Eye (2010) 24, 472–482

www.nature.com/eye

CAMBRIDGE OPHTHALMOLOGICAL SYMPOSIUM

Eales' disease: diagnosis and management

T Das[1], A Pathengay[2], N Hussain[3] and J Biswas[4]

Abstract

Eales' disease is an idiopathic inflammatory venous occlusive disease. It primarily affects young adults and is often bilateral. It is characterized by three overlapping stages of venous inflammation (vasculitis), occlusion, and retinal neovascularization. Diagnosis is mostly clinical and requires exclusion of other systemic or ocular conditions that could present with similar retinal features. Recurrent vitreous haemorrhage is the hall mark of Eales' disease. Treatment is usually corticosteroids in the inflammation stage and photocoagulation in the proliferative stage of the disease. Visual prognosis is good if treated early in the course of the disease.
Eye (2010) **24,** 472–482; doi:10.1038/eye.2009.315; published online 15 January 2010

Keywords: Eales' disease; periphlebitis; vasculitis

[1]LV Prasad Eye Institute, Bhubaneswar, Orissa, India

[2]LV Prasad Eye Institute, Visakhapatnam, Andhra Pradesh, India

[3]Al Zahara Hospital, Sharjah, UAE

[4]Sankara Nethralaya, Chennai, Tamil nadu, India

Correspondence: T Das, LV Prasad Eye Institute, Patia, Bhubaneswar, Orissa 751024, India
Tel: 91 674 3987 201; Fax: 91 674 3987 130.
E-mail: tpd@lvpei.org

Received: 18 October 2009
Accepted: 17 November 2009
Published online: 15 January 2010

Introduction

Eales' disease is an idiopathic inflammatory venous occlusion that primarily affects the peripheral retina of adults. Retinal changes include perivascular phlebitis, peripheral nonperfusion, and neovascularization. Vision loss is characteristically caused by bilateral (often), recurrent, vitreous haemorrhage and its sequelae. In 1880 and 1882, Henry Eales,[1,2] a British ophthalmologist, described the clinical picture of recurrent retinal haemorrhage in young adults. His seven patients were all young men (aged 14–29 years) and all had a common history of headache, epistaxis, variation in peripheral circulation, dyspepsia, and chronic constipation. Henry Eales believed it to be a vasomotor neurosis, and not retinal vasculitis. Wardsworth[3] described the associated signs of retinal inflammation 5 years later.

In the century that has followed, Henry Eales had been honoured with the eponym for the disease characterized by idiopathic recurrent vitreous haemorrhage in otherwise young and healthy adults. The eponym has been retained because of its widespread recognition and the emphasis that it gives to the common clinical features and certain significant therapeutic implications. In later years, a number of early researchers, such as Elliot,[4] Kimura *et al*,[5] Keith Lyle and Wyber,[6] and Cross,[7] have documented various clinical and pathological features of this inflammatory retinal condition.

Patient profile

Eales' disease had been reported form the United Kingdom, the United States, and Canada in the later half of the nineteenth and early twentieth century. But for unclear reasons, it is now rare in developed countries and is more commonly reported from the Indian subcontinent. We wonder whether this is associated with environmental cleanliness, general nutrition, and health of the individuals. The reported incidence in India is one in 200–250 ophthalmic patients.[8]

Eales' disease predominantly affects healthy young adults, mostly male, in the age group of 20–30 years. Most symptoms include vitreous haemorrhage, such as small specks, floaters, cobwebs, or decrease in visual acuity. Others have mild reduction of vision associated with retinal vasculitis but without vitreous haemorrhage. Although many patients will complain of symptoms in only one eye, a detailed fundus examination of the fellow eye will often show the early changes such as periphlebitis, vascular sheathing, or peripheral nonperfusion, detected using fluorescein angiography. Eventually, between 50 and 90% of patients develop bilateral involvement.[9,10]

Clinical picture

The three hallmark signs of the Eales' disease are retinal phlebitis, peripheral nonperfusion, and retinal neovascularization (Figure 1).

