Infectious endophthalmitis after cataract surgery

D S Hughes, R J Hill

Endophthalmitis is potentially the most devastating complication of cataract surgery. For the purpose of this perspective it will be defined as intraocular infection attributed to elective cataract extraction with or without intraocular lens implantation. Ideally, all cases of endophthalmitis would be culture proved but culture negative cases that respond to antibiotic therapy are presumed to be infectious in origin despite lack of definitive proof. To this end, truly sterile postoperative inflammation resulting from phacoanaphylaxis is excluded. However, in phacoanaphylaxis it has been postulated that bacteria act as an adjuvant in stimulating a response to lens protein. Additionally, the exaggerated uveitic response resulting from excessive manipulation or the introduction of foreign material will also be excluded.

There are many controversies and ambiguities in the area of postoperative endophthalmitis, particularly in relation to prevention and management. These usually reflect the large numbers required to make meaningful statements or the assumptions made in extrapolating from animal models to the infected pseudophakic eye. Within the constraints of this article six questions will be asked:

What is the incidence?
What are the causes?
How does it present?
How can it be managed?
What is the outcome?
How can it be prevented?

What is the incidence?

Most authors are agreed that the incidence of endophthalmitis following cataract surgery is declining. Good historical perspectives are provided by Forster, Kattan et al, and Fahmy. It would appear that during this century the incidence has fallen from 1-5% to the region of 0-1%. This improvement has been attributed to better instrumentation allowing more precise surgery, improved operating theatre technique and the use of prophylactic antibiotics. The incidence derived from classic studies may not relate to modern surgical practice. It is important to know the incidence in relation to current techniques of extracapsular extraction or phacoemulsification with or without lens implantation. The effect of any modification or new procedure has to be related to this figure. Additionally, the rate following secondary lens implantation seems to be higher (0·3%). In any study it is difficult to control for all the possible variables — for instance, the type of conjunctival flap, the use and choice of prophylactic antibiotics, and the composition of the implant. However, no matter how good the technique endophthalmitis will inevitably appear.

It is possible that the true incidence is higher than suspected from studies because of underreporting. This could be particularly true of chronic infection which may be treated as persistent uveitis. While phacoanaphylaxis may cause chronic inflammation, in the first instance endophthalmitis should be suspected. In order to get the best modern estimate, an average has been calculated from recent published series. Unfortunately there are no modern series relating to practice in the British Isles and American studies form the basis of the estimate. This is unsatisfactory as there are likely to be differences in the population and practice that could affect the incidence. Risk factors should be assessed independently. Complicated cases are at higher risk and their exclusion will give a baseline on which to work.

Two recent studies are summarised in Table 1. Both studies commenced in 1984 and were reported in 1991. The relatively high number of intracapsular cataract extractions and the low number of phacoemulsifications probably reflects this fact. However, extracapsular cataract extraction technique is unlikely to have changed a great deal. These two studies represent the most up to date figures on incidence. The average appears to be in the order of 0·1%, but despite this seemingly low level there is no room for complacency and every effort should be made to keep the incidence as low as possible. It is probable that this figure does not include cases of chronic bacterial or fungal postoperative endophthalmitis. Reports of these conditions in the literature comprise either single cases or small series so the effect on the overall incidence should be small.

It has been estimated that over 100000 extractions are performed in the United Kingdom each year – 92% using the extracapsular technique with the remainder split between intracapsular and other extracapsular techniques. Using these estimates about 126 cases of postoperative endophthalmitis would be expected annually, but of course this figure is speculative and for confirmation a national survey is needed.

What are the causes?

There is increasing recognition that virtually any organism can cause endophthalmitis if introduced in sufficient quantities. DNA studies in Staphylococcus epidermidis endophthalmitis suggest that the commonest source of infection is the patient’s own flora. Organisms may be carried into the eye as surface fluid refluxes through the wound during surgery.

