

ORIGINAL ARTICLES—Clinical science

Assessment of a standard treatment protocol on visual outcome following presumed bacterial endophthalmitis

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Abstract

Aims—The aim of this prospective study was, firstly, to judge the effect of early aggressive treatment with a standardised regimen of high dose broad spectrum intraocular and systemic antibiotics on visual outcome and, secondly, to assess the sensitivity of isolated organisms to the treatment regimen utilised.

Methods—Thirty two consecutive patients presenting with presumed bacterial endophthalmitis were treated and completed follow up. In every case, intraocular sampling was undertaken and treatment with intraocular vancomycin, amikacin, and systemic ciprofloxacin was commenced immediately, followed by systemic steroids 1 day later.

Results—In 69% of patients vision improved with 47% achieving a final visual acuity of 6/36 or better and 31% achieving 6/12 or better. Of the intraocular samples taken from post-surgical and post-traumatic cases, 10/27 (37%) and 3/5 (60%) were culture positive, respectively. All the bacteria isolated were sensitive to at least one of the three antibiotics used.

Conclusions—The study demonstrated that the combination of vancomycin, amikacin, and ciprofloxacin is adequate as a standard regimen for the treatment of most patients with suspected bacterial endophthalmitis. The prognosis for a good visual outcome, however, remains poor with 15/27 (55%) post-surgical and 2/5 (40%) post-traumatic cases achieving a final acuity of 6/60 or less.

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broad spectrum antibiotics to cover the full range of potential bacterial pathogens. The use of intraocular antibiotics in conjunction with systemic antimicrobials known to penetrate the blood-ocular barrier, has gained wide acceptance for the treatment of suspected bacterial endophthalmitis.¹⁻³ Commonly accepted treatment regimens include the use of intraocular vancomycin and either amikacin or ceftazidime with systemic ciprofloxacin (administered by either the intravenous or oral routes). The aim of this prospective study was, firstly, to judge the clinical effect of early aggressive treatment with a standard regimen of high dose broad spectrum intraocular and systemic antibiotics on visual outcome and, secondly, to assess the sensitivity of isolated organisms to the treatment regimen utilised.

Materials and methods

All cases of suspected post-surgical and post-traumatic bacterial endophthalmitis presenting to Moorfields Eye Hospital were eligible for this prospective study. A total of 39 eyes of 39 patients were examined between March 1991 and January 1993 and considered for enrolment. Of the 39 patients who fulfilled the enrollment criteria, 32 were included in the final analysis. These consisted of 27 post-surgical and five post-traumatic cases and excluded five patients who ultimately proved to have *Streptococcus* and *Fusarium* species as their causative agents of disease (as these patients would require additional and alternative therapy, respectively), and two patients who did not receive systemic treatment. A detailed protocol was followed for every patient which included the completion of a questionnaire (Table 1).

Intraocular (aqueous and/or vitreous) sampling was undertaken on every patient. Aqueous sampling was undertaken under topical anaesthesia at a slit lamp, using a 27 gauge (0.33 mm) needle and 100-200 µl aspirated. Vitreous sampling was undertaken under sterile conditions according to operator preference, either as a biopsy through the pars plana or with a vitreous cutter under the operating microscope, at the time of vitrectomy. After subconjunctival injection of anaesthetic, 200-

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Endophthalmitis is a devastating ocular disease, the incidence of which has been reported as 0.1-0.3% after intraocular surgery, and 2.0-3.0% after penetrating ocular trauma.¹ Currently, confirmation of the diagnosis of bacterial endophthalmitis is dependent on microbiological isolation of organisms and as time to microbiological diagnosis can vary between 2 and 12 days,² the initial treatment of this disease necessarily requires the use of

