MANAGEMENT OF RETINAL DETACHMENT ASSOCIATED WITH CMV RETINITIS IN AIDS PATIENTS

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SUMMARY

In patients with AIDS, the most important ocular opportunistic infection, CMV retinitis, can now be treated effectively with virostatic agents. Associated retinal detachment is encountered frequently, and its management has become increasingly significant to quality of life as improvements in medical care have helped to preserve vision and extend life expectancy. Although retinal detachment in these eyes is typically rhegmatogenous, the pathophysiology is distinctive due to the association with CMV retinitis which, even in remission, is characterised by atrophic changes at all levels of affected retina and alterations of the vitreous. Despite initially successful surgical reattachment, multiple, small, often posterior holes may develop because of progressive CMV infection. For these reasons, vitrectomy and silicone oil injection with scleral buckling may currently provide the best overall means of maintaining retinal reattachment and restoring visual function. Nevertheless, management must be individualised in each case, with the realisation that progressive visual loss frequently ensues from retinitis progression.

During this first decade of the AIDS epidemic, cytomegalovirus (CMV) retinitis has become broadly recognised as the most important cause of visual loss in patients with HIV infection.[1-5] With the development of antiviral agents ganciclovir, foscarnet and other pharmacologic and medical advances, means are now available for arresting active CMV retinitis in the majority of individuals.[5-10] Over the same period, it has also become clear that rhegmatogenous retinal detachment complicates CMV retinitis in a significant number of eyes.[11-14] It is well recognised that these detachments are causally related to small, often difficult to detect holes, usually at the border between atrophic, regressed CMV infection and unaffected retina, and may be precipitated by vitreous traction (Figs. 1, 2).

As with the other evolving statistics about AIDS and opportunistic infections such as CMV retinitis, previously published series probably underestimate the current situation. Jabs, *et al.*, have recently suggested that the probability of retinal detachment may now be 50%, one year following the diagnosis of CMV retinitis.[14] This trend reflects a number of factors including earlier diagnosis of CMV retinitis, better preservation of vision with improvements in care and antiviral agents, and ultimately prolonged patient survival. Less well understood factors may include changes in the systemic patterns of disease or in host susceptibility.

In this paper, aspects of management of retinal detachment related to CMV retinitis are discussed, including manifestations, care options, indications for treatment, and surgical and visual results based upon experience and data accumulated at a major university teaching hospital and referral centre.

PATIENTS AND METHODS

From a review of medical records and photographic files available at the Bascom Palmer Eye Institute, 143 patients

Fig. 1. *Typical active CMV retinitis with retinal detachment, showing the border region between CMV-affected and unaffected retina. Generalised thinning and small atrophic holes exist in this region.*

Fig. 2. *Superior retinal detachment in the presence of regressed CMV activity, confined to the nasal retina, Onset of detachment was associated with posterior vitreous detachment. Note vitreous organisation over atrophic nasal mid-periphery.*

with AIDS were identified between June, 1984 and June, 1991, in whom a diagnosis of CMV retinitis was made. CMV retinitis was the AIDS-defining illness in at least 12 patients. Evidence of typical CMV retinitis had been confirmed by examination, fundus photographs, clinical follow-up and response to anti-CMV therapy in all but 16 of these patients. The latter had not returned for examination after the initial diagnosis of CMV retinitis. All patients underwent complete ophthalmologic examination, including best refracted visual acuity and serial dilated fundus examinations with photography whenever possible.

In 30 eyes of 25 patients with documented CMV retinitis, a diagnosis of retinal detachment was made within a clinical scenario considered appropriate for surgical repair. Of the 25 patients, only five did not have bilateral CMV retinitis at the time retinal detachment was diagnosed. Six patients, all with bilateral retinitis, presented with bilateral retinal detachment. Of the remaining 14 initially with unilateral detachment, three subsequently developed retinal detachment in the second eye as well, during the period of review. Thus, bilateral retinal detachment developed within the period of review in nine of 20 patients with bilateral CMV retinitis. All have been diagnosed and cared for since December, 1988.