Additionally, an intraocular lens can become contaminated if it touches the ocular surface and even after exposure to the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Incidence of infectious postoperative endophthalmitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases of endophthalmitis</td>
<td>Total cataract operations</td>
</tr>
<tr>
<td>Extracapsular extraction*</td>
<td>236</td>
</tr>
<tr>
<td>Phacoemulsification*</td>
<td>14</td>
</tr>
<tr>
<td>Intracapsular extraction*</td>
<td>170</td>
</tr>
<tr>
<td>Extracapsular extraction†</td>
<td>18</td>
</tr>
</tbody>
</table>

*After Jarvis et al.
†After Kattan et al.
(Excludes one phacoemulsification and two complicated cases and comprises 14 culture proved and four culture negative cases.)
Table 2  Bacterial causes of postoperative endophthalmitis

<table>
<thead>
<tr>
<th>Gram positive</th>
<th>Gram negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus epidermidis</td>
<td>Proteus spp</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Pseudomonas aeruginosa</td>
</tr>
<tr>
<td>Streptococcus spp</td>
<td>Haemophilus influenzae</td>
</tr>
<tr>
<td>Propionibacterium acnes</td>
<td>Klebsiella spp</td>
</tr>
<tr>
<td>Bacillus spp</td>
<td>Most coliform species</td>
</tr>
</tbody>
</table>

Table 4  Characteristics of acute and chronic postoperative endophthalmitis

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Symptoms</th>
<th>Signs</th>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-4 days</td>
<td>Ocular pain</td>
<td>Lid oedema</td>
<td>&gt;30 days</td>
<td>Bacterial:</td>
</tr>
<tr>
<td>&gt;30 days</td>
<td>Reduced vision</td>
<td>Conjunctival hyperaemia</td>
<td></td>
<td>Steroid responsive iritis</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>Chemosis</td>
<td></td>
<td>Capsular plaque</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Purulent discharge</td>
<td></td>
<td>Granulomatous iritis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Corneal oedema</td>
<td></td>
<td>Vitritis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anterior chamber reaction</td>
<td></td>
<td>Localised vitreous reaction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypopyon</td>
<td></td>
<td>Fungal:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vitritis</td>
<td></td>
<td>Not usually sterile responsive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poor red reflex</td>
<td></td>
<td>Stringy vitreous reaction</td>
</tr>
</tbody>
</table>

Fox et al. presented a series of 19 cases of chronic postoperative endophthalmitis in which the onset ranged from 2 days to 8 months with a mean of 8 weeks. However, this may be misleading as the time to diagnosis differs from the time of onset. The time to diagnosis probably reflects the time when infection was suspected and this figure ranges from 1 to 36 months (mean 9.4 months). Localised endophthalmitis is a term used to describe chronic infection where it appears that the organism is sequestered in the capsular bag. The predominant feature is the presence of a white plaque on the capsule associated with chronic inflammation. It has been observed that chronic endophthalmitis can develop after Nd:YAG laser posterior capsulotomy. Features of both acute and chronic infection are presented in Table 4.

How is it managed?
Two main issues have to be addressed - namely, how to identify the infecting organism and how to deliver sufficiently high antibiotic concentrations within the eye. A subsidiary is whether removing infected contents - for instance, aspirating a hypopyon, removing the implant and capsule, or performing a vitrectomy, is valuable as a form of 'incision and drainage'.
Apart from the delayed acute form it can be assumed that the infecting organism gained access at the time of surgery. When intraocular infection is suspected cultures should be taken at the earliest opportunity; however, there is some debate as to the best source of material. There is little to be gained from conjunctival swabs. Initially, provided there is no vitreous communication, the posterior capsule will act as a barrier and infection is probably located within the anterior chamber. Unfortunately, this is not the case for long and in acute endophthalmitis infection rapidly spreads to the vitreous cavity. A number of studies have shown the advantages of vitreous biopsy and as it is inappropriate to wait for the result of an anterior chamber tap, both are recommended. However, Driebe et al. did have two cases with positive anterior chamber taps and negative vitreous cultures. These cases had intact posterior capsules with posterior chamber lenses. They postulate that under these conditions infection may be limited to the anterior chamber and this seems to be supported by Heaven et al. Aspiration within the bag and possibly primary partial capsulectomy are advised in chronic endophthalmitis, particularly if associated with a capsular plaque. A manual irrigation/aspiration system is used to collect aspirate from both the anterior chamber and within the capsular bag.