Table 1 Details of questionnaires completed for every patient

Patient demographics
Date of presentation, and duration of symptoms
Past ocular history:
Details of past ocular history: blepharitis, dacryocystitis, atopy, sicca
Surgery:
date:
type: (cataract (ECCE, ICCE, or phaco), glaucoma, corneal, vitreoretinal, secondary lens implantation)
peroperative complications: (capsule rupture plus/minus vitreous loss)
postoperative complications: (immediate and late: wound dehiscence or leak, broken or infected sutures, corneal oedema, raised IOP, uveitis)
Trauma:
date and mechanism:
surgery at referring hospital: primary repair plus/minus removal of intraocular foreign body plus/minus intravitreal antibiotics
Treatment so far in particular antibiotics (systemic, subconjunctival and/or topical) and steroid treatment (systemic and topical)
Past medical history in reference to recent surgery/illness/systemic disease (diabetes, immune deficiency)
Details of ocular examination:
Eye (R/L): Visual acuity:
Anterior chamber activity and flare (0–5):
Intraocular pressure (IOP): Binocular indirect ophthalmoscopy grade (BIO 0–5):
Corneal examination (normal/ulcer/abscess):
Lens (normal/cataract/aphakic/pseudophakic posterior chamber or anterior chamber intraocular lens/other):
Posterior capsule (clear/opacified/abscess/not applicable/no view):
Vitreous abscess (yes/no/no view):
Fundal examination (choroiditis/retinitis/cystoid macular oedema/retinal detachment/no view):
Other tests—for example, ultrasound examination
Details of samples taken:
Culture: lids, conjunctiva, cornea, aqueous, vitreous, capsule, foreign body
Details of treatment both surgical and medical:
Samples: AC tap, vitreous tap, intraocular foreign body, capsule
Procedures: vitrectomy/intraocular lens removal/capsulectomy/intraocular foreign body removal/lensectomy/retinal detachment repair
Intracameral injections: vancomycin, amikacin, steroid
Systemic administration: ciprofloxacin, cefuroxime, gentamicin, steroid (with date of commencement)
Topical therapy: cefuroxime, gentamicin forte, steroid, other
Other therapy: for example, subconjunctival
Follow up at 1, 3, and 6 month
Ocular examination:
Eye (R/L): Visual acuity:
Anterior chamber activity and flare (0–5):
IOP: BIO (0–5):
Fundal examination: (cystoid macular oedema/retinal detachment/epiretinal membrane/macular hole/retinitis/choroiditis/no view):
Treatment: systemic/topical steroids/antibiotics, other
Results of microbiology with antibiotic sensitivities:
Gram stain of intraocular sample
Extraocular and intraocular culture of specimens
Sensitivities to vancomycin, amikacin, ciprofloxacin, penicillin, gentamicin, other
Outcome: 1 = 6/5–6/12, 2 = 6/18–6/36, 3 = 6/60–NPL, 4 = enucleation
Last recorded visual acuity with date:

400 µl of vitreous was aspirated using a 23 gauge needle which was inserted through the pars plana 3 mm behind the limbus in aphakic eyes and 4 mm behind the limbus in phakic eyes.

All samples were plated immediately, after one drop had been placed on a glass slide for Gram staining and microscopy. Once the vitreous sample had been taken, vancomycin (2.0 mg in 0.1 ml) and amikacin (0.4 mg in 0.1 ml) were injected separately into the vitreous cavity through the same injection site. Intravenous ciprofloxacin (200 mg twice

daily) was commenced and changed to oral therapy (750 mg twice daily) after 2 days. Oral prednisolone (60 mg per day) was started 1 day after intracameral antibiotics had been given and once the presence of fungi had been excluded on microscopy.

Intraocular samples were examined by Gram and periodic acid Schiff staining, and cultured on blood agar, chocolate blood agar, and in Robertson's cooked meat broth, brain heart infusion broth, and thioglycolate broth. For aerobic bacteria, only heavy growth from one solid medium or isolation of the same organism from more than one type of medium was considered significant and not a contaminant. Anaerobic growth on any medium incubated anaerobically, was considered significant. Cultures were maintained for 14 days. If no organism was isolated the case was considered culture negative even if organisms were thought to be present on the smear.

Patients were seen regularly according to clinical need but were routinely seen at 1, 3, and 6 month intervals and the data recorded.