Features favouring repair included recently documented good visual function, the lack of active or past CMV infection in the posterior pole, and in general, willingness and demonstrated ability of the patient to continue intravenous anti-CMV therapy. In the few in which surgery was not advised, the most frequent factors were severe loss of vision due to prior CMV retinitis and/or extremely poor systemic health. Overt retinal breaks were not observed in all eyes, such that care was taken to exclude exudative detachment in these cases. Two fellow eyes to those included in this series were observed with stable peripheral detachment throughout the patients lifetime. In 22 of the 25 patients, the retinitis had been documented to have responded to antiviral therapy prior to the development of retinal detachment. Intravenous ganciclo-

vir (Cytovene®) had been used in all of these patients except one, who was treated initially with foscarnet (Foscavir®). One patient underwent surgery while receiving intravenous induction therapy with ganciclovir before clinical regression of active CMV retinitis, having been diagnosed to have rhegmatogenous retinal detachment simultaneous with the diagnosis of CMV retinitis. Because of severe neutropenia and difficulty maintaining intravenous access, another patient received bilateral intravitreal ganciclovir (200 micrograms) following the diagnosis of bilateral active CMV retinitis with retinal detachment. One further patient with indolent, untreated pre-equatorial CMV retinitis and macula-off inferior detachment was operated on with plans to start anti-CMV therapy when retinitis progression became sight-threatening.

No eyes included in this study had atypical CMV retinitis or was suspected of infection with multiple agents. Known central nervous system, neuro-ophthalmic or other significant past ocular diseases were not present. Eyes in which intravitreal injection of ganciclovir had been performed prior to the development of retinal detachment (1) were excluded from review. Patients were not included if there was insufficient post-operative follow-up (minimum two visits).

Surgical Procedures

Retinal reattachment procedures were carried out (Table I) as was considered appropriate, following careful counselling, based upon individual findings and guided by the principles discussed below. Further procedures were considered in the presence of incomplete or failed reattachment, and were undertaken only when the patient's overall status, both mental and physical, and potential for benefit were felt to be favourable.

Procedures were performed under local anaesthesia with intravenous sedation, usually on a one-day stay basis. Vitrectomy and silicone oil injection was performed utilising standard 3-port pars plana vitrectomy techniques, with simple encirclement with a solid silicone band (#41 or #42) employed with greatest regularity when scleral buckling was included. A wider exoplant (#276 tyre or

Table I Surgical Procedures and Final Status

® Eyes	PPV/SB/SO	PPV/SO	SB	PR	Other
Initial	16	5	4	2	1 laser
					1 PPV/MS
Further surgical					1 PPV/GFX/E
procedures	0	3	0	1	3
FINAL					
STATUS	21	5	3	1	

Initial surgical procedures, additional surgery performed and Final Status of 30 eyes of 25 AIDS patients with retinal detachment associated with CMV retinitis. Final Surgical Status was defined as the combination of all surgical procedures performed. Abbreviations used:

PPV   pars plana vitrectomy
SB   scleral buckling
SO   silicone oil injection
PR   pneumatic retinopexy
MS   membrane dissection
GFX   gas-fluid exchange
E   endolaser

silicone sponge) was used in instances in which a large, inferior peripheral break was recognised. Membrane peeling techniques were applied with caution due to the atrophic nature of adjacent and underlying retinal tissues. Whenever possible, the drainage retinotomy was created nasally above the horizontal, within or adjacent to a region previously affected by retinitis.

Certain steps were undertaken with respect to features distinctive to the patient population. Of note, a disposable infusion cannula and disposable endodrainage needle were used, both of which were discarded at the end of the procedure. Silicone oil (1000 or 5000 cS) was injected following complete air-fluid exchange, and all eyes were left phakic. Preplaced sutures were utilised to facilitate rapid closure of the sclerotomies, in order to reduce loss of silicone oil from the vitreous cavity. Cryotherapy was not used, and endolaser, employed infrequently, was used when true peripheral retinal breaks of significant size could be identified. Silicone oil tamponade was relied upon to provide permanent closure of the endodrainage retinotomy and as the primary modality for atrophic holes due to CMV retinitis itself.

Pneumatic retinopexy was performed according to previous published techniques,[15] utilising approximately 0.25 cc filtered 100% C_3F_8 (perfluoropropane), with laser photocoagulation applied four days after gas injection. In addition to the above, extracapsular cataract extraction with posterior chamber intraocular lens implantation was performed at a later date in selected cases, based upon visual potential and other parameters as outlined above.