Simple vitreous aspiration is often unsatisfactory especially if the vitreous is formed. A better alternative is to take a sample of the vitreous core with a suction cutter. The volume aspirated not only serves diagnostic purposes but also creates
space for intraocular injections. When samples are taken using an infusion system they should be passed through a micropore filter as described by Forster or isolated by means of a three way tap. Slides are taken for Gram and fungal staining before immediate inoculation on to a range of aerobic, anaerobic, and fungal culture media. These should include liquid media as they provide a higher yield. A culture is considered positive if there is confluent growth on one or more solid media or growth of the same organism on two or more media, and growth in a liquid medium or scant growth on a solid one is considered equivocal. Anaerobic media should be retained for 14 days if Propionibacterium acnes is to be excluded. It is imperative that there is close cooperation between microbiologist and ophthalmic surgeon if the maximum benefit from sampling is to be gained.

Intravitreal antibiotics are generally advised and should be administered after samples have been taken rather than waiting for results. Broad spectrum antibiotics are used that cover the likely infecting organism. Heaven et al dispute this recommendation favouring the conventional approach (topical, subconjunctival, and systemic antibiotics) in uncomplicated cataract surgery. However, they admit that the poor outcome following vitreous interventions may have been related more to the severity of the disease than the treatment itself. Topical antibiotics do not reach therapeutic levels within the eye and while periocular injections achieve adequate concentrations in the anterior chamber, the levels are inadequate within the vitreous. The systemic route is of limited value because of the blood-eye barrier. However, there is some evidence that therapeutic levels can be achieved with ciprofloxacin and imipenem. Direct injection into the vitreous is the most consistent current method of achieving adequate intraocular levels. It is important to note that the pharmacokinetics of antibiotics differ between phakic, pseudophakic, and vitrectomised eyes.

Great care has to be taken in preparing and administering injections if iatrogenic damage is to be avoided. Protocols for preparation to accurate dilution and volume must be available in the operating theatre. To avoid errors in the administration dose the diluted antibiotic solution should be drawn up into a new syringe which was not used in the preparation of the injection. Gentamicin has been widely used, but is implicated as a cause of macular infarction. Amikacin (0.4 mg in 0.1 ml) is suggested as an alternative combined with vancomycin (1 mg in 0.1 ml). The cephalosporins are also useful with ceftazidime showing promise as an intravitreal agent. Furthermore, probenecid slows the removal of antibiotics that are actively transported from the eye — for example, the cephalosporins, and may be of some benefit. In acute endophthalmitis the use of two agents is recommended to provide the widest possible cover, while vancomycin can be used alone in chronic endophthalmitis. Intravitreal injections must be given slowly and into midcavity to avoid retinal damage. They are not an alternative to other treatments but should be given in conjunction with both subconjunctival and topical antibiotics. Subconjunctival vancomycin (25 mg) and ceftazidime (100 mg) together with topical vancomycin and amikacin form part of the regimen adopted by the Endophthalmitis Vitrectomy Study Group.

Care has to be taken when interpreting data on the half life of antibiotics in the vitreous. A variety of factors affect the persistence of antibiotics in the eye — for example, whether the drug is actively secreted as in the case of the cephalosporins or passively lost from the eye as occurs with gentamicin, the presence of the lens or posterior capsule, infection, and whether or not a vitrectomy has been performed. It may not be feasible to extrapolate from animal studies to the human eye. Bearing this in mind it is probably safe to repeat intravitreal antibiotics after 48 hours, if no improvement is evident. However, Mandell et al have recently demonstrated that the concentration of amikacin is likely to be below therapeutic levels within 24 hours. The choice agent for subsequent injection should be altered in the light of culture results but it is reasonable to repeat with the same agents if these are not available.

The role of vitrectomy in endophthalmitis is controversial and it is hoped that the current multicentre study being conducted in the United States will answer important questions. The dilemma for the clinician is that while animal studies have shown the benefit of vitrectomy and intravitreal injection over injection alone in sterilising the eye the procedure is not a simple one or risk free. Stern et al suggest a simple protocol which can be used pending definitive results. Endophthalmitis is categorised into mild to moderate (<15% hypopyon) and severe (>15% hypopyon, no red reflex). The suggested protocol is outlined in Figure 1. Ultrasound scanning has been advocated as a method of assessing vitreous activity and grading severity. Peyman has advocated the use of antibiotics in the infusion fluids during vitrectomy to avoid the need for bolus injection and theoretically reducing the risk of toxicity. In general, the posterior capsule and intraocular lens can be preserved. However, in chronic endophthalmitis associated with Propionibacterium acnes if partial capsulectomy removing the plaque proves unsuccessful, a total capsulectomy and lens removal are warranted.

