PERIPAPILLARY SUBRETINAL NEOVASCULAR MEMBRANES: THE NATURAL HISTORY

G. SILVESTRI, D. B. ARCHER and P. B. JOHNSTON
Belfast, Northern Ireland

SUMMARY

We studied the natural course of peripapillary subretinal neovascular membranes in 20 eyes. The membranes were either idiopathic in nature or associated with underlying disease. We found that the visual prognosis was related to the behaviour of the membrane and to the patient's age. Patients under the age of 40 years had unilateral disease and a more favourable visual prognosis. Older patients had a uniformly poor visual prognosis and a high incidence of bilateral disease. Fifty-four per cent of patients over 45 years and 62% over 70 years of age had bilateral membranes. In those over the age of 70 years, 75% of untreated eyes lost vision to a level of 3/60 or less in both eyes. The probability of the second eye becoming involved in the older group of patients was 62%. The period of time elapsing between involvement of the first and second eye varied between simultaneous occurrence and a delay of 7 years.

Peripapillary subretinal neovascular membranes (PPNVMs) account for less than 10% of subretinal membranes occurring at the posterior pole. They represent a variant of the more common central form of disciform detachment of the macula. These PPNVMs may be idiopathic or secondary to various conditions such as presumed ocular histoplasmosis syndrome,[1] myopia,[2] optic disc drusen,[3] trauma,[4] chorioretinitis,[5] uveitis[10] and age-related macular degeneration.[6]

The typical appearance of PPNVMs can vary from a discrete subretinal focus at the edge of the optic disc to a sizeable area of fibrovascular tissue and intraretinal exudation extending to involve much of the macula. The lesion typically extends from the disc margin in a 'tongue-like' fashion and can occur in any peripapillary location, but is commonly found close to the temporal aspect of the disc.[7] The natural course of untreated PPNVMs ranges from spontaneous involution and stabilisation to rampant growth towards the foveola.[7] The behaviour of these membranes and their rate of growth is very unpredictable.[3,7–10]

Due to the variable course of most peripapillary membranes there has been some reluctance to treat these membranes early, treatment usually being deferred until the fovea is under direct threat. The purpose of this study was to review the prognosis of patients with PPNVMs, from all causes, who had attended our unit over a 10-year period, with a view to establishing guidelines as to which patients might require treatment.

PATIENTS AND METHODS

The records of all patients with PPNVMs seen in our department between the years of 1980 and 1989 were reviewed. Fourteen patients had symptomatic PPNVMs on presentation. All patients had had a full ophthalmological examination and photographic and angiographic documentation of their membranes. The types of membranes are described in Table I. Eleven of 14 patients attended for review and were re-examined. A full history was taken and special note made of hypertension, smok-

Table I. Age, visual acuity, aetiology and cause of loss of vision in patients with peripapillary subretinal neovascular membranes

Age (yr)	Aetiology	Visual acuity R eye	Visual acuity L eye	Cause of visual loss
10	Toxoplasmosis	6/24[a]	6/6	SFM + fluid
27	Myopia	6/60[a,b]	6/6	HGE
29	Hypermetropic astigmatism	6/6[a]	6/6	HGE + fluid
30	Chorioretinitis	6/6[a]	6/5	HGE + fluid
46	Idiopathic	PL[a]	6/6	SFM
48	Idiopathic	6/60[a]	6/60[a]	SFM
61	Age-related	6/9	CF[a]	SFM + exudate
71	Age-related	6/9	6/60[a]	Exudate
73	Idiopathic	6/60[a]	3/60[a]	SFM + exudate
74	Idiopathic	6/9[a]	6/6	Fluid
78	Age-related	3/60[a]	CF[a]	Exudate
79	Age-related	CF[a]	3/60[a]	Exudate
82	Age-related	6/9[a]	6/60pt[a]	Exudate
82	Age-related	HM[a]	3/60[a]	SFM + exudate

PL, perception of light; CF, counting fingers; HM, hand movement; SFM, subfoveal membrane; HGE, haemorrhage.
[a]Affected eye; [b]amblyopic eye.

Correspondence to: Miss G. Silvestri, Department of Ophthalmology, Queen's University, The Eye and Ear Clinic, Royal Victoria Hospital, Belfast BT12 6BA, Northern Ireland.