Laser photocoagulation demarcation of an inferior detachment was attempted initially in one individual who presented with bilateral retinal detachments. In one patient, a CMV retinitis-associated macular pucker had been removed with vitrectomy and membrane peeling four months prior to the development of retinal detachment. In another, localised retinal detachment developed five months after diagnosis of CMV retinitis and initiation of ganciclovir treatment (related to a tear distant from the CMV retinitis), and was repaired with vitrectomy, air-fluid exchange and endolaser three months prior to retinal detachment adjacent to CMV retinitis.

RESULTS

In this series, the period of observation prior to surgery ranged between one day and nine weeks following diagnosis of retinal detachment, with post-operative follow-up sought to the time of death in all such individuals. This resulted in a mean 4.3 months follow-up (range two weeks—15 months) after surgery, excluding six patients living, with post-operative review in this group ranging between six weeks and 10 months.

The relationship of retinal detachment to CMV retinitis was typical in all cases (Fig. 1). In most cases, small atrophic holes were distributed along the border region between affected and normal retina, at varying distances from the posterior pole. Overt retinal tears were noted infrequently. In all patients in whom this could be determined reliably by initial examination and/or documented records (11 of 25 patients), retinal detachment developed (first or solely) in the eye first affected by CMV retinitis. In those who had been examined prior to retinal detachment, new vitreous detachment was frequently evident clinically around the time of retinal detachment. Intraoperatively, partial posterior vitreous detachment associated with a prominent posterior hyaloid face was confirmed in the majority of eyes, with a uniform observation being that of early degeneration or liquefaction of the vitreous.

The initial surgical procedures performed on these eyes, and subsequent re-operations are shown in Table I. Final surgical status was defined as the combination of all surgical procedures performed, perhaps sequentially. The number of procedures performed on individual eyes was low, with one re-operation in four cases, and three re-operations on one eye. Side effects and complications were observed infrequently intra- and post-operatively, which was well tolerated and accompanied by apparently normal healing. Limited retinal and preretinal haemorrhage was associated with the removal of transvitreal and epiretinal membranes, and mild posterior capsular lens 'feathering' was noted at the end of the procedure. No persistent elevation of intra-ocular pressure developed in any of the eyes. Silicone oil was not removed from any of the eyes, and no complications were clearly related to its use other than progressive lens changes and acquired hyperopia. Macular pucker was recognised to affect visual function significantly in one eye.

In the post-operative period, periodic patient review including fundus photographs was sought in all patients. There appeared to be no effect attributable to surgery or silicone oil upon the clinical response of CMV retinitis to antiviral therapy. The presence of silicone oil itself did not interfere with monitoring of retinitis response, detection of recurrent CMV activity or photographic documentation. Similarly, nuclear and posterior subcapsular lens changes did not interfere with clinical care, though cataract was considered significant to vision in five eyes (4–9 months post-operatively). Extracapsular cataract extraction (ECCE) and posterior chamber IOL implantation was undertaken in three of these cases during the period of review.

To attempt to analyse the surgical results in a way relevant to patient function, these were subdivided into several categories (Table II). 'Total' was used to designate eyes with complete and long-term reattachment, throughout the period of review (Fig. 3). Degrees of 'subtotal' or partial reattachment were defined relative to restoration of and/or protection of macular function. That is, eyes were considered partially reattached if (a) there was recurrent inferior detachment, but stable reattachment of the macula, or if (b) a non-macular retinal detachment was never fully reattached, but the macula remained unaffected. A 'failed' procedure was one in which surgery did not change the natural course of progressive retinal detachment.

Table II Retinal Reattachment Results

® Eyes	PPV/SB/SO	PPV/SO	SB	PR
FINAL STATUS	21	5	3	1
Total reattachment	12(5)	(3)	–	1
Subtotal reattachment	2(1)	1	–	–
Failed	1	1	2(1)	–

Eyes from Table I in Final Status categories (as defined by previous surgical procedures: PPV = pars plana vitrectomy, SB = scleral buckling, SO = silicone oil injection, PR = pneumatic retinopexy) were assigned to retinal reattachment categories according to definitions below. Eyes in which the macula was not clinically detached pre-operatively are shown in parenthesis.