Results

Twenty seven post-surgical cases and five post-traumatic cases were enrolled in the study (total 32 patients). The average age was 68 years for the post-surgical cases (range 19–91 years) and 33 years for the post-traumatic cases (range 20–40 years). All the post-traumatic cases were male but among the post-surgical cases 15 patients were female and 12 male (χ^2 $p < 0.001$) (Table 2).

POST-SURGICAL CASES AT PRESENTATION

The visual acuity at presentation was 6/24 or less in all patients with 24/27 (89%) patients at 6/60 or less (range 6/24–POL, mode HM, median HM). The left eye was affected in 56% and the right eye in 44% of patients. The surgical procedures and associated complications are described in Table 3. The majority of patients had undergone routine extracapsular cataract surgery (20/27) which had proceeded without intraoperative or postoperative complications (14/20). Four patients had had a trabeculectomy performed and time from operation to presentation with endophthalmitis secondary to bleb abscess formation was recorded as between 19.5 months and 14.8 years.

POST-TRAUMATIC CASES AT PRESENTATION

The five post-traumatic patients presented with three penetrating injuries (two ferrous metal and one glass foreign body) and two retained intraocular foreign bodies (both ferrous metal). The left eye was affected in 4/5 cases. Four patients presented within 24 hours of the event. One patient presented within 24 hours of developing symptoms, 5 days post-trauma.

TIME TO PRESENTATION

Of the 27 post-surgical patients 10 presented in the early postoperative period—that is, the first 10 days postoperatively (mean 4.9 days,

Table 2 Patient details

Case no	Age/sex/eye	Time from operation or trauma to first symptoms	Time from presentation to first sampling	Pre-Rx	AC tap	Vit tap or biopsy	Vit	Initial visual acuity	Final visual acuity	Outcome	Microbiology results
Post-surgical cases:											
Culture positive cases											
1	62/F/R	5 days	1 day	Y	N	N	Y	PL	Phthisis	3	Coagulase negative <i>Staphylococcus</i> spp
2	82/F/L	3 weeks	21 months	N	Y	Y	N	HM	NPL	3	Coagulase negative <i>Staphylococcus</i> spp and <i>Staphylococcus aureus</i>
3	80/F/R	4.8 months	<1 day	N	N	N	Y	6/60	6/12	1	Coagulase negative <i>Staphylococcus</i> spp
4	69/F/R	8 months	1 day	N	Y	Y	N	PL	6/18	2	Coagulase negative <i>Staphylococcus</i> spp
5	52/M/R	14.8 years	4 days	Y	Y	N	N	HM	6/12	1	Coagulase negative <i>Staphylococcus</i> spp
6	51/M/R	2 months	6 weeks	Y	N	N	Y	HM	6/60	3	<i>Propionibacterium acnes</i>
7	69/F/L	6 months	18 months	Y	Y	Y	N	6/24	6/36	2	<i>Propionibacterium acnes</i>
8	76/L/M	5 days	<1 day	Y	Y	Y	N	PL	CF	3	<i>Proteus mirabilis</i>
9	62/M/L	2.7 years	8 days	N	N	N	Y	HM	Phthisis	3	<i>Neisseria</i> spp
10	66/M/L	11.6 years	7 days	N	N	Y	N	HM	CF	3	<i>Haemophilus</i> spp
11	19/F/R	1 day	6 months	N	N	N	Y	HM	6/12	1	No growth
12	42/M/R	1 day	8 days	N	Y	Y	N	HM	PL	3	No growth
13	35/M/L	2 days	<1 day	N	Y	Y	N	6/60	6/60	2	No growth
14	84/F/L	3 days	<1 day	Y	Y	Y	Y	PL	NPL	4	No growth
15	50/M/L	5 days	2 days	Y	N	Y	N	HM	6/60	3	No growth
16	81/F/R	8 days	2 weeks	Y	Y	Y	N	HM	6/9	1	No growth
17	80/F/L	9 days	42 days	Y	Y	N	Y	6/36	6/9	1	No growth
18	79/M/L	10 days	<1 day	Y	Y	Y	N	6/60	6/9	1	No growth
19	76/M/L	1 month	14 days	Y	Y	N	Y	6/60	6/18	2	No growth
20	71/F/L	2 months	12 months	Y	Y	Y	Y	6/36	6/9	1	No growth
21	58/F/R	2 months	9.6 years	N	Y	N	Y	CF	CF	3	No growth
22	51/M/L	3 months	9 months	N	Y	Y	N	6/60	6/12	1	No growth
23	87/F/R	3 months	11 months	Y	N	N	Y	PL	CF	3	No growth
24	72/F/R	5 months	3 weeks	N	N	N	N	6/60	6/18	2	No growth
25	78/M/L	12 months	8 weeks	Y	N	N	Y	PL	HM	3	No growth, <i>Monaxella keratitis</i>
26	71/F/R	20 months	2 days	Y	N	Y	N	PL	6/60	3	No growth
27	70/F/L	2.2 years	<1 day	N	Y	Y	N	PL	PL	3	No growth
Post-traumatic cases											
Culture positive cases											
28	35/M/L	<1 day	<1 day	Y	Y	Y	N	PL	6/60	3	Coagulase negative <i>Staphylococcus</i> spp
29	33/M/L	<1 day	2 days	N	N	N	Y	6/5	6/12	1	Coagulase negative <i>Staphylococcus</i> spp
30	40/M/L	5 days	<1 day	Y	Y	Y	Y	6/36	6/9	1	Coagulase negative <i>Staphylococcus</i> spp
Culture negative cases											
31	20/M/L	<1 day	4 days	Y	Y	Y	Y	HM	6/36	2	No growth
32	40/M/R	1 day	1 day	Y	N	N	Y	HM	CF	3	No growth