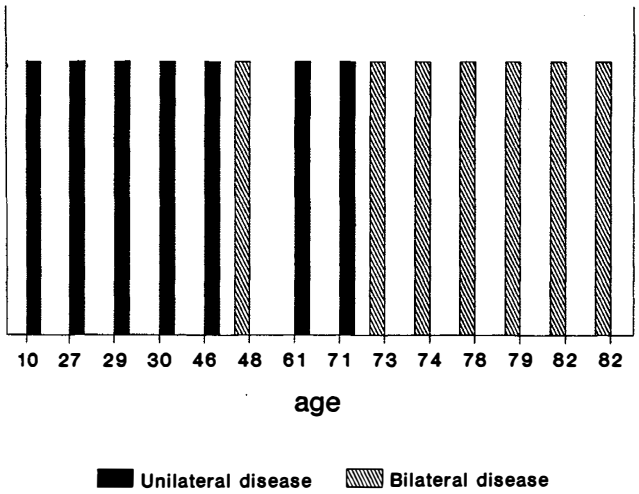

Fig. 1. *Incidence of bilateral disease versus age.*

ing and progression of visual complaints. A full ophthalmic examination of both eyes was carried out and a search made for any precipitating pathology.[1] Fluorescein angiography was carried out to elucidate the location, morphology and nature of the subretinal neovascular membranes.[2] Patients judged to have end-stage fibrovascular complexes did not have angiography.

RESULTS

Fourteen patients (20 eyes) were included in the study. Only 3 of the 20 eyes received laser photocoagulation. Patient ages ranged between 10 and 82 years and 78.2% of patients were female. All 4 patients under the age of 40 years (referred to below as the 'younger patients') were female. Five patients had hypertension. The follow-up time was between 9 months and 14 years with a mean of 24 months. We examined all patients or, if the patients were not available, the colour slides in our records in an effort to establish a cause for the membrane. The aetiology of the membranes was as follows (Table I). The 4 younger patients had membranes secondary to myopia, toxoplasma scarring and diffuse chorioretinitis. One patient had hypermetropic astigmatism. The significance of this is questionable. In patients over 40 years old 4 of 10 (40%) had idiopathic PPNVMs and 6 of 10 (60%) had membranes associated with age-related degenerative changes.

Visual Acuity

Although the numbers reported are small it seemed the younger patients suffered unilateral disease which could usually be attributed to associated pathology. Visual prognosis in this group was favourable. Two of 4 younger patients who had poor vision due to serous detachment of the retina have recovered 6/6 vision, 1 is stable at 6/60 in a previously amblyopic (6/60) eye and the fourth patient has a visual acuity of 6/24. Older patients typically had a poor visual outcome as shown in Table I. All eyes but one in those over the age of 40 years showed either direct progression of the membrane or deposition of lipid exudate subfoveally with resultant visual loss to a level of 6/60 to counting fingers (CF). The 1 patient aged 74 years with remaining good vision in the affected eye does, however, have a progressing membrane.

Bilaterality

Sixty per cent of the older group developed bilateral PPNVMs in the follow-up period. In 2 of these patients an early neovascular membrane was suspected in the fellow eye on initial presentation. None of the younger patients showed bilateral disease (Fig. 1).

Laser Treatment

Three patients were treated by laser photocoagulation. One of these was a 10-year-old diabetic. Treating this membrane was technically difficult because of the patient's young age and therefore poor compliance. The membrane was not completely ablated and there was continued growth. The other patients treated were 79 and 82 years old respectively. Treatment was carried out late in the disease process when the membrane was already encroaching on the fovea. Visual outcome was poor: 3/60 each eye.

Case 1

This 30-year-old woman presented with a history of blurring of vision in her right eye. She was noted to have a unilateral multi-focal choroiditis (Fig. 2a). Visual acuity at this time was 6/6 right, 6/5 left. The choroiditis was self-limiting and vision in the right eye settled at 6/5. Six weeks later she presented again with a further decrease in vision in the right eye. On examination visual acuity was 6/9 and she was noted to have a PPNVM (Fig. 2b) which was confirmed on angiography (Fig. 2c). Over a number of weeks the lesion progressed as shown in Fig. 2d and 2e and visual acuity dropped to hand movement. The presence of intraretinal haemorrhage was considered a contra-indication to laser treatment and therefore the lesion was left untreated. Over a period of 4 months the lesion regressed spontaneously and visual acuity has been stable at 6/9 for 2½ years (Fig. 2f, g).

