

Endogenous Endophthalmitis

Por Yong Ming *MRCSEd, MMed (Ophth)*,¹ Chee Soon-Phaik *FRCS (G), FRCOphth*¹⁻³

¹ Singapore National Eye Centre

² Singapore Eye Research Institute

³ National University of Singapore

ABSTRACT

Intraocular infection occasionally arises from the spread of organisms from a remote source. Although rare, the visual consequences are often devastating. Various organisms including bacteria, fungi and protozoa have been implicated. In East Asian countries, the most common situation is that of *Klebsiella* endophthalmitis in the setting of hepatobiliary infection. Intensive systemic antibiotic treatment together with judicious use of intravitreal antibiotics and surgery may salvage some vision for the patient. However, the outcome in most cases remains poor.

Keywords: bacterial, East Asian, endogenous endophthalmitis, fungal, *Klebsiella*, protozoal

INTRODUCTION

Endogenous endophthalmitis is a rare but devastating intraocular infection resulting from spread of pathogens from a remote focus. Overall, it accounts for a minority of cases of endophthalmitis, most of which arise post-operatively or after trauma. However, it often entails a poorer prognosis because of late diagnosis and underlying severe sepsis. Aggressive and early treatment with appropriate antibiotics may salvage some vision for the patient.

Endogenous endophthalmitis can affect patients of any age and sex. Although affected patients often have impaired host defense systems, immunocompetent patients have been affected as well.¹⁻³

Among previously healthy patients, a small proportion had an iatrogenic cause of endogenous endophthalmitis. Direct inoculation of organisms from dental surgery, contaminated intravenous fluids and intravesicular injections of *M. bovis*-bacille Calmette-Guerin for bladder carcinoma have been reported.^{4,7} Trauma including burns can predispose to a peripheral focus of infection and sepsis.⁸

General risk factors for endogenous endophthalmitis include those in Table 1. More specific risk factors and septic sources associated with particular microorganisms are set out in Table 2.

MICROBIOLOGY

A variety of organisms have been implicated in this condition. Bacteria and fungi are more commonly implicated but endogenous amoebic endophthalmitis has also been described.^{5,9}

Most cases of endogenous endophthalmitis are associated with an identifiable source of sepsis. In general, patients with Gram-positive infections often have underlying conditions such as endocarditis, septic arthritis and cutaneous infections. Gram-negative infections are more often associated with hepatobiliary, chest and urinary tract infections. Fungal organisms may also originate from a focus of infection in the chest or urinary tract. They frequently colonise indwelling catheters, especially if broad-spectrum antibiotics are also used. Where no obvious infective focus can be found, a history of direct inoculation either iatrogenically or via intravenous drug abuse can sometimes be elicited.

Table 1. Risk factors for bacterial and fungal endogenous endophthalmitis.

Chronic metabolic diseases Diabetes mellitus Chronic renal failure
Malignancy
Immunosuppression Acquired Immune Deficiency Syndrome Drug induced
Intravenous drug abuse
Long term intracorporeal foreign bodies
Invasive surgery

Table 2. Associated micro-organism, risk factors and septic source (Adapted from Chee et al¹⁹).

Organism	Risk Factors	Septic Source
<i>Klebsiella pneumoniae</i>	Diabetes mellitus	Hepato-biliary disease, urinary tract infection, prostatitis
<i>Escherichia coli</i>	Diabetes mellitus	Urinary tract infection, endocarditis
<i>Staphylococcus aureus</i>	Diabetes mellitus, renal failure, intravenous catheters, arterio-venous fistulas	Cutaneous infections, septic arthritis
<i>Streptococcus</i> species		Meningitis, cutaneous infections
<i>Bacillus cereus</i>	Intravenous drug abuse	
<i>Candida</i> species	Gastro-intestinal surgery, parenteral hyperalimentation, broad-spectrum antibiotic use, indwelling catheters, immunosuppressive therapy, low-birth weight infant, intravenous drug abuse	
<i>Aspergillus</i> species	Chronic pulmonary disease, intravenous drug abuse	Pulmonary infection

Table 3. Incidence of different bacteria causing endogenous endophthalmitis (Adapted from Wong et al²).