'Total'   No clinically detectable subretinal fluid
'Subtotal' Initial full reattachment followed by recurrent detachment sparing the macula, or never fully reattached with macula initially unaffected
'Failed'   Remains completely detached, or did not prevent progressive macular detachment

The impact of surgery upon visual function was assessed by comparing pre-operative vision to best post-operative vision (Fig. 4). For eyes with pre-operative macular detachment and adequate follow-up, best post-operative vision was attained at intervals ranging between two weeks and three months, mean 1.1 months. Final acuity (Fig. 5) as determined by death or loss of vision was recorded up to 15 months following surgery and was frequently much poorer due to progressive, 'smouldering' retinitis, diseases independent from CMV, and factors other than retinal detachment. Six patients remain alive at the time of submission of this manuscript, with post-operative follow-up in this group of six weeks to 10 months.

DISCUSSION

Histopathologically, in the presence of treated or untreated CMV infection, there is a necrotic retinitis which progresses from acute to chronic stages over months.[8] With time, virtually the entire thickness of the retina is replaced by atrophic remnants, with little in the way of recognis-able cytoarchitecture (Fig. 6). Posterior vitreous detachment frequently if not always exists in such eyes, at least in part, and degrees of proliferative vitreoretinopathy (PVR) are observed with regularity. Inflammatory factors have been identified within the vitreous[16] of eyes with infectious retinitis and potentially contribute additionally to subsequent pathophysiologic events. A further observation is that tight adherence to atrophic retinal remnants is created by apparent retinal pigment epithelial (RPE) metaplasia and hyperplasia. As vitreous traction is superimposed, it is not unanticipated that atrophic holes, microscopic or larger may develop, especially at or adjacent to points of traction, retinal atrophy and adhesion. Loss of any previous barrier effect to water movement[17] attributable to normal vitreous and retinal structure may also contribute to detachment.

Current data suggests a profile for eyes with CMV retinitis which are at highest risk to develop retinal detachment.[14] Greater rather than lesser extent of retinitis and involvement of the retinal periphery were definite hallmarks in our series. We regularly noted the presence of vitreous inflammation and organisation, with an association between posterior vitreous detachment and the development of retinal detachment. There are undoubtedly yet unrecognised host and other factors, as well as possible 'generic' determinants of risk for detachment (i.e., high myopia, family history, trauma, etc).

The development of retinal detachment and its repair revolve around the inherent characteristics of CMV retinitis, its progressive nature and the frequency with which multiple, microscopic or larger breaks develop, as well as other distinct pathological features. Because of the unpredictable course of both the systemic and ocular disease under consideration, all steps which may have a future impact upon visual function deserve consideration in each patient. With regard to management and in parallel with current management of peripheral CMV retinitis itself,
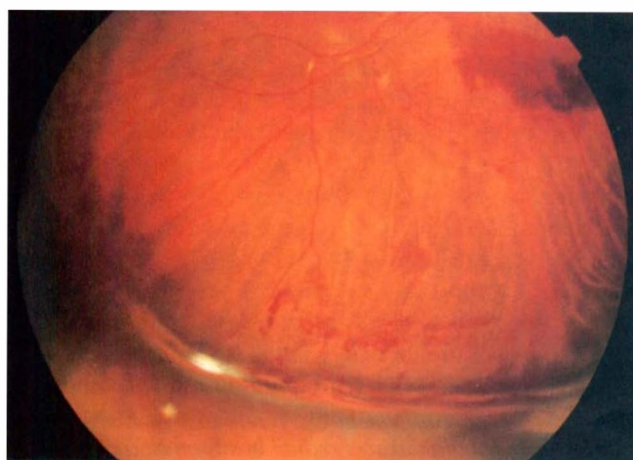