Case 2

This 82-year-old woman presented with decreased vision in her left eye. Visual acuity on presentation was 6/12 due to a PPNVM with intraretinal exudation extending to the fovea (Fig. 3a, 3b). At the time of initial presentation a decision was made to follow the lesion closely. However, due to patient illness follow-up was not possible and on eventual review the visual acuity was found to be 3/60 due to subfoveolar extension of the membrane.

At this time argon green laser photocoagulation was carried out to stabilise vision. Following treatment left vision stabilised at 6/36–1. The right fundus was found to be clinically normal. Three months later the right fundus was found to have peripapillary exudation (Fig. 3c) and fluorescein angiography confirmed the presence of a right

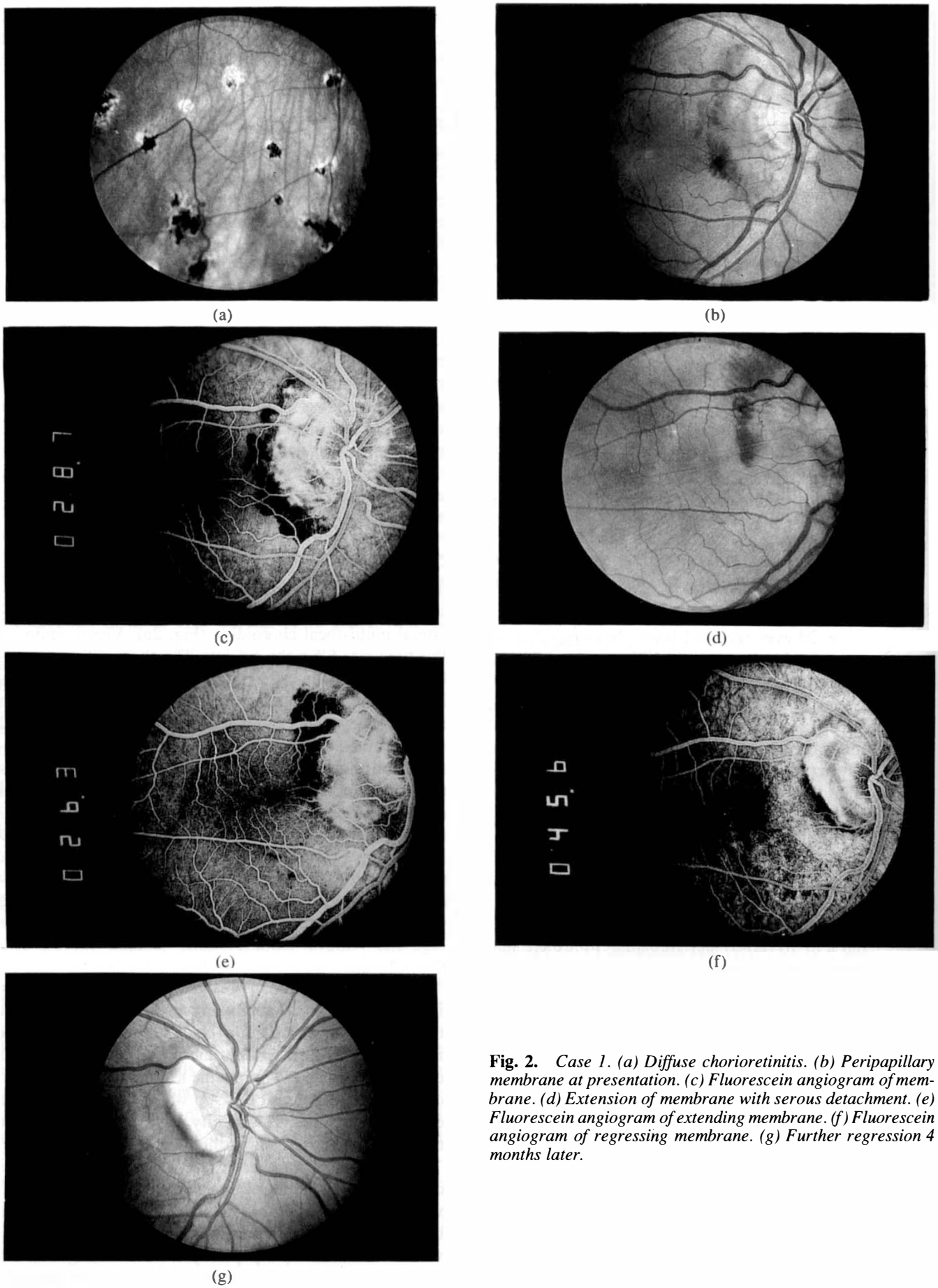

Fig. 2. *Case 1. (a) Diffuse chorioretinitis. (b) Peripapillary membrane at presentation. (c) Fluorescein angiogram of membrane. (d) Extension of membrane with serous detachment. (e) Fluorescein angiogram of extending membrane. (f) Fluorescein angiogram of regressing membrane. (g) Further regression 4 months later.*

