and pigment epithelium in the adjacent areas.) Other coexisting pathologies (e.g., tears, detachment) are also treated as if appearing in an eye without

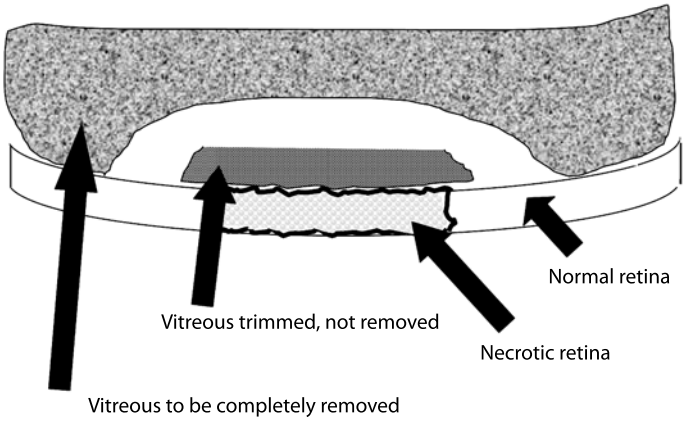

Fig. 5.5 Trimming the vitreous over necrotic retina. Instead of detaching the posterior hyaloid, it is trimmed parallel to the retina, then cut circumferentially, allowing safe detachment and removal of the vitreous in the adjacent area. (Schematic representation, cross-sectional image)

infection. Gas tamponade may also be used, and medications can be injected into an eye with tamponade. (Alternatively, an incomplete fluid–gas exchange is performed and the drugs are injected into the fluid component.) The use of silicone oil tamponade is discussed separately below.

5.7.10 Enucleation/Evisceration

These are performed only if absolutely necessary: an infection that is (about to be) breaking through the sclera and causing panophthalmitis (tissue melting) or an eye whose anatomy cannot be restored to normal appearance and there is no hope for even light perception vision. Extensive counseling [11] must precede eye removal.

5.7.11 Pharmacological Treatment

It is not the scope of this chapter to discuss this in detail. The authors use heavy topical, occasionally subconjunctival, antibiotic and corticosteroid treatment in every case; antibiotics and corticosteroid intravitreally; and oral antibiotics [5]. (Even if there is corneal erosion; the benefits more than outweigh the risks. Topical corticosteroid therapy, however, is discontinued after 1 week if the erosion remains unhealed.) Intraoperatively, the authors use antibiotics and corticosteroids in the infusion fluid only if silicone oil is to be used (see below).

5.8 Surgical Decision-Making and Complications

5.8.1 Decision-Making

It must be emphasized that the decision whether to undergo surgery is the patient's; the ophthalmologist should inform the patient about the condition and the risks/benefits of each treatment option in a way that allows the patient to make a choice that he is comfortable with [9]. The authors strongly believe that the primary line of treatment for the vast majority of eyes with endophthalmitis should be vitrectomy; i.e., purely medical treatment is the exception, not the rule (Fig. 5.6). The decision whether surgery is performed is driven not by the visual acuity (i.e., light perception versus better, see the EVS recommendation [3]), but by the clinical appearance and course. This is especially important since deterioration can be rapid, leading to irreversible but otherwise preventable damage.

If performed on an eye with early disease, the risk of serious retinal complications is no greater than it is for other conditions such as a "simple" vitreous hemorrhage. Vitreoretinal surgeons with decent experience should be able to perform this surgery.

With increasingly advanced cases, the degree of surgical difficulties and the risk of complications grow exponentially. It is therefore best for the less experienced surgeon to refer such cases.

Finally, the authors do not automatically render an eye with no light perception vision inoperable [12]. If the eye had good vision before, the loss of light perception is recent, the eye's anatomical condition permits surgery, and the patient understands that the chance of visual improvement is low, surgery should be offered as an option. Cleaning the eye's interior, even if light perception does not return, helps cosmesis, comfort, and reduces the incidence of enucleation/evisceration. (Eye removal is a major additional psychological trauma to the patient.)

5.8.2 Complications and Their Management

Only retinal complications are discussed here; it must also be understood that these can occur as the result of the disease itself, not only as a surgical complication.

5.8.2.1 Retinal Break

Breaks can occur via several mechanisms (e.g., as a "normal" complication in the periphery, as a direct injury from an intravitreal instrument, or as a result of trying to detach the vitreous over a necrotic retina [a common site, not surprisingly, is the fovea.]). The breaks can be surrounded with laser or if longer-term tamponade is felt necessary, silicone oil may be used; the laser treatment can be deferred.