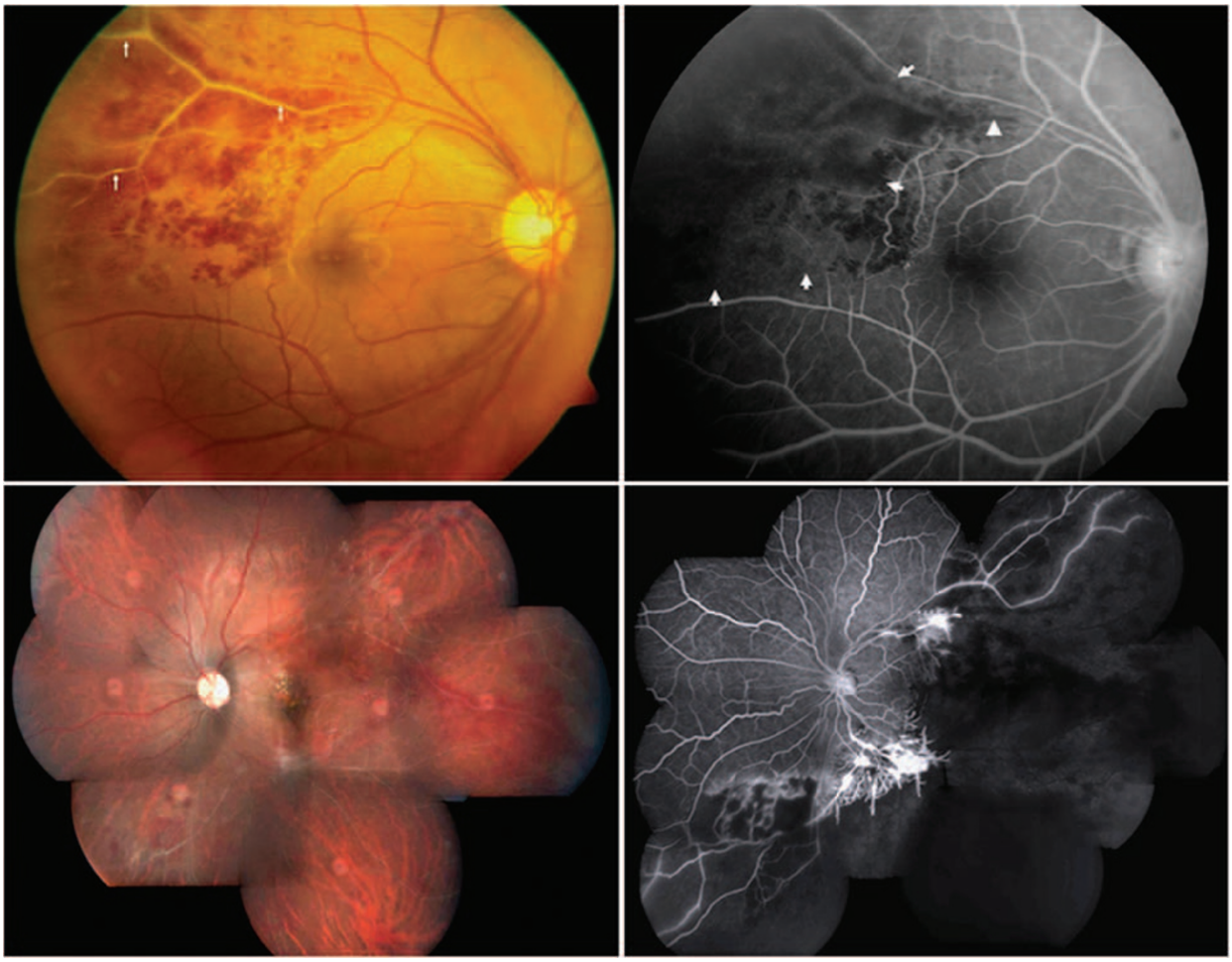

Figure 1 A typical fundus picture in Eales' disease. The colour fundus (top left) of right eye shows obliterated vessels as white lines (arrows), surrounded by retinal haemorrhages; the corresponding angiogram (top right) shows areas of capillary nonperfusion (arrow head) distal to the obliterated vessels. The colour fundus photograph of the left eye (bottom left) shows several areas of obliterated vessels, and suspected new vessels; the corresponding fluorescein angiograph (bottom right) confirms the retinal new vessels, and an extensive area of capillary non perfusion.

Retinal phlebitis

Retinal phlebitis is characterized by mid-peripheral venous dilation, perivascular exudates along the peripheral veins, and superficial retinal haemorrhages. Vascular sheathing ranges from thin white lines limiting the blood column on both sides to segmental heavy exudative sheathing.

Peripheral nonperfusion

Most patients develop varying degrees of peripheral retinal nonperfusion. Find solid white lines representing the remains of obliterated large vessels are commonly observed in the area of nonperfusion. These fine lines retain configuration of normal retinal vasculature. This junction between the anterior peripheral nonperfusion and the posterior perfused retina is usually sharply demarcated. The vascular abnormalities at the junction between the perfused and nonperfused zones include micro-aneurysm, veno-venous shunts, venous beading, and occasionally hard exudates and cotton-wool spots.[11,12]

Neovascularization

Neovascularization of retina occurs in up to 80% of patients. The new vessels form either on the disc (NVD) or elsewhere on the retina (NVE). The NVEs are usually located at the junction of the perfused and nonperfused retina. Bleeding from neovascularization is common, is usually recurrent, and is one of the major causes of vision loss. A few days after vitreous haemorrhage, blood settles in the lower vitreous, and fundus details could be

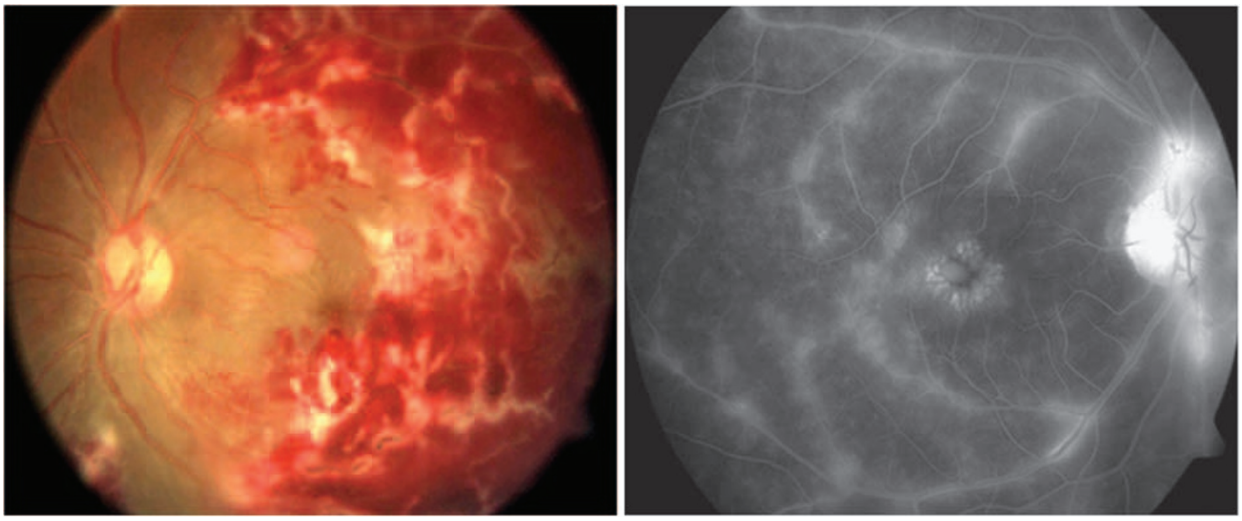

Figure 2 Central Eales' disease: fundus and fluorescein angiography. The colour fundus photograph of left eye shows massive areas of retinal haemorrhages and periphlebitis in the posterior pole (left) and fluorescein angiography of the right eye shows gross staining of vessels and cystoid macular oedema (right). The colour fundus (left) shows obliterated vessels as white lines (arrows), surrounded by retinal haemorrhages; the corresponding angiogram (left) shows areas of capillary nonperfusion (arrow head) distal to the obliterated vessels.

visible again. In some favourable case, there may not be any recurrence after the first episode of vitreous haemorrhage; however, in many cases there will be a second or more than two episodes of fresh vitreous bleeding. In recurrent bleeding, the fundus will show evidence of old blood, with signs of fibrous organization, retinitis proliferans, or even tractional retinal detachment. Untoward sequel includes uveitis, complicated cataract, rubeosis iridis, and secondary neovascular glaucoma in the later stage of the disease.