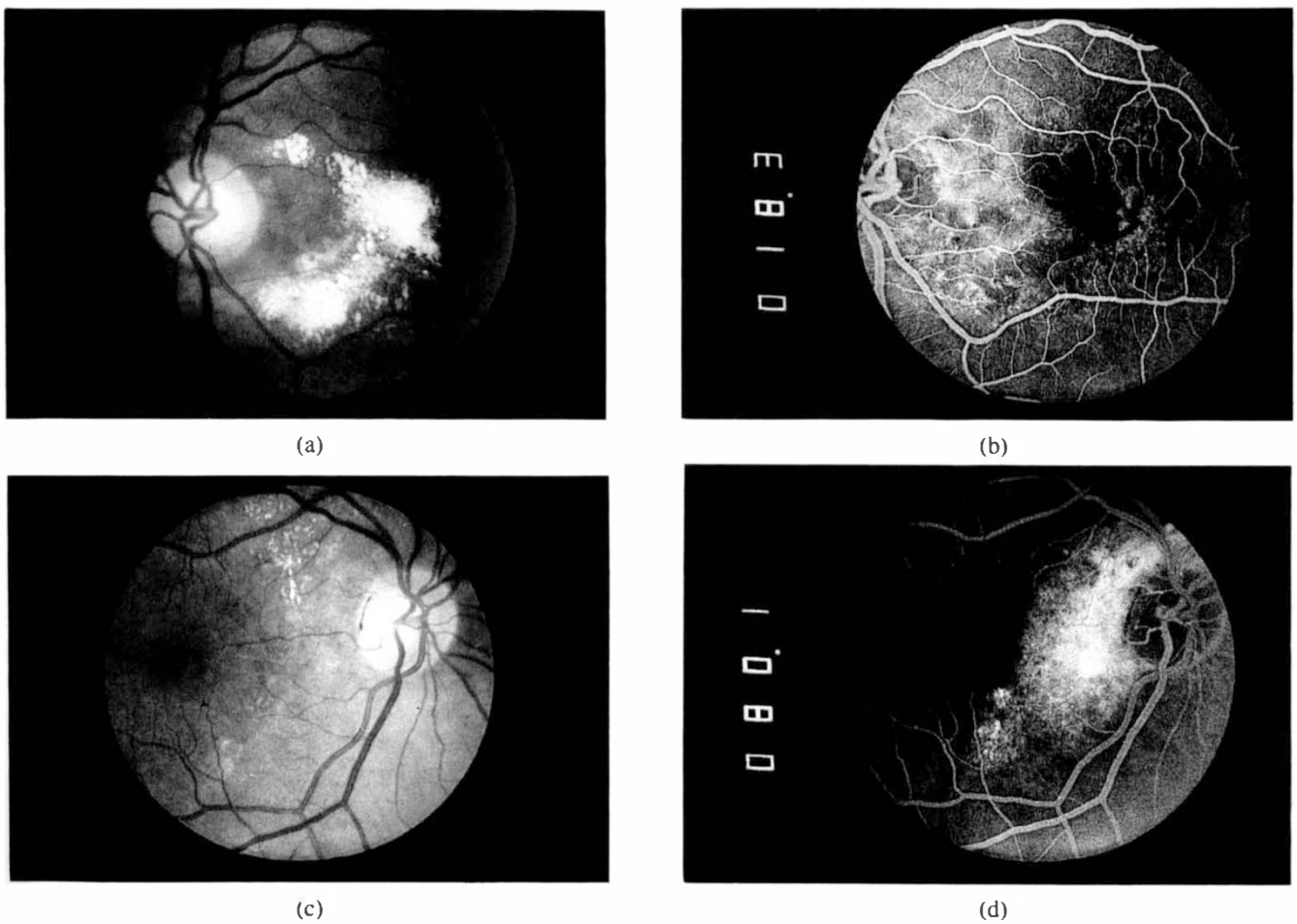

Fig. 3. *Case 2. (a) Peripapillary membrane at presentation. (b) Fluorescein angiogram. (c) Asymptomatic right fundus 4 months after treatment of the left eye. (d) Peripapillary membrane in right eye confirmed on fluorescein angiography.*

PPNVM (Fig. 3d). This was treated and vision remains at 6/9 12 months following treatment.

DISCUSSION

As yet there are no established guidelines for the management of patients with PPNVMs nor randomised trials to evaluate the efficacy of laser photocoagulation in controlling the disease process. Conservative management is encouraged by the possibility that the membrane may regress or stabilise before reaching the fovea. Nevertheless in a significant number of cases it is known that the membrane will progress relentlessly and invade the foveal avascular zone causing severe loss of vision.

The current policy of waiting to demonstrate growth of the neovascular membrane prior to therapy is a reasonable one. However, the membrane may extend rapidly between examinations or the patient may fail to attend for review (case 2). This study was an attempt to identify clinical features of PPNVMs which would determine their natural course and final visual prognosis.

The membranes in this series had varying causes. In 3 patients the membranes were caused by chorioretinitis, toxoplasmosis and myopia respectively, 7 were idiopathic and 10 were related to macular degeneration. Of the patients over the age of 40 years, 70% were female. This female preponderance is in keeping with the fact established from previous studies that this condition is more common in females.[6] One striking finding which was unanticipated was that 54% of patients over 45 years old had bilateral membranes and 62% of those over the age of 70 years had bilateral disease. Two patients had bilateral disease on presentation. In the other patients with bilateral disease the second eye became involved while under observation. The time interval from presentation to disease in the fellow eye varied from simultaneous through asymmetrical presentation to a delay of 7 years. This obviously has important implications for long-term follow-up of these patients. The visual acuity in this group was generally poor: 6/60 to counting fingers. In no case in this older group was there a membrane which stabilised or regressed and in no patient did we fail to show progression. It is interesting to consider the direct cause of the visual loss in these patients. The pathological changes responsible for actual visual loss were intraretinal haemorrhage, serous retinal detachment, lipid exudation into the macula or direct subfoveal extension of the membrane. The causes of visual loss are shown in Table I.