Organism	Incidence (%) in East Asian Countries from 1986–1998	Incidence (%) in Singapore Institutions from 1994–1997
Gram Positive		
<i>Streptococcus</i> species	3.6	7.4
<i>Staphylococcus aureus</i>	3.6	11.1
<i>Enterococcus faecalis</i>	1.2	–
Gram Negative		
<i>Klebsiella pneumoniae</i>	77.4	59.3
<i>Escherichia coli</i>	4.8	3.7
<i>Neisseria meningitidis</i>	1.2	3.7
<i>Salmonella</i> species	1.2	3.7
<i>Enterobacter agglomerans</i>	2.3	–
Acid Fast		
<i>Nocardia asteroides</i>	2.4	3.7
<i>Mycobacterium</i> species	2.4	7.4

Bacterial Endogenous Endophthalmitis

Among East Asians, most cases of bacterial endogenous endophthalmitis are caused by Gram-negative bacteria, the majority being *Klebsiella pneumoniae* (77.4%).² Most cases of *Klebsiella* endophthalmitis were found to be related to hepatobiliary infection,

which also appears to be most common in East Asians.^{2,10} A recent report of 5 patients with Group B *Streptococcus* endogenous endophthalmitis in our population found that 4 were associated with septic arthritis.¹¹ The difference in incidence of different causative bacteria in East Asia are further elaborated on in Table 3.

In the West, Gram-positive cocci including *Staphylococcus aureus*, *Streptococcus pneumoniae* and other streptococcal species are the most common causes of bacterial endogenous endophthalmitis.³ In the paediatric population, *Haemophilus influenzae* and *Neisseria meningitidis* account for a significant proportion of cases.³

Fungal Endogenous Endophthalmitis

Endophthalmitis due to systemic fungaemia is less commonly reported in East Asian countries. Contributing factors include lower rates of indwelling catheters and other long-term intracorporeal foreign bodies, and previously lower rates of HIV infection and intravenous drug abuse. Underlying immunosuppression is common although a case of *Aspergillus* endophthalmitis occurred in a healthy 5-year-old child.¹²

Organisms implicated include *Candida albicans* and *Aspergillus* species.¹³⁻¹⁶ Less commonly, *Cryptococcus neoformans*, *Histoplasma capsulatum* and other dimorphic fungi, and *Fusarium* species have been implicated in endogenous endophthalmitis.^{16,17} Increasingly, early systemic antifungal therapy appears to be reducing the incidence of *Candida* endogenous endophthalmitis despite the increasing prevalence of Candidiasis.¹⁸

Protozoal Endogenous Endophthalmitis

Although we have not seen any cases in our institution, amoebic endogenous endophthalmitis has been reported in the literature recently.^{5,9} One case was due to an unspecified *Acanthamoeba* species, while the other was presumed to be caused by *Entamoeba gingivalis* following a dental procedure. In this case, there was co-infection with *Staphylococcus epidermidis* and the presence of these 2 organisms could have contributed to an abrupt onset of endophthalmitis.

PATHOPHYSIOLOGY

From a remote infective focus or direct intravenous inoculation, organisms usually reach the eye via the bloodstream.¹⁹ Direct spread of fungal infection has been described from the central nervous system via the optic nerve.¹⁶

Septic emboli lodge in arterioles and capillaries, from where organisms breach the blood ocular barriers. Structures with a high blood flow, including the retina, choroid and ciliary body, are preferentially affected.¹⁹ Apart from microbial toxins, retinal damage is exacerbated by ischaemia caused by septic emboli. Indeed, bilateral central retinal artery occlusion occurred in a patient with bilateral *Klebsiella* endogenous endophthalmitis.²⁰

CLASSIFICATION

Cases of endogenous endophthalmitis can be classified according to the site of ocular involvement as well as the extent of involvement. This also provides a gauge of visual prognosis. Greenwald *et al* subdivided these cases into anterior and posterior cases, with each subset having further focal and diffuse categories. Focal disease occurs where intraocular inflammation is concentrated at discrete foci while diffuse disease is associated with intense, generalised inflammation of the affected ocular compartment. Panophthalmitis denotes involvement of both anterior and posterior segments as well as inflammation of the orbital structures.³