A large study of 144 eyes[13] have documented distribution of common retinal lesions as follows: periphlebitis and sheathing of vessels in 84% of eyes, kinky tortuous venules and irregularity in vessel caliber in 37% of eyes, pigmentation in the course or at bifurcation of vessels and circumscribed pigmented areas suggestive of healed chorioretinitis in 35% of eyes, surface or elevated retinal new vessels in 50% of eyes, and vitreous haemorrhage in 34% of eyes. The macula is usually not involved primarily in Eales' disease despite extensive peripheral nonperfusion, but when it does, named central Eales' disease, all mid-peripheral lesions appear in the posterior pole and cause reduction of vision in the early stage of the disease, often due to cystoid macular oedema (Figure 2).

Fluorescein angiography

Active vasculitis is characterized by staining of the vessel wall or even frank extravasation[14] (Figures 1 and 2). Vascular sheathing due to gliosis without active inflammation does not stain. The inflammation of the venous segments results in various degrees of obstruction to the venous flow. Venous stasis consequent to venous obstruction is manifested by engorged tortuous veins distal to the obstruction, and engorgement of the capillary bed. The newly formed blood vessels become distinctly outlined during the arteriovenous phase with their abnormal branching patterns and dye leak. The dye leakage and later dye staining stop after resolution of venous inflammation. Often one notices patches of deep choroiditis along the inflamed veins in various stages of development and healing.

Natural course

The natural course of Eales' disease is quite variable with temporary or even permanent remission in some cases and relentless progression to total blindness in others. The diagnostic clinical feature of Eales' disease is the evidence of peripheral venous inflammation, either past or present. Active inflammation is manifested by characteristic perivascular clustering, either mild or massive, or isolated or multiple. The inflammation of vein causes variable degrees of venous insufficiency.

Retinal ischaemia stimulates neovascular growth from the surrounding normal vasculature. The common site is just proximal to the site of obstruction. When there are extensive areas of retinal ischemia, both retinal new vessels (more often) and disc new vessels follow. These new vessels are the most important cause of repeated vitreous haemorrhage. Occasionally, the new vessels

Table 1 Grading of Eales' retinopathy

Lesion	*I*	*II*	*III*	*IV*
Angiopathy				
Venous changes	1/12	<2/12	<3/12	>3/12
Retinal haemorrhages	<1/12	<2/12	<3/12	>3/12
Proliferative retinopathy				
New vessels	—	<1/12	<2/12	>2/12
Fibrous tissue	<1/12	<2/12	<3/12	>3/12
Vitreous haemorrhages obscured	<2/12	<4/12	<8/12	>8/12

1/12 = 30 degree of an arc.

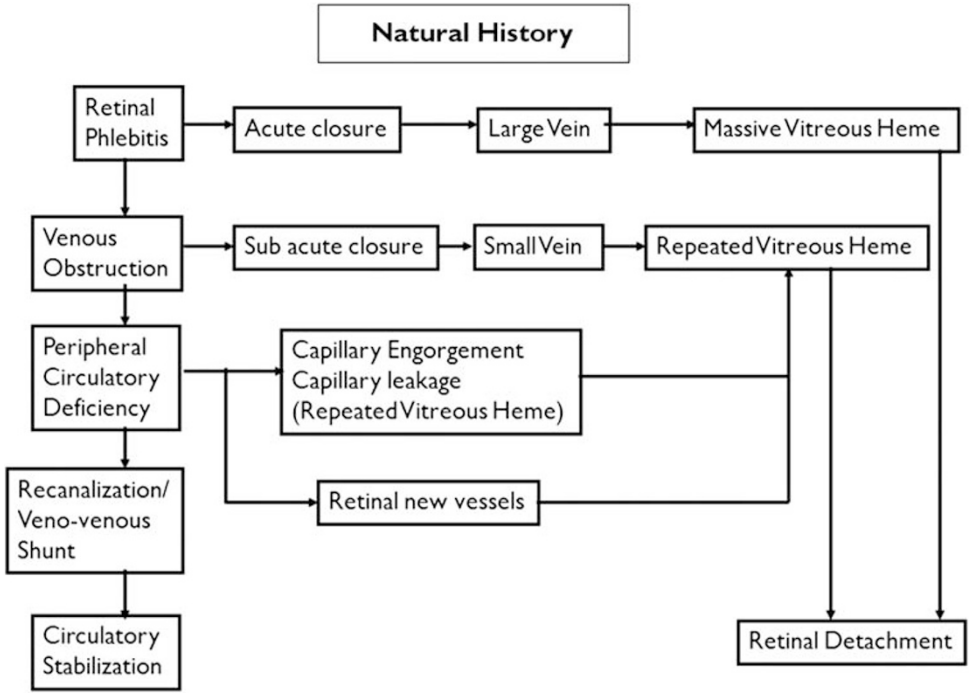

Figure 3 Natural history of Eales' disease.

regress spontaneously; they sclerose and stop perfusing with blood, and finally the regressed new vessels get replaced with glial tissue. The regressing new vessels often cause traction on the retina and lead to either traction or combined retinal detachment when it also causes a slit-like traction tear of the retina.

Not all cases follow this classic course. We do not know what exactly determines the variable course of Eales' disease. Charmis[15] classified Eales' disease into four stages: stage I is the very early stage of evolution and is characterized by mild periphlebitis of small peripheral retinal capillaries; in stage II the perivasculitis of the venous capillary system is widespread and larger veins are also affected; stage III is characterized by new vessel, and retinal and vitreous haemorrhage occurs in this stage; and stage IV is the end result of massive and recurrent vitreous haemorrhages with retinitis proliferans and tractional retinal detachment.