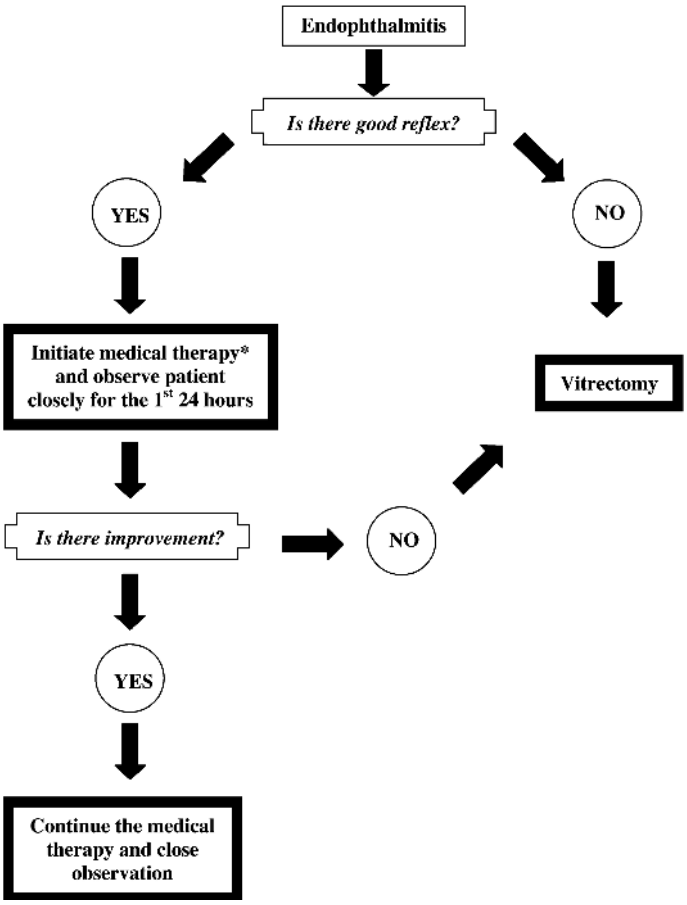

Fig. 5.6 Treatment algorithm of CEVE for acute postoperative endophthalmitis

5.8.2.2 Retinal Detachment

Whether caused by the disease or, less commonly, by the surgeon, a retinal detachment is treated as if occurring in a noninfected eye. First the vitreous (and pus) removal is completed, then the break is sealed with laser (see above) once the subretinal fluid is removed, and some type of tamponade is used. The fact that this is an eye with endophthalmitis should have no bearing on the choice of the tamponade.

5.8.2.3 Silicone Oil as a Long-Term Tamponade

The authors consider using silicone oil if they know they have created a retinal break or are uncertain whether or not they have; if a retinal detachment is present; or if there are large areas of retinal necrosis.

It is not a goal to routinely use silicone oil in the management of endophthalmitis; rather, it represents an exception, reserved for the worst/most difficult cases. Nevertheless, silicone oil has several unique advantages:

- Bacteria do not multiply in silicone oil [1];
- Silicone oil prevents/treats retinal detachment of a rhegmatogenous nature;
- The intravitreal silicone oil remains clear, allowing visualization of the retina throughout the postoperative period.

A few rules about silicone oil use in eyes with endophthalmitis must be observed:

- Do not implant silicone oil if the vitreous cavity has not been adequately cleansed. The remaining pathogens, while unable to freely

circulate, may be pressed against a circumscribed area, causing localized retinal damage.

- The authors use antibiotics and corticosteroids in the infusion fluid if silicone oil is to be used. (Without silicone oil use, medications are not used in the infusion fluid.) The dosages are identical to those used in an intravitreal injection (i.e., the drugs are not diluted).
- Antibiotics and corticosteroids are injected into the oil at the end of the procedure. As demonstrated by the authors, triamcinolone is observed to be spread fairly evenly against the retinal surface the next day. (Appears as a ping-pong ball immediately after the injection.)

5.9 Results with CEVE and Their Comparison with the EVS

Table 5.4 shows the results the authors achieved in a consecutive series of 47 eyes with acute postoperative endophthalmitis. The inclusion criteria were identical to those used in the EVS except that eyes were not excluded, as in the EVS, for lack of iris visibility due to corneal or anterior chamber problems, nor for the presence of even high retinal detachment. (If anything, the cohort in the authors' series was in worse condition than eyes in the EVS.) Although the authors' study was not randomized or prospective, the selection criteria allow a careful comparison between the two studies (Table 5.4).

Statistically significantly better anatomical and functional results were found with CEVE than in either management arm in the EVS. The authors attribute this improvement to vitrectomy being early (in other words: vitrectomy is the primary treatment option; its application is the rule, not the exception) and complete, and to its being the primary line of treatment, rather than being applied as a last resort.