In Greenwald *et al*'s series, focal disease of either the anterior or posterior segments were associated with good outcomes when treated appropriately with antibiotics. Anterior diffuse disease with severe anterior segment inflammation also responded well to treatment. However, resolution was sometimes delayed and complications such as corneal oedema, glaucoma or cataract could occur. Posterior diffuse disease and panophthalmitis were generally associated with very poor outcomes consistent with rapid and widespread retinal involvement.³

CLINICAL FEATURES

Symptoms

In most cases, the patient complains of ocular symptoms in the setting of established septicaemia or an extraocular focus of infection. Occasionally, ocular infection may be the first sign of a systemic disorder or occur in healthy people. Certain organisms, such as *K pneumoniae* and *L monocytogenes*, have been implicated in such circumstances.^{1,2}

Generally, ocular symptoms occur within a week after the onset of systemic illness. However, in a recent local case series, 2 out of 27 patients developed eye problems a month or more after their systemic disease was diagnosed.² An affected patient, if not moribund, will often complain of ocular pain, decreased vision accompanied by floaters, redness, swelling and discharge.

Systemic symptoms of sepsis are often nonspecific and include malaise, nausea, loss of appetite or weight and abdominal discomfort.¹⁹ Other symptoms, including fever, chills and rigors, may be transient and may only be obtained on direct questioning. History taking for these patients also requires a systematic search for symptoms referable to a focus of infection, including the gastrointestinal, urinary, respiratory, dermatological and dental systems.

Signs

Bacterial Endogenous Endophthalmitis

Although most cases are unilateral, bilaterality has been reported in 14 to 25% of cases.^{1,2} Appropriate systemic therapy does not preclude second eye involvement, which may be delayed.

Anterior focal disease is rare and involves inflammation confined to discrete foci, which may appear as iris nodules or microabscesses. More severe generalised inflammation is seen in diffuse disease. The latter is usually accompanied by chemosis, lid swelling, corneal oedema, anterior chamber fibrinous reaction and hypopyon. The intraocular pressure is often elevated. If the fundus is not visible, B-scan ultrasonography will reveal the lack of posterior segment echoes.

Posterior focal disease manifests as whitish nodules or plaques usually in the choroid and rapidly involves the retina. Infections caused by Gram-positive organisms may be multifocal, associated with Roth spots and retinal vasculitis, and tend to be severe. Gram-negative infections usually cause a single large choroidal abscess involving the posterior pole. In between suppurative foci, the intervening uvea and retina may be largely normal. Diffuse disease is a more severe condition characterised by intense vitreous inflammation which usually obscures the fundus. This may arise from virulent organisms such as Group B Streptococcus or from posterior focal infection, especially if these are misdiagnosed as autoimmune uveitis and treated with periocular steroid injections. Perivascular haemorrhages and arterial emboli have been noted in cases where the fundi could be visualised.¹⁹ Ultimately, frank retinal necrosis occurs. Globe perforation may occur at the site of an abscess, especially if a marked rise in intraocular pressure exists (Fig. 1).

Panophthalmitis denotes disease involving the entire globe which has spread to orbital tissues. Signs of orbital cellulitis include lid oedema, chemosis, proptosis and limited ocular movements. In our experience, severe chemosis is often seen in infections caused by Klebsiella and Pseudomonas species (Figs. 2 and 3).

Specific signs have been described which may suggest a specific infecting organism. For example, Bacillus infections characteristically demonstrate a chocolate brown anterior chamber exudate with a ring-shaped white corneal infiltrate (Fig. 4). Serratia infections may be associated with a pink or dark hypopyon. An eye with Klebsiella or Group B Streptococcus endogenous

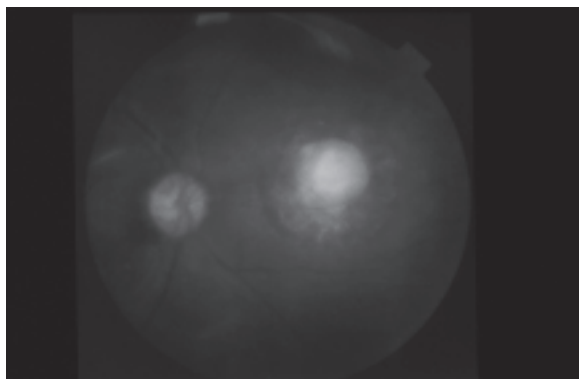


Fig. 1. Posterior pole choroidal abscess in a patient with *Staphylococcus aureus* endogenous endophthalmitis. There is little vitritis in this particular case.