We[16] have proposed a grading system of Eales' retinopathy based on the degree and extent of microangiopathy, proliferative retinopathy, and vitreous haemorrhage (Table 1). This classification is useful in assessing and monitoring the effect of treatment.

The natural course of the Eales' disease is either circulatory stabilization or repeated vitreous haemorrhages (Figure 3).[17] There are three different ways that vitreous haemorrhage can occur in Eales' disease. First, acute phlebitis with rapid or sudden obstruction to the venous flow can cause a haemorrhage large enough to break into the vitreous. When a large-caliber vein is involved the haemorrhage can be massive, which may not clear for months. Second, when a smaller peripheral

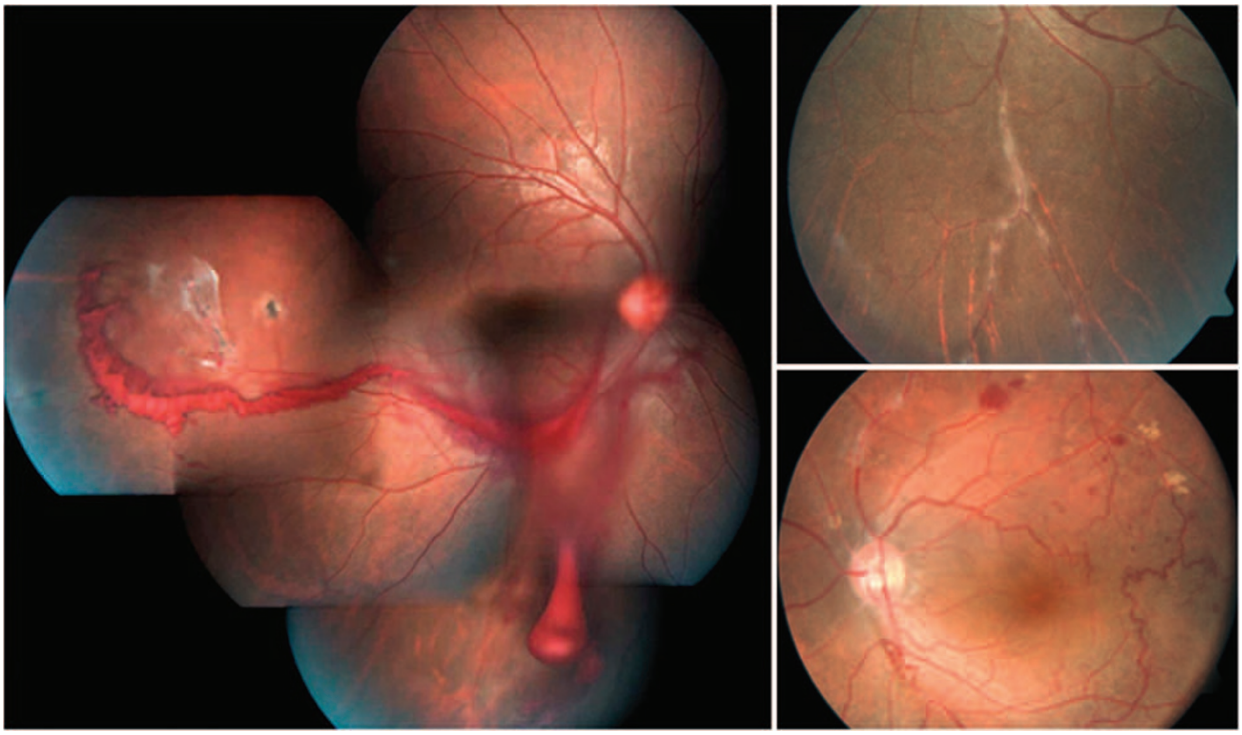

Figure 4 Stages in Eales' retinopathy. (Left) Fundus photograph of the right eye records an event of fresh vitreous haemorrhage; an area of fibrovascular proliferation is observed in temporal equator with an adjacent healed chorioretinal atrophy. (Right) The top and bottom pictures show healed stage of Eales' retinopathy; veno-venous anastomosis is observed temporal to macula in the left bottom.

venule is involved, haemorrhage is relatively small and gets absorbed with time. Occasionally, sequential acute involvement of small-caliber venules lead to repeated vitreous haemorrhage. Finally, a persistent state of circulatory deficiency and retinal ischaemia may lead to neovascular proliferation, which is the commonest source of repeated vitreous haemorrhage. Occasionally, in the course of time, circulatory stabilization may ensue through recanalization, veno-venous capillary shunts, and tissue atrophy (Figure 4).

Aetiopathogenesis

The aetiopathogenesis of Eales' disease to date has remained controversial and ill-understood. Since the description of Wardsworth,[3] Eales' disease is recognized as primary vasculitis of unknown aetiology in young adults. Retinal vasculitis and peripheral retinal revascularization associated with various systemic and ocular diseases could mimic Eales' disease in the inflammatory and proliferative phases, respectively (Tables 2 and 3).

Systemic diseases associated with Eales' disease

The association of several systemic conditions with Eales' disease has been reported. But, in several large series many such associations have not been proved and we presume that most of these associations are only occasional. However, as tuberculosis has often been directly or indirectly implicated, a brief survey of the literature and the possible causal association is justified.