Pre-Rx = antibiotic treatment at presentation; AC tap = anterior chamber tap; Vit tap = vitreous humour tap or biopsy; Vit = vitrectomy. Outcome: 1 = 6/5-6/12; 2 = 6/18-6/36; 3 = 6/60-NPL/phthisis; 4 = enucleation.

Table 3 Operative procedures and complications associated with cases of post-surgical endophthalmitis in this series

	No of patients
Operation:	
Extracapsular cataract extraction and intraocular lens implant	20
Trabeculectomy	4
Corneal surgery	2
Vitreoretinal surgery	1
Intracapsular cataract extraction	1
Total:	28*
Complications:	
No complications	20
1, 2, or 3 complications	7†
Peroperative:	
Vitreous loss	0
Capsule rupture	0
Postoperative:	
Raised intraocular pressure	1
Wound or bleb leak	1
Broken sutures	1
Corneal oedema	1
Uveitis	5

*One patient underwent penetrating keratoplasty and trabeculectomy within 10 days of the first procedure.

†One patient suffered two peroperative and postoperative complications and another suffered three.

mode 1 day, range 1–10 days) and 17 patients (63%) presented after 11 days, the range varying widely between 21 days and 14.8 years. Overall, 59% of all patients presented more than 1 month after surgery. There was no statistically significant correlation between time to presentation from onset of symptoms and final visual acuity better than 6/60 for those patients presenting at 1 day or less, at 1 week, and greater than 1 month after onset of symptoms ($p = 0.33, 0.30, \text{ and } 0.67$ respectively).

SAMPLING AND TREATMENT

Culture of vitreous humour was undertaken in all patients (15 by vitreous tap only, 14 by vitrectomy, and three by vitreous tap followed by vitrectomy). Anterior chamber (AC) tap and culture was performed on 56% of all patients. An AC tap was always accompanied by vitreous sampling.

All patients received intravitreal amikacin and vancomycin immediately after the samples had been collected. Systemic ciprofloxacin was administered in 97% of patients. One patient with delayed onset endophthalmitis secondary to *Propionibacterium acnes*, did not receive ciprofloxacin as this had already been administered at the referring hospital and the organism was fully sensitive to vancomycin and amikacin. Systemic steroids were commenced in 78% of patients after 24 hours. Treatment with topical antibiotics was variable with 55%, 44%, and 41% of patients receiving topical cefuroxime, gentamicin, and/or chloramphenicol, respectively. Topical steroids were adminis-

tered to all patients after sampling was complete.