The patients in the younger age group, i.e. less than 40 years of age, tended to develop peripapillary haemorrhage and/or serous detachment of the macula, whereas those older than 40 years had a propensity for either direct sub-

foveal extension of the membrane or for chronic lipid exudation into the macula. Those patients who developed haemorrhage and/or serous detachment of the macula generally had a favourable prognosis due to resolution of these factors. However, those who had chronic lipid exudation had a uniformly poor visual prognosis.

It is therefore our impression from this study that even though a PPNVM may not be encroaching directly on the fovea, older patients are at risk of visual loss from intrafoveal lipid exudation. Once the exudates are established at the fovea the visual prognosis is poor even if the membrane resolves or is treated.

None of the 4 patients in the younger age group showed any evidence of chronic lipid exudation, whereas lipid exudation appeared to be a very prominent feature of the patients in the older age group (Table I). It is interesting to speculate on the reason for this. It is postulated that in older patients the macrophage scavenging system may not be as efficient in clearing debris caused by the membrane, thus resulting in chronic intraretinal lipid deposition.

In our series 3 patients had had laser photocoagulation. One patient was inadequately treated due to her young age and technical difficulties, and the two older patients were treated when the disease process was already advanced. These membranes all progressed; however, in the 10-year-old patient the membrane has stabilised and vision has been stable at 6/24 for 18 months. We feel, however, that because of the timing and technical difficulties it is not an accurate representation of the results expected from laser treatment.

Galdini *et al.*[12] recently treated eyes with PPNVMs using monochromatic argon green photocoagulation. After a follow-up time of 37.7 months they had a 92% success in achieving closure of the new vessels and an 80% rate of visual stabilisation.