Table 2 Retinal vasculitis mimicking Eales' disease

Systemic	*Ocular*
Leukaemia	Behcet's disease
Lyme borreliosis	
Multiple sclerosis	Birdshot retinochoroidpathy
Sarcoidosis	Coat's disease
Syphilis	Pars planitis
Systemic lupus erythematosis	Viral retinitis
Toxoplasmosis	
Tuberculosis	
Wegener's granulomatosis	

Table 3 Proliferative vascular retinopathy mimicking Eales' disease

Systemic	*Ocular*
Diabetes mellitus	Branch retinal vein occlusion
Sarcoidosis	Central retinal vein occlusion
Sickle cell disease	Coat's disease
	Pars planitis
	Retinopathy of prematurity

Tuberculosis
Two studies[18,19] have histopathologically shown the presence of tubercle bacilli in the pathologic specimens. The assumption of tubercular aetiology is based on observations of active or healed tuberculosis in some patients of primary vasculitis. But such association was not more than 1.3% in a large clinical study.[20]

Hypersensitivity to tuberculoprotein
Hypersensitivity to tuberculoprotein is based on the observation of positive Mantoux reaction.[21,22] Tuberculin hypersensitivity develops after exposure to tuberculosis. Cutaneous sensitivity is known to yield a fairly reliable index of ocular sensitivity in experimental animals that are infected with tuberculosis. Ashton[23] hypothesized that the retina of patients with Eales' disease could be selectively sensitized against tuberculoprotein. Re-exposure to this antigen could result in allergic vasculitis in the retina. But Eales' disease has also been reported in Mantoux-negative patients.[24] As the Matoux is positive in 67–90% of healthy adults in India[25] (and possibly other developing countries), the role of tuberculoprotein in Eales' disease is questionable.

Immune-mediated mechanism
Immune-mediated mechanism has been proposed by some researchers as a possible cause of Eales' disease.[19,20] The clinical picture of acute onset, favourable response to systemic corticosteroid, lymphocytic infiltration in the histopathological study of vitreous and epiretinal membranes, and abnormal immunological parameters observed in retinal vasculitis is similar to Eales' retinopathy. This is suggestive of an immunological mechanism, although the precise nature has not been identified so far in Eales' retinopathy.

Light microscopic and immunohistochemical studies have shown predominant T-cell involvement in the lymphocytic infiltration of epiretinal and subretinal membrane of Eales' disease.[26,27] Presence of predominant T cells in the epiretinal and subretinal membrane of Eales' disease probably indicate that a cell-mediated immune mechanism might be having a role in the proliferative phase of the disease with membrane formation on the surface of the retina.

Biochemical studies in Eales' disease
Raised *á*-globulins and reduced albumin levels,[28] and detection of a distinct protein spot at iso-electric point (pi) of 5.9 with a molecular weight of approximately 23 kDa[29] in the serum samples is reported in patients with Eales' disease. These and other studies suggest that certain peptide growth factors, for example, platelet-derived growth factor (PDGF), insulin-like growth factor I (IGF-I), epidermal growth factor (EGF), transforming growth factors (TGF-α and TGF-β), vascular endothelial growth factor (VEGF) and so on, have a key role in the process of neovascularization by both direct and indirect means.[30,31]

Pathology

The clinical manifestation of this disease is due to three basic pathological changes: inflammation, ischaemia, and neovascularization and its sequelae. The site of involvement is predominantly the peripheral retina. Inflammation involves both peripheral veins (predominant) and arterioles. Histopathological studies of Eales' disease are few as the disease occurs in young healthy individuals. Most researchers have shown chronic inflammatory cell infiltration.[5,18,19,21,32]

With the advent of vitreoretinal surgery, many eyes with Eales' disease receive vitrectomy for non-resolving vitreous haemorrhage and/or tractional retinal detachment. This has allowed obtaining intraocular tissue sample in the proliferative phase of the disease. The vitreous composition does not seem to be different from eyes with other retinal vascular disease.[33] The epiretinal membrane in Eales' disease is usually composed of several neovascular channels with glial cells, macrophages, fibrocytes, retinal pigment epithelial cells with variable amount of collagen material, and basement membrane. In comparison to other vascular retinopathies, the epiretinal membrane in Eales' disease contains significant lymphocytic infiltration. These lymphocytes are observed around the newly formed vascular channels and diffusely within the ERM itself. These infiltrates are usually T-cell and a few B-cell type[27] (Figure 5). This is suggestive of a cell-mediated immune reaction involved in the formation of these membranes. Stock[18] and Gilbert[19] have shown acid fast bacilli in the peripheral retinal lesion and perivascular sheaths in eyes with primary phlebitis. Madhavan *et al*[34] have shown *M. tuberculosis* complex DNA using IS6110 primers in polymerase chain reaction.

Treatment

The treatment of Eales' disease is symptomatic. It is aimed at reducing retinal perivasculitis and associated vitritis, reducing the risks of vitreous haemorrhage from new vessels on the retina and/or the optic nerve head by retinal ablation, and surgical removal of non-resolving vitreous haemorrhage and/or vitreous membranes. The present-day modalities of treatment are confined to corticosteroids, anti-VEGF therapy, photocoagulation with or without anterior retinal cryoablation, and vitrectomy at various stages of the disease process.