Fig. 3. Post-operative appearance of total reattachment eight weeks following pars plana vitrectomy, silicone oil injection and scleral buckling. Note the distinctive reflection along curvature of scleral buckle, indicating confluent silicone oil—retina contact.
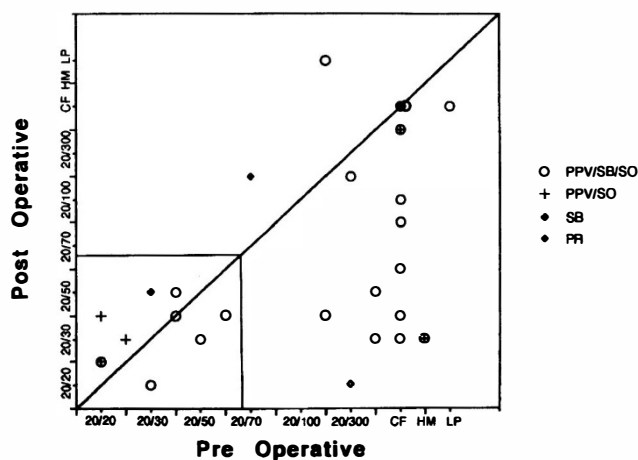
Best Post-operative Acuity

Fig. 4. Best post-operative visual acuity following retinal attachment procedures in comparison with pre-operative visual acuity. Final status categories are symbolised according to the key shown. Eyes in which the macula was not clinically detached pre-operatively are clustered within the box.
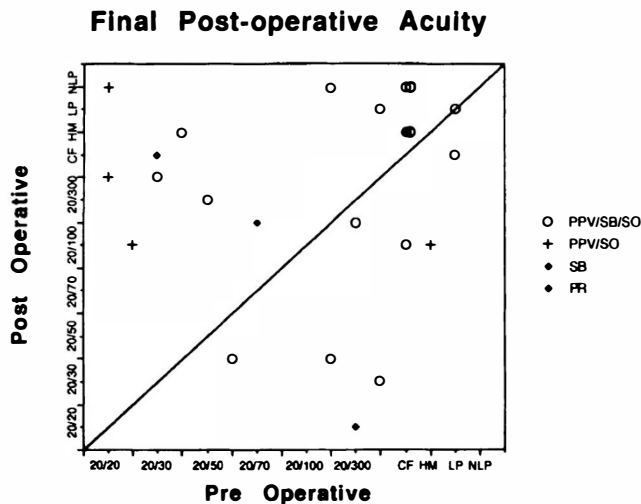
Final Post-operative Acuity

Fig. 5. *Final post-operative visual acuity following retinal attachment procedures in comparison with pre-operative visual acuity. Final status categories are symbolised according to the key shown.*

observation alone is altogether appropriate in selected cases. Procedures such as pneumatic retinopexy or simple scleral buckling may be successful in specific cases. Though the risk of recurrent detachment may be higher following such procedures, these modalities remain useful options in patient management. Regardless of the chosen procedure, visual function depends upon appropriate post-operative management of the underlying CMV infection through conscientious and standardised monitoring of fundus appearance[18] and effective communication with all those involved, physicians and otherwise.

In contrast to most cases of acute retinal necrosis (ARN) in which long-acting tamponade is not mandatory,[19,20] the nature of retinal detachment with CMV retinitis in AIDS patients may require permanent internal tamponade. Overall, as has been suggested by others,[11–14,20,21] the use of silicone oil appears to be the most ideal method for long-term reattachment in infectious retinitis cases of this sort. We feel that in those eyes in which scleral buckling was included, the decision was based less upon the desire to support a standard retinal break, but rather relates to the geometric characteristics of buckled *vs* unbuckled silicone-filled eyes, especially in the setting of HIV infection and CMV retinitis (Fig. 7). It would appear that scleral buckling provides more confluent or continuous silicone oil-retinal contact and therefore tamponade of retinal breaks. This is of importance in the setting of CMV retinitis, especially when located inferiorly, in the presence of incomplete filling of the vitreous cavity (seen as a refractile change at the interface between oil and aqueous). In our series, this may have contributed to the low number of recurrent detachments. When previous retinitis has not involved the inferior retina, such considerations may be of lesser importance. As an important corollary, however, the change in axial length induced by circumferential scleral buckling generally reduces the hyperopia induced by silicone oil in a phakic eye, which can produce considerable image dis-