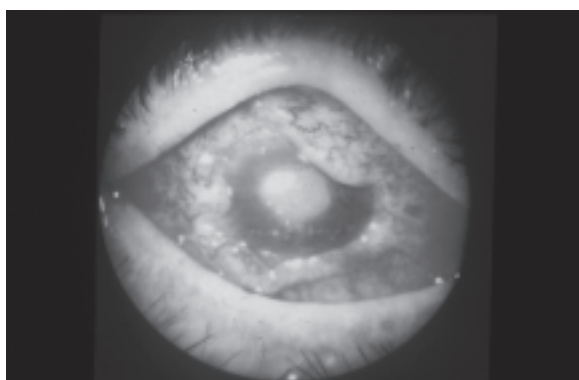


Fig. 2. Severe chemosis associated with Klebsiella endogenous endophthalmitis.



Fig. 3. Left panophthalmitis due to Klebsiella. There is marked lid oedema associated with the orbital inflammation.

endophthalmitis often has a pupillary hypopyon (Fig. 5).¹⁹ The hypopyon associated with Group B Streptococcus often does not organise and shifts to occupy the most dependent portion of the anterior chamber. This has been termed a “sliding hypopyon”.

Fungal Endogenous Endophthalmitis

A characteristic sign of endogenous *Candida* endophthalmitis is a creamy, white, well-circumscribed

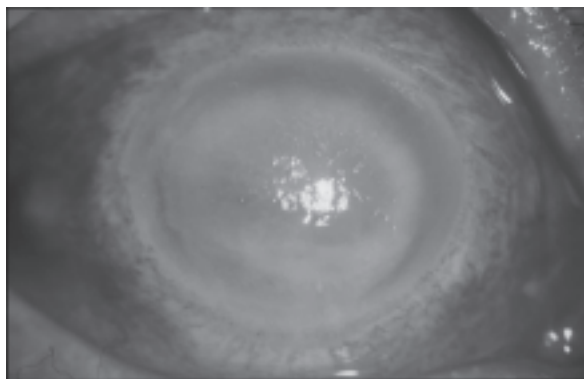


Fig. 4. Ring infiltrate in a patient with endogenous endophthalmitis after percutaneous transluminal coronary angioplasty. No organism was cultured from this eye, which eventually underwent enucleation.

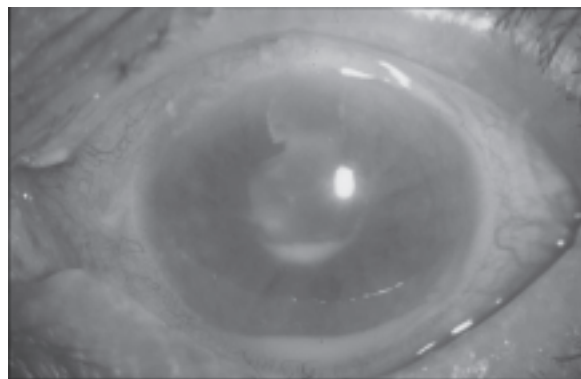


Fig. 5. Pupillary hypopyon in a patient with Group B streptococcus endogenous endophthalmitis. Note the suppurative anterior chamber exudate forming a level in the inferior anterior chamber angle as well as at the inferior margin of the pupil.



Fig. 6. B-scan ultrasound of the same eye as in Figure 2. There are multiple echogenic areas in the pre-retinal space consistent with vitreous debris. Superiorly, there is an exudative retinal detachment which was not visible on funduscopy.

lesion, involving the retina and choroid in the posterior pole. If multiple, these lesions may occur in a satellite pattern similar to that seen in fungal keratitis. Intraretinal haemorrhage may surround the white patches, giving the appearance of a Roth spot. Vitreous opacities may be connected by strands, producing a “string of pearls” appearance. More general features of anterior segment inflammation may be present including raised intraocular pressure and mutton-fat keratic precipitates.