Overall, seven patients had capsulectomy and culture of capsule remnants. Removal of the IOL was performed in only two of these cases but a further four cases were treated with IOL removal in the absence of capsulectomy.

Four of the five post-traumatic patients underwent vitrectomy. The one patient who did not undergo vitrectomy after admission had already undergone vitrectomy and removal of intraocular foreign body at the referring hospital.

COMPLICATIONS AT PRESENTATION AND POST-SAMPLING

At presentation two post-surgical endophthalmitis patients (cases 1 and 6) were noted to have retinal detachments (0.07%). Both of these cases were culture positive and had poor final visual outcomes.

Advanced ophthalmic conditions in existence before presentation and contributing to poor final visual outcome were noted and include advanced glaucoma (two cases), Behçet's disease (one case), and high myopia with longstanding nystagmus (one case). Complications of endophthalmitis and its treatment include cystoid macular oedema (three cases), macular hole (two cases), epiretinal membrane (two cases), retinal detachment (two cases both at 1 month, one vitrectomy, one tap), decompensated corneal graft (three cases). Patient 21 underwent vitrectomy for a worsening clinical picture, and later removal of IOL and capsule which was complicated by expulsive haemorrhage and the eye was enucleated shortly afterwards.

FINAL VISUAL OUTCOME

Final visual outcome was assessed after at least 6 months, and categorised as in Table 4. Comparing initial and final visual acuities, 22/32 (69%) patients showed an improvement in their vision. Overall, 12/27 (44%) post-surgical patients and 3/5 (60%) post-traumatic cases had a final visual acuity of 6/36 or better, with 8/27 (29%) and 2/5 (40%) achieving 6/12 or better, respectively. Compared with culture positive cases, culture negative cases were associated with a higher percentage of cases with a final visual acuity of 6/12 or better (35% (6/17) *v* 20% (2/10)) and a smaller proportion with vision of 6/60 or less (52% (9/17) *v* 60% (6/10)) ($\chi^2 p = 0.16$). The prognosis for a good visual outcome, however, remains poor with 15/27 (57%) post-surgical and 2/5 (40%) post-traumatic cases achieving a final acuity of 6/60 or less.

MICROBIOLOGICAL RESULTS AND ANTIBIOTIC SENSITIVITIES

Intraocular and extraocular cultures were positive in 13/32 (40%) and 20/32 (58%) of all patients respectively. In the post-surgical subgroup of patients 10/27 (37%) had positive intraocular and 19/27 (70%) positive extraocular cultures. In one case aqueous fluid was culture positive in the absence of a culture positive sample of vitreous and in one other, samples

Table 4 Final visual outcome of all patients

	Post-surgical patients (%)			Post-traumatic patients (%)		
	Culture +	Culture -	All	Culture +	Culture -	All
1 = 6/5–6/12	2	6	8	2	0	2
2 = 6/18–6/36	2	2	4	0	1	1
3 = 6/60–NPL	6	8	14	1	1	2
4 = enucleation	0	1	1	0	0	0
Total	10	18	27	3	3	5

Table 5 Comparison of final visual acuity post-treatment of presumed bacterial endophthalmitis (NA= not available)

Reference	Vision 6/60 (20/200) or less	
	Culture positive	Culture negative
Post-surgical cases only:		
Bohigan 1985 ³	77% (39/51)	48% (15/31)
Driebe 1986 ⁵	60% (41/67)	27% (5/18)
Kattan 1990 ⁶	56% (14/25)	40% (2/5)
Heaven 1992 ⁷	25% (6/20)	8% (1/12)
Doft 1994 ⁸	22% (13/60)	17% (1/6)
Okhravi 1997	60% (6/10)	53% (9/17)
Post-traumatic cases only:		
Peyman 1979 ⁹	33% (4/12)	NA
Alfaro 1994 ¹⁰	81% (17/21)	87% (13/15)
Okhravi 1997	33% (1/3)	50%

from the posterior capsule were culture positive in the absence of a culture positive aqueous or vitreous. Nine of the 11 culture positive patients were also culture positive from an extraocular site but this was reflected in only 12 out of 21 culture negative cases (χ^2 p= 0.4).