parity and visual disability due to aniseikonia, in addition to possible effects on accommodation.[21] Our data tends to support this effect; although the small number of patients does not lend itself to statistical analysis, the average ani-
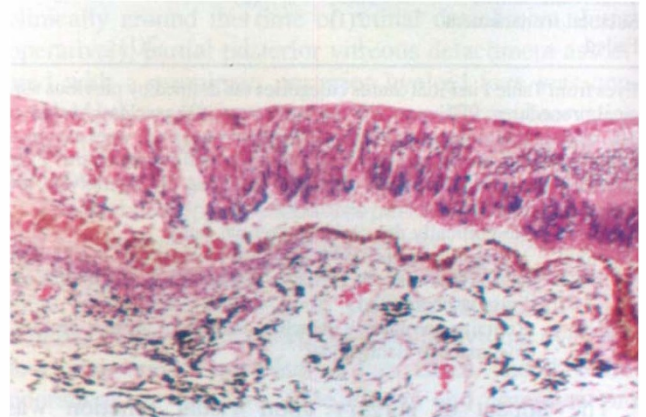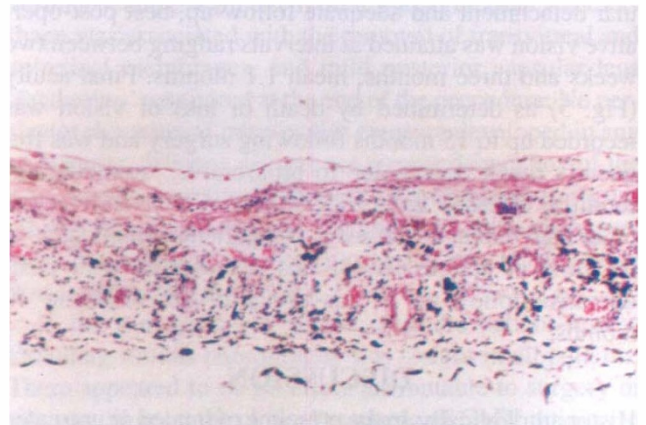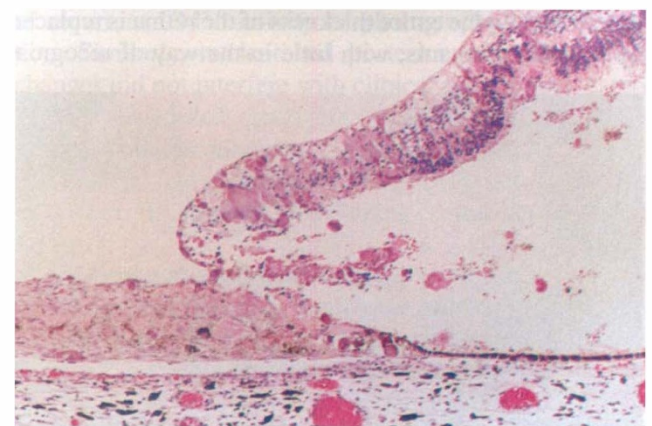

Fig. 6a.

Fig. 6b.

Fig 6c.

Fig. 6. *Histology of typical CMV retinitis: A. Active border showing acute, full thickness retinal involvement (left and midfield), including pigment epithelium and choroid (original magnification = 20×). B. Sequelae of CMV retinitis with destruction of all layers, disorganisation of the RPE, and atrophy of the choroid. (original magnification = 10×). C. Retinal detachment at the transition zone between past CMV retinitis and normal, unaffected retina (original magnification = 10×).*
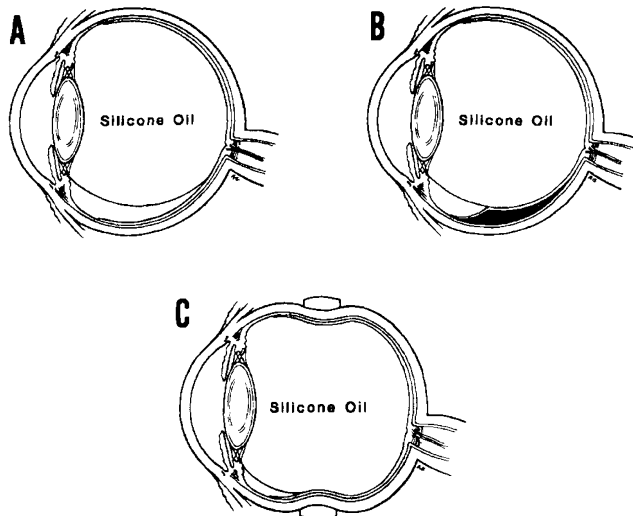
Fig. 7. *Diagrammatic representations of: A. Silicone oil-filled eye with 'subtotal' fill, but complete retinal reattachment beneath the silicone oil; B. Subtotal silicone oil fill may allow recurrent inferior retinal detachment with posterior holes; C. In the presence of a scleral buckle, inferior retina-silicone oil contact is more confluent, reducing likelihood of recurrent retinal detachment when fill is subtotal. Also note increased axial length of globe.*