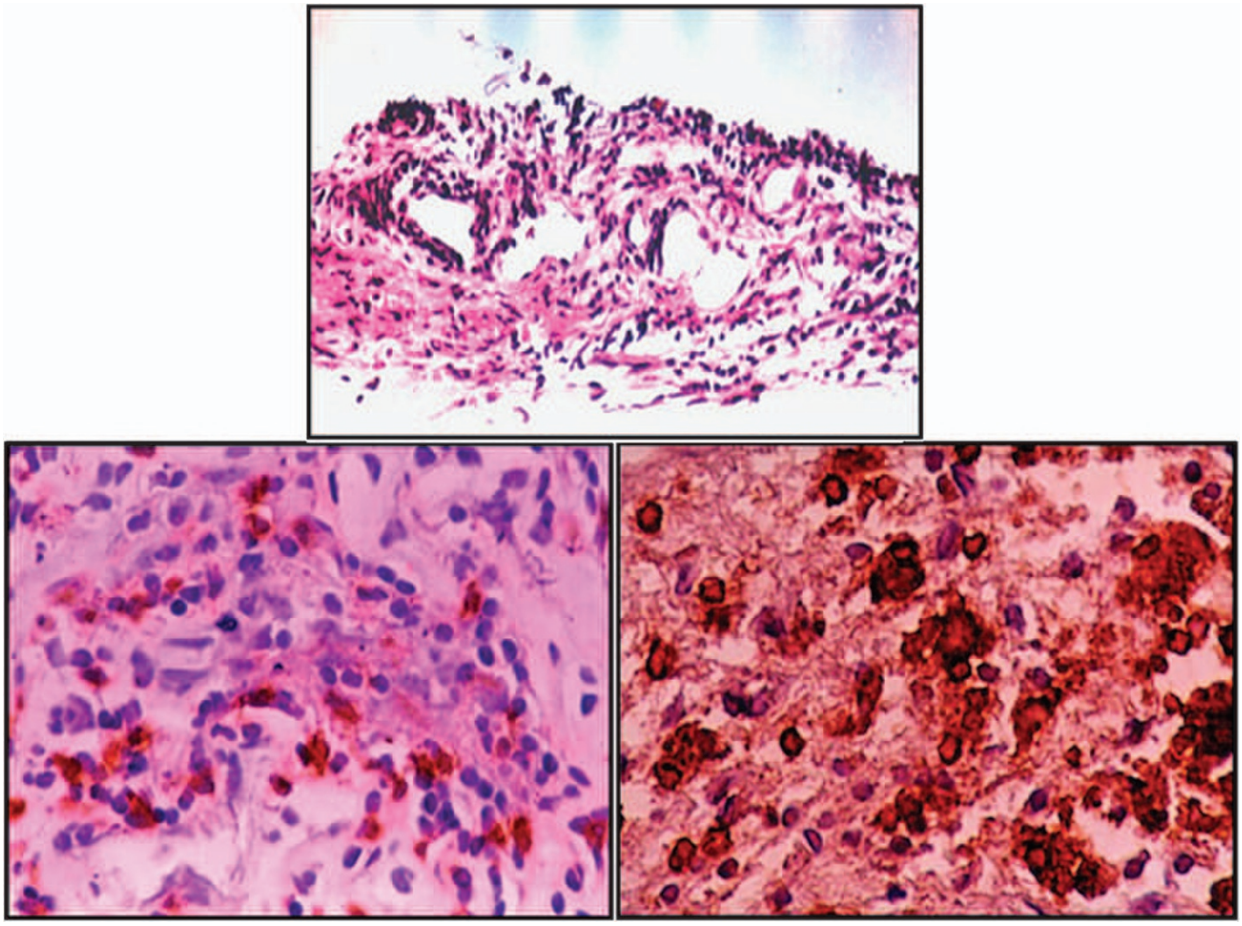

Figure 5 Photomicrograph of an epiretinal membrane in Eales' disease. (Top) it shows diffuse lymphocytic infiltration and infiltration around vascular channels (H&E $\times 100$). (Bottom left) Immunohistochemical staining by pan T-cell marker showing positivity of most of the lymphocytes (diaminobenzene $\times 200$); and (bottom right) immunohistochemical staining by pan B-cell marker showing positivity of few lymphocytes (diaminobenzene $\times 200$).

Corticosteroids

Corticosteroids form the mainstay of treatment in the active perivasculitis stage of the disease. Oral and periocular corticosteroids are used for control of retinal vasculitis. Initially, high doses of oral corticosteroids, for example, prednisolone (up to 2 mg/kg body weight), are given and gradually tapered as vasculitis begins to wane (Figure 6). Posterior sub-Tenon injection is considered in very active retinal vasculitis. In selected cases intravitreal triamcinolone can be tried. We and others[35,36] have documented the beneficial effects of such therapy (Figure 7).

Antitubercular treatment (ATT)

When considered, ATT is given for 9 months. The ATT protocol is usually reserved for patients with acute phlebitis with massive infiltration, nodule formation, and complete obliteration of segments of the vein.

Anti-VEGF therapy

This therapy is currently considered as a definitive therapy in Eales' disease, as recent studies have indicated a close relationship between the prominent neovascular proliferation in Eales' disease and the intense expression of VEGF. There is one published report of the benefits of intravitreal bevacizumab in regression in new vessels and reduction in vitreous haemorrhage in two patients with Eales' disease.[37] We have similar experience in three patients (unpublished), but similar to many other retinal vascular diseases, intravitreal bevacizumab is an adjunct to subsequent photocoagulation or vitreous surgery, depending on the stage of the disease.

Photocoagulation

Photocoagulation is the mainstay of treatment in the proliferative stage of Eales' disease. In the era when retinal laser was not available in India, we had suggested