Aspergillus endogenous endophthalmitis, although less common, is frequently a more fulminant disease.¹⁵ Nearly all patients have anterior chamber cells and keratic precipitates. The inflammation may result in a hypopyon, pupillary membrane, rubeosis iridis, and an anterior chamber inflammatory mass. Posteriorly, chorioretinitis may appear as fluffy yellow-white elevated chorioretinal opacities. Gravitational layering of inflammatory cells may produce a subhyaloid or subretinal “hypopyon”, especially since subretinal and subretinal pigment epithelial infection tends to occur

with *Aspergillus*.²¹ Retinal detachment may complicate the infection. Retinal haemorrhages and perivasculitis may be present. Ultimately, full thickness retinal necrosis may occur.

Protozoal Endogenous Endophthalmitis

These cases can range from those with a fairly indolent course to others with an abrupt onset of ocular inflammation. The latter may suggest co-infection with bacteria. In a recent HIV positive case caused by *Acanthamoeba*, there was the gradual increase of anterior chamber inflammation from a mild anterior chamber reaction to a severe granulomatous anterior uveitis with mutton-fat keratic precipitates over 2 weeks.⁹ At vitrectomy, peripheral choroidal granulomatous inflammation was found. Other posterior segment signs include white retinal lesions around the optic disc.⁵

INVESTIGATIONS

If the fundal view is obscured, imaging with B-scan ultrasonography is useful in displaying the extent of vitreous involvement, choroidal abscesses, retinal detachment and scleral thickening (Fig. 6). Computed tomography (CT) scans allow high resolution orbital imaging in cases of suspected panophthalmitis to detect abscess formation or confirm the presence of contiguous orbital involvement.¹⁹

As in all infectious diseases, microbiological tests aimed at identifying the causative organism(s) are crucial. Blood (72%), urine (28%), and cerebrospinal fluid (CSF) (50%) specimens for culture allow early and reliable identification of microorganisms in at least 80% of cases of bacterial endogenous endophthalmitis.^{1,3} Blood and urine specimens should

be obtained immediately before initiation of antibiotic therapy and sent for culture. CSF specimens should also be obtained unless meningitis can be excluded.

Organisms are cultured from ocular fluid in 36 to 73% of cases.¹⁻³ In many cases, prior treatment for systemic infection with intravenous antibiotics had already been instituted and this would reduce the culture positive rate from ocular fluids. A second factor resulting in a negative culture is sampling from an inappropriate compartment within the eye. Both aqueous and vitreous cultures should be obtained unless the organism has been identified from a non-ocular source. Beyond an initial diagnostic aqueous and vitreous tap, a pars plana vitrectomy can provide additional material for culture. The following nutrient media should be inoculated: blood agar, chocolate agar, brain-heart infusion broth/agar, thioglycollate broth and Sabouraud agar. A specimen sent for Gram stain may allow provisional categorisation of the organism. Polymerase chain reaction may allow rapid identification of organisms with very high sensitivity, but specificity may be a problem and facilities for this test are not widely available.²²

In comparison with bacterial endogenous endophthalmitis, those cases caused by fungi rarely have a positive blood culture. However, vitreous cultures will often reveal the offending organisms in these cases.²³ Systemic fungaemia was either transient or not recognised prior to the eye infection. On the other hand, screening of several series of patients with candidaemia did not reveal any cases of endophthalmitis.^{24,25} The benefit of screening lucid, asymptomatic patients thus remains doubtful at this point in time.

Amoebic endogenous endophthalmitis has only rarely been reported in the literature. These organisms can be difficult to identify, as they will not grow on routine microbiological media. Although they may be visible on Gram-stain, special stains such as calcofluor white will definitively reveal the organisms. Specimens sent for cytology and stained with haematoxylin and eosin will also show the trophozoites.⁵

Apart from microbiological investigation, other tests may be required according to the clinical picture if the original source of infection has not already been identified. These would include chest radiographs, echocardiography and ultrasonography or CT scan of the abdomen. If no obvious source of sepsis is suggested on careful clinical examination, a Gallium-67 scan may help to reveal foci of inflammation.²⁶ HIV testing should be considered for cases involving seemingly healthy individuals, especially if they also involve opportunistic pathogens.