Treatment of these membranes does pose certain problems. As noted by Kies and Bird,[6] once the fovea is threatened the area occupied by the new vessels is often difficult to outline because the areas of neovascularisation are poorly defined. It is also difficult to determine the significance of small points of hyperfluorescence beyond the main lesion. If possible it is recommended that a wide margin of 'normal-appearing' fundus should be treated around the lesion.[6] It would therefore appear reasonable to treat early and not to wait until the lesion approaches the fovea.

Our findings are as follows: There appears to be a spectrum of disease, patients younger than 40 years of age in this series having unilateral disease with a favourable visual outcome. In contrast patients over the age of 40 years all showed progressive membranes, a high incidence of bilateral disease (62%) and an ultimately poor visual prognosis without any or inadequate treatment.

We therefore recommend the following guidelines:

1. In the younger patient with a unilateral membrane and an underlying cause there is a high expectancy of resolution and a good ultimate prognosis. In these cases we feel that it is reasonable to adopt an expectant policy.
2. In the older patient the disease appears to be uniformly progressive although at varying rates. We also note that in this group of patients lipid exudation poses a severe and permanent threat to vision. We recommend the early and aggressive treatment of these eyes, with treatment extending well into normal retina. The high incidence of bilateral involvement makes it imperative to document the fellow eye fully and to carry out fluorescein angiography to detect any occult disease (case 2).

Treatment of peripapillary membranes was initially thought to cause treatment scotomas due to nerve fibre damage in the papillomacular bundle. However, it has been shown that if the treatment is carried out using the argon green laser and the intensity of burns is limited to 'grey' discoloration, arcuate scotomas are not a problem.[12] It therefore appears that it is the patient's age and the related behaviour of the membrane that is the key to whether the membrane is likely to progress or regress. A prospective trial is currently in progress to assess the visual outcome following treatment as recommended here.

We are indebted to Mrs Marilyn McDermott for providing us with such excellent colour slides and fluorescein angiograms.

Key words: Age-related degeneration, Natural history, Peripapillary subretinal neovascular membranes, Visual prognosis.

REFERENCES

1. Cantrill HL, Burgess D. Peripapillary neovascular membranes in presumed ocular histoplasmosis. Am J Ophthalmol 1980;89:192–203.
2. Hotchkiss ML, Fine SL. Pathologic myopia and choroidal neovascularization. Am J Ophthalmol 1981;91:177.
3. Wise GN, Henkind P, Alterman M. Optic disc drusen and sub-retinal haemorrhage. Trans Am Acad Ophthalmol Otolaryngol 1974;78:212.
4. Hilton GF. Late serosanguinous detachment of the macula after traumatic choroidal rupture. Am J Ophthalmol 1975; 79:999.
5. Jampol L, Orth D, Daily MJ, Rabb MF. Subretinal neovascularisation with geographic (serpiginous) choroiditis. Am J Ophthalmol 1979;88:683.
6. Kies JC, Bird AC. Juxtapapillary choroidal neovascularisation in older patients. Am J Ophthalmol 1988;105:11–9.
7. Jack RL. Peripapillary disciform degeneration of the retina: diagnosis and treatment. Ann Ophthalmol 1978;10:15–31.
8. Gass JDM. Pathogenesis of disciform detachment of the neuroepithelium. III. Senile disciform macular degeneration. Am J Ophthalmol 1967;63:617–44.
9. Gass JDM. Pathogenesis of disciform detachment of the neuroepithelium. VI. Disciform detachments secondary to heredo-degenerative, neoplastic and traumatic lesions of the choroid. Am J Ophthalmol 1967;63:689–711.
10. Arkfeld DF, Brockhurst RJ. Peripapillary subretinal neovascularisation in peripheral uveitis. Retina 1985;5:157–60.
11. Sarks SH. New vessel formation beneath the retinal pigment epithelium in senile eyes. Br J Ophthalmol 1973;57:951–65.
12. Galdini AP, Jalkh AE, Trempe CL, Nasrallah FP, Schepens CL. Argon green laser treatment of peripapillary choroidal neovascular membranes. Ophthalmic Surg 1989;20(2): 93–9.
13. Duane TD, Jaegar EA. Retinal pigment epithelium: Bruch's membrane layer. In: Biomedical foundations of ophthalmology, vol. 1. Philadelphia: Lippincott, 1986:11–12.