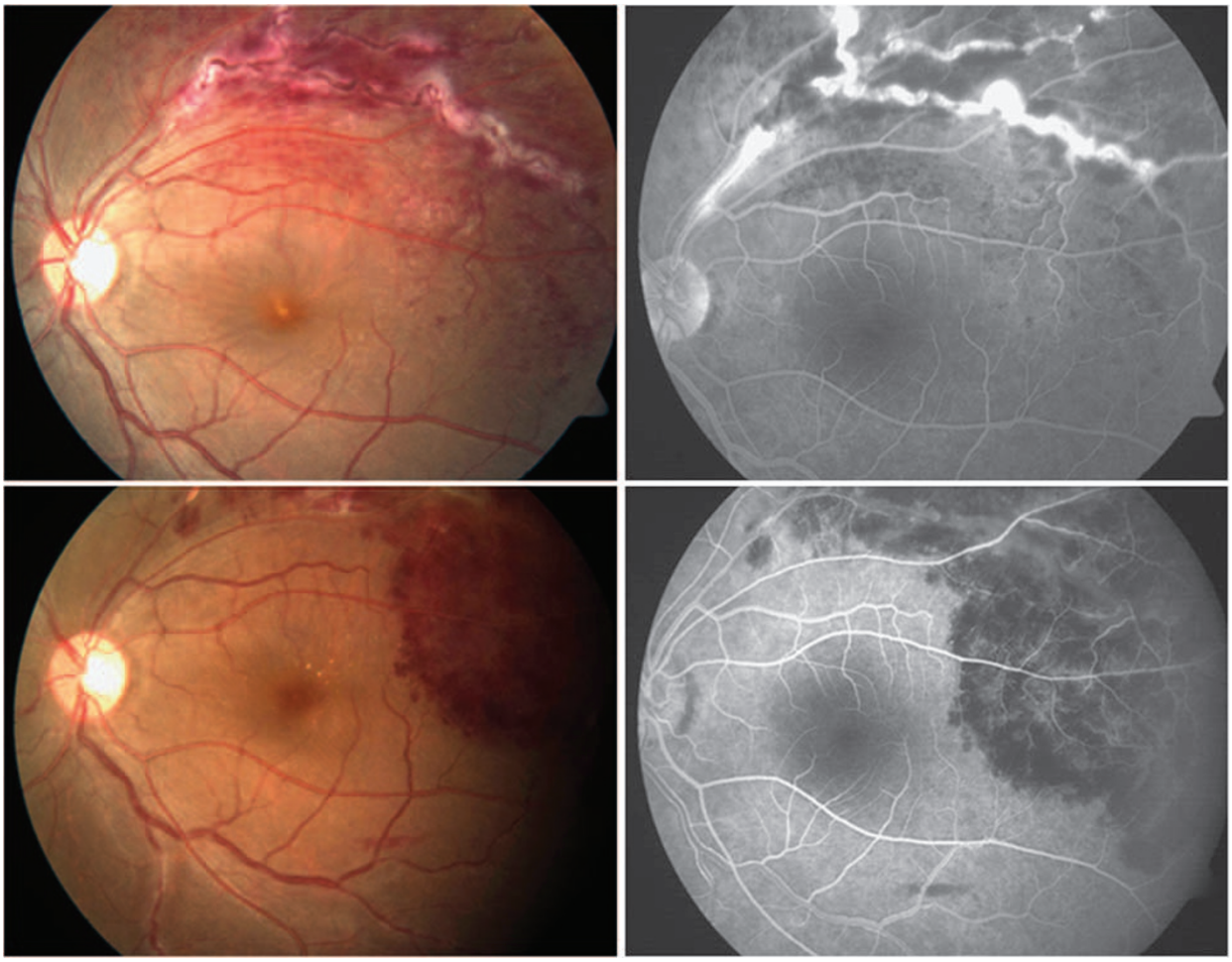

Figure 6 Oral corticosteroid in the treatment of Eales' disease. (Top) At presentation and (bottom) at 6 weeks after corticosteroid therapy. This 25-year-old man presented with massive vasculitis and retinal haemorrhages. He was treated with oral prednisolone (2 mg/kg of body weight) for a week and then gradually tapered. At 6 weeks, there was a reduction in vasculitis and a normal configuration of the vessels.

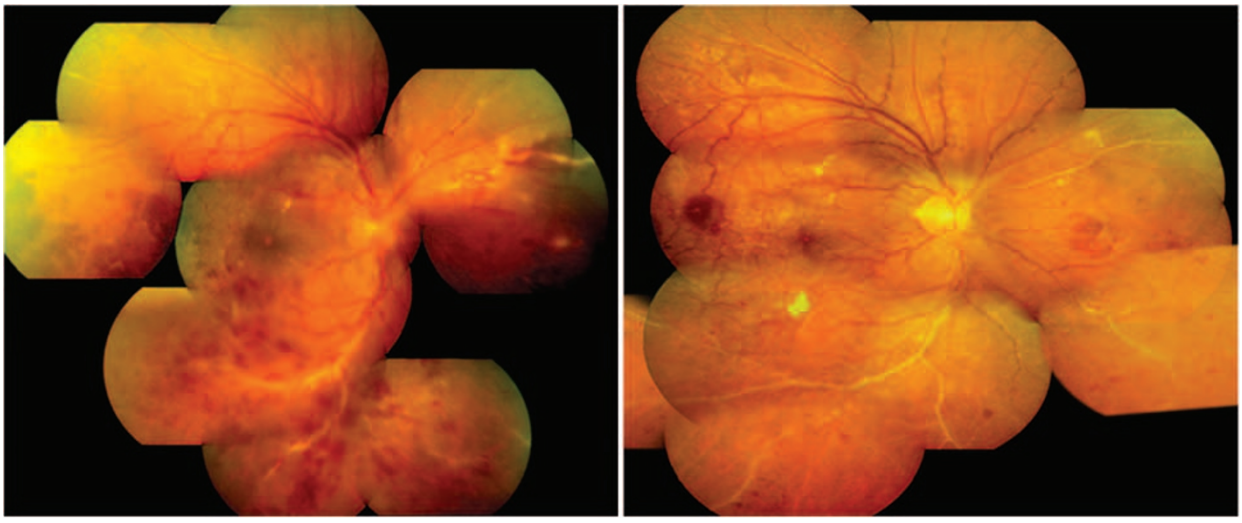

Figure 7 Intravitreal triamcinolone acetonide in the treatment of Eales' disease. (Left) At presentation, there are several areas of retinal vasculitis; (right) at 6 weeks after treatment, the retinal vasculitis was replaced with obliterated vessels. This eye had received one injection of intravitreal traimcinolone acetonide 4 mg in 0.1 ml.