sometropia at the time of best post-operative vision in eyes with silicone oil alone was +5.50 diopters (range +4.00 to +6.00), compared to +3.70 diopters (range +2.25 to +5.50) in those with silicone oil and an encircling scleral buckle.

In the decision-making process of offering repair of retinal detachment in the setting of AIDS and CMV retinitis, criteria and principles come into consideration which differ from usual circumstances. Most relevant among these are the risks to the patient for overall retention of visual function. As was the case in 12 patients in this series, CMV retinitis may be the AIDS-defining illness in patients otherwise generally healthy, as has previously been reported.[22] The improved outlook for long-term survival in these and other patients may modify our future therapeutic recommendations. In addition to considerations of systemic prognosis, there are those which pertain to ocular status. Of the 20 patients in this study with bilateral CMV retinitis at examination, six presented with bilateral retinal detachments, and three additional patients developed retinal detachment in the fellow eye during the period of review. Thus, almost half of the patients with bilateral retinitis in this series experienced bilateral retinal detachment. Over the same period, vision was lost due to CMV retinitis (three patients) or other complications of AIDS in the unoperated eye, such that the operated eye ultimately became the better eye in four of the 25 patients. With regard to preservation of visual function, it is therefore important to recognise the threat implied by bilateral CMV infection in terms of loss of vision due to retinitis as well as to detachment, when counselling patients. This may also come to importance in the decision of whether or not antiviral therapy should be started, if unilateral infection is diagnosed, since contralateral retinitis rarely if ever develops during anti-CMV therapy.[4]

Thus, the decision to undertake surgical repair having been considered carefully, the most consistently beneficial treatment in terms of anatomic reattachment has been pars plana vitrectomy with silicone oil injection, most frequently combined with scleral buckling. The use of cryotherapy or endolaser except in extraordinary circumstances has been avoided, and the ease of postoperative recuperation in our patients may be in part attributed to this. In the silicone oil setting, their use probably contributes more to inflammation and other morbidity than to strengthening retinal attachment. For those in whom cataract becomes the vision-limiting factor, cataract extraction with IOL implantation can be performed when appropriate.

In conclusion, we are destined to encounter a significant number of CMV-related retinal detachments. Care for these patients defies codification, but some considerations are notable. Given the bilateral nature of CMV retinitis and the gradual overall deterioration so common in these patients, therapy for the 'first eye' detachment may be tolerated better than at a later stage in the disease. Furthermore, a temporary period of improved visual function may be of relatively great value in this patient setting, such that published final visual results are difficult to interpret. An attempt to limit hospitalisation and surgical morbidity from the patient's standpoint is a further issue. Exposure of health care workers is also a realistic consideration, and steps should be taken to eliminate risk to future patients. This may apply in particular to surgical instruments which may trap blood products, such as those with connectors and attached tubing, in addition to routinely disposed items.

Despite surgical recommendations, unanswered questions remain in defining optimal care for eyes affected with CMV retinitis-associated detachment. For example, little is known about possible changes in drug delivery to ocular tissues or potential toxicity in silicone-filled eyes when the retinal vasculature and choroidal circulation are altered by CMV retinitis. Does CMV retinitis behave differently after vitrectomy and in the presence of silicone oil? Most relevant, to what practical degree is useful vision restored or maintained by virtue of these surgical and medical efforts? As further investigation is undertaken and therapeutic approaches are improved with regard to prophylaxis and treatment of CMV retinitis and possibly of associated retinal detachment, careful counselling and individualisation of care remain the best guidelines.

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