In only three post-surgical patients and in one post-traumatic case did a positive culture from the extraocular surface correspond to the same species of organism grown from the intraocular samples. All four of these were culture positive for coagulase negative staphylococci.

Culture of the posterior capsule was positive in two cases and in a third, microscopy confirmed the presence of organisms consistent with *P. acnes* already grown from the vitreous sample (Table 6 case 7). In one case lens capsule culture was positive in the absence of a positive culture from either aqueous or vitreous and revealed a mixture of causative organisms, namely coagulase negative *Staphylococcus* species and *Staphylococcus aureus*.

Gram positive organisms accounted for 7/10 (70%) culture positive post-surgical and 3/3 (100%) post-traumatic cases of endophthalmitis. All the bacteria isolated were sensitive to at

least one of the three antibiotics used (Table 6). In four cases sensitivities were only available to gentamicin (patients 2, 4, 5, and 10). In these cases organisms sensitive to gentamicin were judged sensitive to amikacin. Only one of the two isolates of *P. acnes* was resistant to gentamicin and partially resistant to amikacin (patient 7). Considering the isolates of coagulase negative *Staphylococcus*, one was found to be partially resistant and another fully resistant to vancomycin.

Discussion

FINAL VISUAL ACUITY

The final outcome results for vision worse than 6/60 varies from 22–77% in the literature (Table 5).^{4–10} Comparison of these reports is, however, confounded by the use of widely differing management regimens at different centres. It is clear, however, that culture negative cases are associated with a lower percentage of cases with final visual outcome of 6/60 or less. In this series, despite adequate antibiotic coverage of the pathogens responsible with at least one antibiotic in every case, final visual outcome results remain unsatisfactory. Perhaps a combination of this antibiotic regimen with a more aggressive surgical approach would be of more benefit. The recent publication of the Endophthalmitis Vitrectomy Study (EVS)¹¹ has highlighted the benefits of vitrectomy in patients who present with a visual acuity of perception of light. The results of this study cannot, unfortunately, be applied globally to all cases of severe endophthalmitis, as many patients were excluded from the trial, notable among them those with corneal oedema, no view of iris, no perception of light vision at presentation, prior intraocular surgery other than lens related (five post-cataract cases in this series), retinal detachment at presentation (two cases in this series), previous injection of

Table 6 Final visual acuity by microbiological results

Case number	Aetiology	Final visual outcome	Organism/s isolated	Culture positive samples			Antibiotic sensitivities		
				AQ+	Vit+	Cap+	V	A	C
1	Post-surgical	3	Coagulase negative <i>Staphylococcus</i> spp	NA	Y	NA	Y	Y	Y
2	Post-surgical	3	Coagulase negative <i>Staphylococcus</i> spp and <i>Staphylococcus aureus</i>	N	N	Y	NK	Y(G)	Y
3	Post-surgical	1	Coagulase negative <i>Staphylococcus</i> spp	NA	Y	Y	NK	Y(G)	NK
4	Post-surgical	2	Coagulase negative <i>Staphylococcus</i> spp	N	Y	N	N(PR)	Y	Y
5	Post-surgical	1	Coagulase negative <i>Staphylococcus</i> spp	NI	NI	NA	NK	Y(G)	NK
6	Post-surgical	3	<i>Propionibacterium acnes</i>	NA	Y	NA	Y	Y	NK
7	Post-surgical	2	<i>Propionibacterium acnes</i>	N	Y	Ya	Y	N(PR)	Y
8	Post-surgical	3	<i>Proteus morgagni</i>	Y	N	NA	N	Y	Y
9	Post-surgical	3	<i>Neisseria</i> spp	NA	Y	NA	N	Y	N
10	Post-surgical	3	<i>Haemophilus</i> spp β	NA	N	NA	N	Y(G)	N
29	Post-traumatic	3	Coagulase negative <i>Staphylococcus</i> spp	N	Y	Na	Y	Y	Y
30	Post-traumatic	1	Coagulase negative <i>Staphylococcus</i> spp	NA	Y	NA	NK	Y	NK
31	Post-traumatic	1	Coagulase negative <i>Staphylococcus</i> spp	Y	Y	NA	N	Y	Y