MANAGEMENT

Medical

Systemic Therapy

Prompt institution of intensive intravenous antibiotics is critical in endogenous endophthalmitis. This not only treats the remote focus of infection and sepsis, but also the ocular disease. Prolonged intravenous therapy is usually required for 2 to 4 weeks, until it is certain that the systemic infection has been eradicated.

Before culture results are known, initial therapy should be with broad-spectrum antibiotics at the highest recommended dosage. For Gram-positive cover, intravenous vancomycin is warranted in view of the potential severity of the disease and consequences. Good Gram-negative coverage is provided by third-generation cephalosporins, ciprofloxacin and aminoglycosides. Although intravenous antibiotics can reach therapeutic concentrations in affected eyes, the use of systemic antibiotics that have good intraocular penetration and bioavailability is preferred. In particular, it should be borne in mind that aminoglycosides do not have good intraocular bioavailability when given intravenously.

In specific situations, certain antibiotics would be preferred. For example, the high incidence of *Bacillus* infection among intravenous drug abusers mandates the initial use of either vancomycin or clindamycin. On the other hand, cutaneous infections often involve *Staphylococcus aureus*, and cloxacillin or a first-generation cephalosporin antibiotic would be recommended. Subsequent therapy can be tailored according to sensitivity results and response to treatment.

In cases of fungal sepsis and endophthalmitis, amphotericin B provides good efficacy and broad coverage. However, side effects are significant and include hepato- and nephrotoxicity. The azole antibiotics are less toxic and have better ocular penetration. Specifically, fluconazole alone may be sufficient in early *Candida* endophthalmitis and itraconazole is useful in *Aspergillus* and *Fusarium* infections. Fluconazole has also been found to be effective against amoebic endophthalmitis.⁵

Intravitreal Therapy

Although the value of intravitreal antibiotics over and above the use of intravenous antibiotics has not been definitively established, most cases in our experience are of posterior diffuse disease and panophthalmitis which denote severe infection with extension of

Table 4. Visual outcome of bacterial endogenous endophthalmitis.

	Count fingers or better	Hand movements or worse	Enucleated/eviscerated
	No. of eyes (percentage)		
Singapore hospitals 1994–1997 ²	10 (33)	22 (27)	2 (6)
Literature review 1986–1998 ²	80 (34)	154 (66)	41 (16)

organisms into the vitreous. These cases should be treated as aggressively as possible with both systemic and intravitreal antibiotics.

In cases caused by bacteria, intravitreal injection of vancomycin 1mg/0.1ml and ceftazidime 2mg/0.1ml provides good coverage and avoids the toxicity associated with aminoglycosides. Repeated injections may be required since the half-life of these drugs in the vitreous cavity is short.

In most cases of fungal endophthalmitis, an intravitreal injection of 5 to 10µg amphotericin B is recommended. Using amphotericin in this manner avoids its numerous systemic side effects, but its potential for retinal toxicity should be noted. In the one case of amoebic endophthalmitis in an immunocompetent host, vitrectomy with an infusion solution containing 0.1mg/ml gentamicin, together with 0.2% fluconazole and systemic fluconazole, appeared sufficient to counter the amoebic component of the disease.⁵

Topical antibiotics are definitively indicated if keratitis develops and adjunctive therapy includes the use of cycloplegics, ocular hypotensives and topical steroids.

The use of intravitreal and systemic steroids in the management of endophthalmitis remains controversial, with systemic steroids being contraindicated in patients with inadequately controlled sepsis. Intravitreal steroids are usually avoided in the early management of endogenous endophthalmitis, especially in the presence of large choroidal abscesses in which the infection may not be adequately and rapidly controlled by intravenous or intravitreal antibiotics. The use of intravitreal or systemic steroids is contraindicated when a fungal cause of the endophthalmitis is suspected or confirmed.