Summary for the Clinician

- An overriding principle of surgery is its step-by-step progression from the corneal epithelium toward the macular surface.
- Make sure that no undue pressure is exerted on the eye.
- Do not open the pars plana infusion until the cannula's position can be verified later during the operation.
- Scraping the epithelium dramatically increases visibility of the deeper structures and thus increases the safety and scope of surgery.
- It is mandatory to always have some type of irrigation in place before aspirating.

Table 5.4 Results with complete and early vitrectomy for endophthalmitis (CEVE) and their comparison with those in the EVS

Variable	EVS, vitrectomy	EVS, no vitrectomy	CEVE
Number of eyes	218	202	47
Retinal detachment*	2.9%	7.2%	0%
Enucleation/evisceration/phthisis*	2.5%	6.2%	0%
Expulsive hemorrhage*	1.9%	4.9%	0%
Repeat vitrectomy*	0%	6.0%	0%
No light perception final vision*	4%	5%	0%
Final visual acuity 20/40 or greater*	54%	52%	91%

*$p<0.0001$, Fisher's exact test, comparing EVS and CEVE outcomes

Summary for the Clinician

- Early filling of the anterior chamber with viscoelastics has several advantages.
- Saving the lens or any of its capsules should not compromise curing the infection or its consequences.
- Unless the vitreous is very hazy, the posterior hyaloid is rather easy to identify since it is somewhat opaque, not transparent as usual. If the vitreous is hazy, however, surgery is very difficult, and considerable experience is required to distinguish between vitreous layers and the necrotic, occasionally already detached retina.
- The central vitreous must be completely removed to minimize the bacterial load ("reservoir") inside the eye.
- Curing the infection requires as complete a vitrectomy as possible; if the vitreous cannot be separated from necrotic retina, it must be circumcised (trimmed), to avoid creating an iatrogenic retinal detachment. This is rare, however, and represents a strong argument in favor of early rather than late intervention.
- The macular surface should always be vacuumed.
- The decision regarding whether or not surgery is performed is driven not by the visual acuity but by the clinical appearance and course.
- With increasingly advanced cases, the degree of surgical difficulties and the risk of complications grow exponentially. It is therefore best for the less experienced surgeon to refer such cases.
- Silicone oil is reserved for the worst/most difficult cases. Bacteria do not multiply in silicone oil. The "dead space" for therapeutic antibiotic levels is eliminated. Intravitreal drug dosages are identical to those used in eyes without vitreous substitutes.

5.10 Summary and Recommendations

The organizers of the EVS deserve a lot of credit for introducing a systematic, statistically well-analyzed approach to the management of eyes with acute postoperative endophthalmitis. Because of the fear of iatrogenic retinal damage during an operation where visibility is a serious problem, however, the EVS protocol called for a vitrectomy that was not radical. Indeed, the EVS compared eyes with no vitrectomy (small, diagnostic biopsy) with eyes with limited vitrectomy (medium biopsy). As a result, the EVS was unable to demonstrate any difference between surgical and nonsurgical treatment, except in eyes that were in their final stage of damage. (It is very likely that if vitrectomy in the surgical arm of the EVS had been complete, similar outcomes would have been found.)

Two decades have passed since planning for the EVS started. Among other factors, better understanding of the pathophysiology, safer vitrectomy machines, improved intraoperative visualization technologies, increasingly efficacious techniques of retinal reattachment (now there is fear of the infection more than of the complications of surgery), new antibiotics (more effective/potent and able to penetrate the blood–retina barrier in higher concentrations) are now available; consequently, it is time to reevaluate the role of vitrectomy in the treatment of eyes with acute postoperative endophthalmitis.

If we compare the "no-vitrectomy" and "partial" vitrectomy arms of the EVS, we must notice that the surgical group faired better in terms of retinal detachment, anatomical failure, expulsive hemorrhage, and reoperation rates. If we compare these results with those achieved with CEVE, both the anatomical and functional outcomes show a statistically significant improvement over either of the EVS groups. The authors therefore strongly advocate the CEVE approach, and also recommend using new generation systemic antibiotics: administered orally, these reach the vitreous cavity in sufficiently high concentration, providing for "bacterial kill"; removal of the inflammatory debris then completes the process, allowing maximum treatment of an otherwise sight-threatening condition.

A.C. Celsus declared two millennia ago: "*Ubi pus, ibi evacua*." Today, when vitrectomy is a routine procedure and our armamentarium to treat not only an ever-growing array of conditions, but also the occasional complications of surgery, CEVE for acute postoperative endophthalmitis is proving to be a superior approach than recommended by the EVS in 1995.

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