AQ+ = aqueous sample culture positive; Vit+ = vitreous sample culture positive; CAP+ = capsule biopsy culture positive; Y = yes; N = no; NA = not applicable; NI = no information from referring hospital; V = vancomycin sensitivity; A = amikacin sensitivity; C = ciprofloxacin sensitivity; Y = fully sensitive; N = resistant; (G) = sensitive to gentamicin; test was not performed for amikacin; PR = partially resistant; NK = sensitivity test not performed/no result available.

α = Organisms compatible with *P. acnes* were seen on microscopy of the capsule fragment but this sample was culture negative. β = *Haemophilus* isolated from cultures of sutures and plomb removed at the time of surgery.

intravitreal antibiotic (eight cases in this series), and known previous ocular disease known to reduce visual acuity to less than 20/100 (eight cases in this series). Twenty of 27 of the patients in our study had endophthalmitis secondary to cataract surgery or secondary IOL insertion. Overall 9/20 (45%) of this subgroup of patients would be excluded if the EVS criteria were to be used: 4/9 of whom had POL, and 3/9 had hand movements vision at presentation. Four of nine of these patients were treated with vitrectomy. If one were to exclude from the analysis the patients who did not fulfil the EVS criteria, the final visual outcome figures would be very similar to those obtained by the EVS group: 7/11 (64%) would have a final visual acuity of 6/12 or better and only 2/11 (18%) would have a final visual acuity of counting fingers or worse in our series, compared with 53% with final acuity of 20/40 or better and 15% with visual outcome of 5/200 or worse as reported in the EVS. Perhaps the patients to whom the EVS conclusions apply are those currently judged less severe in relation to the full spectrum of disease and who should be treated more aggressively when presenting with POL vision.

ANTIBIOTIC SENSITIVITY

For the purposes of this study, a standard antibiotic regimen of vancomycin, amikacin, and ciprofloxacin was chosen for the treatment of patients presenting with presumed bacterial endophthalmitis. Amikacin is useful for the treatment of Gram negative infections and is less frequently associated with retinal toxicity and macular infarction seen with the use of gentamicin.¹² Aminoglycosides were chosen in preference to ceftazidime because they demonstrate a concentration dependent bactericidal action, which increases with bacterial load and, unlike ceftazidime, show synergistic activity with vancomycin against *Staphylococcus*, *Streptococcus*, and *Enterococcus* species.^{13 14}

Vancomycin has excellent coverage of Gram positive organisms and is especially useful in the treatment of disease secondary to *Streptococcus* and methicillin resistant isolates of *Staphylococcus*. Its use has been advocated for therapy of severe ocular infection and discouraged for prophylaxis of endophthalmitis as concern is growing regarding emerging resistance in *Staphylococcus*, *Enterococcus*, and *Pneumococcus* species.¹⁵ Its use for endophthalmitis caused by Gram positive organisms has been advocated as no organisms were found to be resistant.^{3 16} In this group of ocular isolates, however, one isolate of coagulase negative *Staphylococcus* was partially resistant and another was fully resistant to vancomycin on MIC testing. Both these isolates were fully susceptible to amikacin and ciprofloxacin (Table 6).

Ciprofloxacin is useful systemically, both after oral and intravenous administration, achieving intravitreal concentrations higher than the minimum inhibitory concentration (MIC₉₀) of most causative organisms except *Staphylococcus aureus*, *Pseudomonas* spp,¹⁷ and *Streptococcus* spp.¹⁸ Kowalski *et al* have, however, noted that the minimum intraocular

levels expected after systemic administration are sufficient to treat only 60% of the ocular organisms isolated.¹⁹ All isolates sensitive to ciprofloxacin, however, were also sensitive to at least one of the other two agents which had been administered via direct injection.