Surgical

The timing of and necessity for vitrectomy remains unclear in endogenous as compared with post-operative endophthalmitis. Vitrectomy can remove opacities, debris and microorganisms in the vitreous with good efficacy, simultaneously allowing irrigation

of the vitreous cavity with antibiotics and treatment of complications such as retinal detachment. Several important factors arise when considering surgery. Vitrectomy will be more useful in posterior diffuse disease and should be considered especially if such cases appear to be progressing despite adequate medical therapy. In cases of fungal endophthalmitis, vitrectomy provides a good specimen for microbiology and effectively reduces the number of organisms. It is also crucial to consider the overall status of these individuals, many of whom will be desperately ill from systemic sepsis. In some cases, these patients may pose too great an anaesthetic risk for surgery. In others, the patient may be moribund and near death.

PROGNOSTIC FACTORS AND OUTCOMES

Despite aggressive antimicrobial therapy, most patients with endogenous endophthalmitis have an extremely poor outcome. In a recent study surveying cases in Singapore over a 4-year period, 17 of 32 affected eyes ended up with no light perception.² The virulence factor of the organism and age of the patient were important factors predicting outcome. Other variables resulting in poorer outcome include severity of underlying systemic illness, misdiagnosis or delay in diagnosis, and inappropriate, inadequate or delayed treatment.

In general, Gram-positive infections involving microbes such as *Staphylococcus* and *Streptococcus* species result in a better outcome. However, *Bacillus* infections are typically rapidly progressive with a poorer prognosis. Gram-negative organisms, including *K pneumoniae*, *E coli* and *P aeruginosa*, often result in severe infection and a very poor prognosis. Exceptions include *Haemophilus* and *Neisseria*, but these are uncommon causes of endophthalmitis in our population. Fungal endogenous endophthalmitis usually results in very poor outcomes, but those caused by *Candida* species can often be treated effectively if early and appropriate antifungals are used. Table 4 details the visual outcomes in cases of bacterial endogenous endophthalmitis.

CONCLUSION

Endogenous endophthalmitis continues to occur among our patients despite the continuing development of effective antibiotics. In our local context, the most common source of infection was a liver abscess and the organism most often implicated was *K pneumoniae*.

Although it is devastating, vision can sometimes be salvaged, especially if diagnosis was made early and prompt systemic therapy instituted. The role of intravitreal antibiotics and vitrectomy is still not well defined but they have a definite role in cases which progress despite medical therapy and also where fungi have been implicated. Future challenges ahead include our ageing population with more people developing chronic systemic illnesses and the development of new microbial antibiotic resistances. A coordinated multidisciplinary effort will be required to keep abreast of this difficult condition.