In the rare case of a fungal infection intravitreal amphotericin B (0.005–0.01 mg in 0.1 ml) has been recommended. This may be combined with intravitreal miconazole (0.025 mg in 0.1 ml). A sub-Tenon injection of miconazole or amphotericin B is administered together with topical antifungal preparations. To avoid toxicity systemic treatment is avoided but the situation needs to be kept under review and the use of oral imidazoles should be considered.

The last issue that must be dealt with is the use of corticosteroids in combating the destructive effects of the inflammatory reaction on the eye. Steroids have been advocated by all routes (topical, subconjunctival, intravitreal, and systemic) but should be avoided if fungal endophthalmitis is suspected. While Forster recommends subconjunctival triamcinolone 40 mg or dexamethasone 4-0 mg, Diamond suggests dexamethasone 0.4 mg given intravitreally. However, Baum in a comment on the work of Maxwell et al notes that there is no evidence regarding the best method of delivering corticosteroids to the eye.

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**Figure 1** Protocol for the management of postoperative endophthalmitis (adapted from Stern et al).
Table 5 Results of treatment in acute endophthalmitis; outcome by infecting organism

<table>
<thead>
<tr>
<th>Organism</th>
<th>Vision</th>
<th>&lt;CF</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>7</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>14</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>Streptococcus faecalis</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Gram negative organisms</td>
<td>4</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Fungal organisms</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Culture negative</td>
<td>15</td>
<td>1</td>
<td>16</td>
</tr>
</tbody>
</table>

After Dreibe et al.11.  
CF=counting fingers.  
Minimum 3 months' follow up.  
12 of 61 culture positive eyes lost all vision.

What is the outcome?

Many variables affect outcome. Untreated, the prognosis for vision and the integrity of the eye is poor. Outcome relates to the identity of the infecting organism, delay before treatment is started, and the severity or extent of infection. With modern treatment it should be possible to salvage the eye, although the aim must be to preserve visual function. Toxic effects of bacterial products or antibiotics may cause irreparable damage even when the eye has been sterilised. Furthermore, there may be a need for secondary surgery to remove persistent vitreous opacities, treat retinal detachments, or reinsert an intraocular lens. Recurrence of infection or persistent inflammation may also occur.18 19 23

Success could be measured by comparing visual results with preinfection vision rather than vision on presentation. Visual rehabilitation after cataract surgery is now so rapid that best postoperative vision should be used as the benchmark.

While visual outcome relates to the severity of infection, it is well known that culture negative endophthalmitis has a relatively good prognosis, but endophthalmitis due to Staphylococcus aureus, Streptococcus pneumoniae, or Gram negative organisms is poor.10

Vitrectomy is reserved for the most severe disease and this may be the reason why presumed benefits of vitrectomy have not been substantiated.1 Any comparison between therapeutic regimens must include an assessment of severity and a grading system is needed.

The visual outcomes of the series of acute pseudophakic endophthalmitis published by Dreibe et al.11 and Heaven et al.21 are outlined in Tables 5 and 6. In both series Staphylococcus epidermidis comprises the most common organism isolated and there is agreement that visual results are second only to the culture negative group. Heaven et al. document the range of complications from evisceration through presumed antibiotic toxicity to retinal detachment, macular pucker, and oedema. Chronic endophthalmitis has a relatively good prognosis as outlined in Table 7, although relapses may occur.28

Table 6 Results of treatment in acute endophthalmitis; outcome by infecting organism

<table>
<thead>
<tr>
<th>Organism</th>
<th>Vision</th>
<th>&lt;CF</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>7</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>9</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Streptococcus pneumonia</td>
<td>nil</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Gram negative organisms</td>
<td>5</td>
<td>nil</td>
<td>5</td>
</tr>
<tr>
<td>Culture negative</td>
<td>11</td>
<td>1</td>
<td>12</td>
</tr>
</tbody>
</table>

After Heaven et al.21.  
CF=counting fingers.