Based on microbiological sensitivity profiles from culture positive cases, the combination of vancomycin, amikacin, and ciprofloxacin appears adequate for the treatment of patients with suspected bacterial endophthalmitis. The emerging resistance to vancomycin is of concern, however, and needs careful monitoring.

CULTURE POSITIVE RATE

The culture positive rate in several studies has been reported and varies widely from 51–75%,^{4 5 7 20–24} and seems much higher than that found in our study. Our figure of 40% may be a reflection of the high percentage of cases already commenced on both topical and intraocular antibiotics which are referred to this centre.

The importance of undertaking both aqueous and vitreous sampling is highlighted by the culture positivity of aqueous in the absence of a positive culture from vitreous in one of our patients. Although vitreous samples are of greater benefit the value of aqueous and capsule/IOL culture should not be underestimated. Kent *et al* found aqueous samples to be positive by culture in eight cases when culture of vitreous proved unhelpful²⁴ and Busin *et al* used scanning electron microscopy and detected bacteria on all removed lenses in 11 patients in whom cultures were negative before IOL removal, five of which were culture positive from samples taken at the time of IOL removal.²⁵

In common with other reports of culture positive post-traumatic endophthalmitis the vitreous sample was positive in all cases and the aqueous sample in very few.⁹

COAGULASE NEGATIVE STAPHYLOCOCCI

Coagulase negative staphylococci including *Staphylococcus epidermidis* account for 27.5–61% of culture positive cases of endophthalmitis in many series,^{3 20 26} and have been grown from 44% of aqueous aspirates from routine surgical cases which did not develop endophthalmitis.²⁷ In this series of patients, overall 8/15 (53%) of the patients were culture positive for this organism (this figure includes isolates of streptococci). Coagulase negative staphylococci have traditionally been associated with a less virulent course of disease and a good visual outcome. In our series of patients, however, 2/5 post-surgical and 1/3 post-traumatic cases had a final visual acuity of 6/60 or less. Increasingly the possibility of a poor visual outcome secondary to infection with this organism is being recognised.^{24 28}

Excluding the case of bleb associated endophthalmitis (patient 5) the time to presentation was variable with a range of 1 day to 8 months. This range is much greater than the 2–18 days reported previously.²⁹ There was no correlation, however, between final visual outcome

better than 6/60 and time to presentation or treatment ($p=0.2$).

DELAYED POSTOPERATIVE ENDOPTHALMITIS

Olson *et al* reported 35/40 cases (87%) as presenting in the first 6 weeks postoperatively.²⁶ In this series only 41% of cases presented within the first 6 weeks. This may be a reflection of the use of this hospital as a tertiary referral centre for cases of unresponsive uveitis. Seven of 10 cases of delayed onset uveitis so referred were found to be culture positive. In keeping with other reports coagulase negative staphylococci and *P. acnes* were the organisms most frequently isolated.

POST-TRAUMATIC ENDOPTHALMITIS

The culture positive rate of 60% seen in this small series reflects that reported by other investigators.¹⁰ Coagulase negative staphylococci are often the most common causative agent in cases of post-traumatic endophthalmitis.^{9 10} In this series 60% of patients achieved a final visual acuity of 6/36 or better with 40% achieving 6/12 or better.

Conclusion

Full coverage of all possible pathogens is mandatory in the treatment of presumed bacterial endophthalmitis and has been achieved by using a combination of vancomycin, amikacin, and ciprofloxacin. Despite this coverage, however, the prognosis for a good visual outcome remains poor, with 55% of post-surgical and 40% of post-traumatic cases achieving a final visual acuity of 6/60 or less. The emerging resistance to vancomycin is of concern and should be carefully monitored.

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Assessment of a standard treatment protocol on visual outcome following presumed bacterial endophthalmitis

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