REFERENCES

- Okada AA, Johnson RP, Liles WC, D'Amio DJ, Baker AS. Endogenous bacterial endophthalmitis: report of a ten-year prospective study. *Ophthalmology* 1994; 101:832-8.
- Wong JS, Chan TK, Lee HM, Chee SP. Endogenous bacterial endophthalmitis: an east Asian experience and a reappraisal of a severe ocular affliction. *Ophthalmology* 2000; 107:1483-91.
- Greenwald MJ, Wohl LG, Sell CH. Metastatic bacterial endophthalmitis: a contemporary reappraisal. *Surv Ophthalmol* 1986; 31:81-101.
- May DR, Peyman GA, Raichand M, Friedman E. Metastatic Peptostreptococcus intermedius endophthalmitis after a dental procedure. *Am J Ophthalmol* 1978; 85:662-5.
- Matsuo T, Notohara K, Shiraga F, Yumiyama S. Endogenous amoebic endophthalmitis. *Arch Ophthalmol* 2001; 119:125-8.
- Gupta A, Gupta V, Dogra MR, Chakrabarti A, Ray P, Ram J, et al. Fungal endophthalmitis after a single intravenous administration of presumably contaminated dextrose infusion fluid. *Retina* 2000; 20:262-8.
- Han DP, Simons KB, Tarkanian CN, Moretti ST. Endophthalmitis from *Mycobacterium bovis*-bacille Calmette-Guerin after intravesicular bacilli Calmette-Guerin injections for bladder carcinoma. *Am J Ophthalmol* 1999; 128:648-50.
- Jain ML, Garg AK. Metastatic endophthalmitis in a patient with major burns: a rare complication. *Burns* 1995; 21:72-3.
- Heffler KF, Eckhardt TJ, Reboli AC, Stieritz D. Acanthamoeba endophthalmitis in acquired immunodeficiency syndrome. *Am J Ophthalmol* 1996; 122:584-6.
- Chee SP, Ang CL. Endogenous *Klebsiella* endophthalmitis—a case series. *Ann Acad Med Singapore* 1995; 24:473-8.
- Lee SY, Chee SP. Group B *Streptococcus* endogenous endophthalmitis: case reports and review of the literature. *Ophthalmology* 2002; 109:1879-86.
- Smith JR, Chee SP. Endogenous *Aspergillus* endophthalmitis occurring in a child with normal immune function. *Eye* 2000; 14:670-1.
- Brod RD, Flynn HW Jr. Endophthalmitis: current approaches to diagnosis and therapy. *Curr Opin Infect Dis* 1993; 6:628-37.
- Brod RD, Flynn HW Jr, Clarkson JG, Pflufelder SC, Culbertson WW, Miller D. Endogenous *Candida* endophthalmitis: management without intravenous amphotericin B. *Ophthalmology* 1990; 97:666-74.
- Weishaar PD, Flynn HW Jr, Murray TG, Davis JL, Barr CC, Gross JG, et al. Endogenous *Aspergillus* endophthalmitis: clinical features and treatment outcomes. *Ophthalmology* 1998; 105:57-65.
- Samiy N, D'Amico DJ. Endogenous fungal endophthalmitis. *Int Ophthalmol Clin* 1996; 36:147-62.
- Louie T, el Baba F, Shulman M, Jimenez-Lucho V. Endogenous endophthalmitis due to *Fusarium*: case report and review. *Clin Infect Dis* 1994; 18:585-8.
- Banerjee SN, Emori TG, Culver DH, Gaynes RP, Jarvis WR, Horan T, et al. Secular trends in nosocomial primary bloodstream infections in the United States, 1980-1989. National Nosocomial Infections Surveillance System. *Am J Med* 1991; 91:86S-89S.
- Chee SP, Jap A. Endogenous endophthalmitis. *Current Opinion in Ophthalmology* 2001; 12:464-70.
- Liew GC, Khoo BK, Yap EY. Bilateral central retinal artery occlusion as a complication of bilateral *Klebsiella* endogenous endophthalmitis. *Retina* 2000; 20: 682-4.
- Rao NA, Hidayat A. A comparative clinicopathologic study of endogenous mycotic endophthalmitis: variations in clinical and histopathologic changes in *Candidiasis* compared to *aspergillosis*. *Trans Am Ophthalmol Soc* 2000; 98:183-93.
- Lohmann CP, Heeb M, Linde HJ, Gabel VP, Reischl U. Diagnosis of infectious endophthalmitis after cataract surgery by polymerase chain reaction. *J Cataract Refract Surg* 1998; 24:821-6.
- Essman TF, Flynn HW Jr, Smiddy WE, Brod RD, Murray TG, Davis JL, et al. Treatment outcomes in a 10-year study of endogenous fungal endophthalmitis. *Ophthalmic Surg Lasers* 1997; 28:185-94.
- Donahue SP, Greven CM, Zuravleff JJ, Eller AW, Nguyen MH, Peacock JE Jr, et al. Intraocular candidiasis in patients with candidaemia: clinical implications derived from a prospective multicenter study. *Ophthalmology* 1994; 101:1302-9.
- Krishna R, Amuh D, Lowder CY, Gordon SM, Adal KA, Hall G. Should all patients with candidaemia have an ophthalmic examination to rule out ocular candidiasis? *Eye* 2000; 14:30-4.
- Kao PF, Tzen KY, Tsai MF, Yang KJ. Gallium-67 scanning in endogenous *Klebsiella* endophthalmitis with unknown primary focus. *Scand J Infect Dis* 2000; 32:326-8.