How can it be prevented?

Despite improvements in treatment, visual outcome after endophthalmitis is often poor and prevention is of utmost importance. If the inoculum is sufficiently large postoperative infection is likely and the aim is to reduce risk factors and minimise entry of organisms during surgery. A lot of recommendations are empiric and suggested as important by various authors. Many seem sensible measures to adopt in reducing postoperative infection.

Detailed preoperative examination is an important step in prevention. This should be directed to exclude cases with infectious blepharitis, and infections of the conjunctiva or nasolacrimal system. Patients with keratoconjunctivitis sicca have a high rate of staphylococcal colonisation.41 Similarly, it should be noted that individuals with a history of atopic dermatitis have a high carriage rate for Staphylococcus aureus.42 Although we have not found any studies implicating atopy as a risk factor in postoperative endophthalmitis, care should be exercised with these patients. Potential sources of infection elsewhere in the body — for example, leg ulcers, need treatment before elective surgery. Patients with diabetes mellitus form a significant proportion of those undergoing cataract extraction. It is important to be aware that this group is prone to infection and is at higher risk of postoperative endophthalmitis.3

Genetic analysis studies in Staphylococcus epidermidis proved endophthalmitis' suggest that in the majority of these cases the causative organisms originate from the patient's own lid flora. Despite this evidence it is accepted that routine preoperative conjunctival swabs do not have a role in preoperative preparation.43 Culture positive eyes are commonplace44–46 and yet only a small proportion go on to develop endophthalmitis. The list of potential pathogens grows ever larger and it is difficult to decide on risk from the results of swabs. There appears to be variability in the isolation of potential pathogens using daily swabs such that Staphylococcus aureus was isolated from over 20% of lid margin samples despite previously negative cultures.47 The act of taking a swab may of itself modify lid flora.

The argument for the use of prophylactic perioperative antibiotics is far from conclusive and while it seems logical to attempt reduction of the bacterial load a corresponding reduction in the rate of endophthalmitis in modern practice has not been proved. Topical antibiotics are effective in reducing the periocular flora48 and in this respect it has been suggested that gentamicin is more effective than chloramphenicol. Topical ofloxacin has a similar spectrum to gentamicin although its effectiveness on normal flora has not been investigated in vivo.49 While most studies investigating the role of topical antibiotics are flawed the balance probably lies in favour of their ability to reduce the postoperative endophthalmitis rate.11

Subconjunctival antibiotics may be given before or at the end of surgery. Therapeutic levels are achieved in the anterior chamber and in theory this should prevent infection.48 Rabbit studies have given some support to this theory but this has not been demonstrated in humans. Perlman50 showed the effectiveness of subconjunctival antibiotics but the study was small and uncontrolled, while in another study Kolker et al.51 demonstrated that this route was better than no prophylaxis at all. Claims that infection may be delayed rather than prevented52 have not been confirmed. There is no evidence for
Infectious endophthalmitis after cataract surgery

Infectious endophthalmitis after cataract surgery is a rare but serious complication that can lead to loss of vision. The risk is increased with certain surgical procedures and the use of certain medications. The infection can be caused by a variety of microorganisms, including bacteria, fungi, and viruses. The symptoms of endophthalmitis can include pain, redness, and decreased vision.

The infection can occur in the anterior chamber, posterior chamber, or vitreous cavity. The risk of infection is increased with certain surgical procedures, such as intraocular lens implantation, vitrectomy, and laser procedures.

The diagnosis of endophthalmitis is based on clinical findings and laboratory tests. Antimicrobial therapy is the primary treatment for endophthalmitis, and surgery may be necessary to remove infected tissues.

Prevention of endophthalmitis is crucial to minimize the risk of infection. Measures include the use of topical antibiotics before surgery, strict aseptic techniques, and the use of prophylactic intraocular antibiotics.

For more information on endophthalmitis, please refer to the following resources:

232

Hughes, Hill


Infectious endophthalmitis after cataract surgery.

D S Hughes and R J Hill

doi: 10.1136/bjo.78.3.227