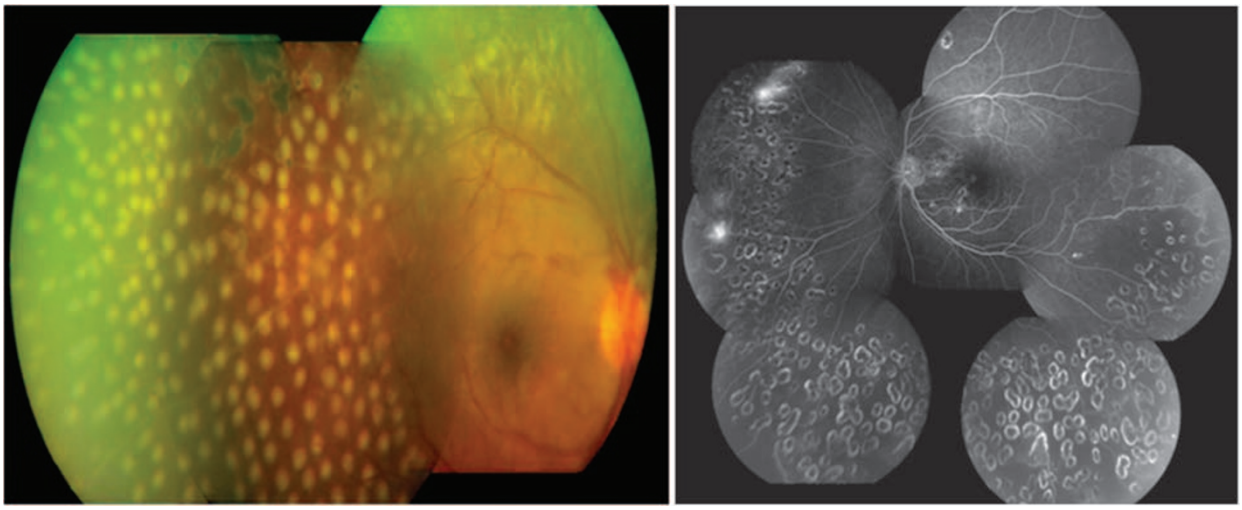

Figure 8 Laser in the treatment of Eales' retinopathy. (Left) Scatter photocoagulation in Eales' disease. Fresh laser marks are observed. (Right) Fluorescein angiogram of another patient. The right eye had received laser treatment before, but the new vessels nasally are not completely regressed.

to combine xenon arc photocoagulation (applied in the paracentral zone) with anterior retinal cryopexy (applied to peripheral retina).[16] Currently, retinal laser has completely replaced the use of both xenon photocoagulation and anterior retinal cryopexy. As vitreous haemorrhage could occur at any stage of Eales' disease, we are unclear whether laser photocoagulation could be beneficial in the inflammatory stage of the disease. It is also unclear whether panretinal photocoagulation involving all four quadrants is necessary, similar to diabetic retinopathy, or a segmental scatter photocoagulation of the involved quadrants of the retina, similar to branch retinal vein occlusion, will suffice.

We addressed these questions in a prospective randomized clinical trial; the results showed that photocoagulation was beneficial in stages II and III (proliferative stage with active new vessels) of Eales' disease.[38] The study also showed that many of those with stage I (stage of retinal vasculitis alone) Eales' retinopathy do not require photocoagulation, whereas those with stage IV (proliferative stage with massive vitreous haemorrhage or traction retinal detachment) Eales' retinopathy are too advanced to benefit from such treatment. Focal treatment of flat retinal new vessels, sectoral scatter photocoagulation of capillary nonperfusion area, and direct treatment of neovascular frond into the vitreous are beneficial in proliferative Eales' retinopathy. After laser photocoagulation, regression of retinal neovascularization and vitreous neovascular fronds has been observed in 89 and 80% of cases, respectively.[39] In general, only a moderate power is required for laser treatment in Eales' disease and panretinal photocoagulation is rarely necessary. Fluorescein angiography helps in monitoring the response to treatment (Figure 8).

Vitrectomy

Vitreous haemorrhage is the prime cause for gross reduction of vision in Eales' disease. The first episode of vitreous haemorrhage usually clears but recurrent vitreous haemorrhages may lead to formation of traction bands and membranes in the vitreous and subsequent complications. But the episodes of vitreous haemorrhage do not necessarily correlate with the retinal changes. The main indications for vitrectomy include unresolving vitreous haemorrhage, tractional retinal detachment involving the posterior pole, multiple vitreous membranes with or without tractional retinal detachment, and combined tractional and rhegmatogenous retinal detachment.

In general, the prognosis of vitrectomy in Eales' disease is good. Posterior vitreous usually detaches from the retinal surface early except the attachment at the optic disc, and unlike diabetic retinopathy there are less often multiple retinal attachments and vitreous schisis. The latter helps the surgeon in getting into the right plane for a safe vitreous surgery. Application of endolaser is mandatory at conclusion of vitreous surgery. Additional procedures, such as belt buckling and lensectomy, are occasionally required. The major postoperative complications are recurrent vitreous haemorrhages, and early development of cataract. We

have shown a direct relationship between the episodes of vitreous haemorrhage and visual improvement after vitreous surgery.[40] Visual improvement is better with fewer episodes and shorter duration of vitreous haemorrhage. It has also been shown that the patients who had photocoagulation before vitreous surgery had a better prognosis.[41]

Future direction of research

Future direction of research should be directed towards developing an animal model of Eales' disease with tuberculoprotein or biochemically isolated specific protein from patients with Eales' disease. This could unravel many of the riddles and help us in developing a definitive therapy.

Conflict of interest

The authors declare no conflict of interest.

References

1 Eales H. Retinal haemorrhages associated with epistaxis and constipation. *Brim Med Rev* 1980; **9**: 262.
2 Eales H. Primary retinal haemorrhage in young men. *Ophthalmic Rev* 1882; **1**: 41.
3 Wardsworth. Recurrent retinal haemorrhage followed by the development of blood vessels in the vitreous. *Ophthalmic Rev* 1887; **6**: 289.
4 Elliot AJ. Recurrent intraocular haemorrhage in young adults: Eales' disease. A preliminary report. *Trans Cand Ophthalmol Soc* 1948; **46**: 39.
5 Kimura SJ, Carriker FR, Hogen MJ. Retinal vasculitis with intraocular haemorrhage. Classification and results of special studies. *Arch Ophthalmol* 1956; **56**: 361.
6 Keith-Lyle T, Wybar K. Retinal vasculitis. *Br J Ophthalmol* 1961; **45**: 778.
7 Cross AC. Vasculitis retinae. *Trans Ophthalmol Soc UK* 1963; **83**: 133.
8 Puttamma ST. Varied fundus picture of central retinal vasculitis. *Trans Asia Pacific Acad Ophthalmol* 1970; **3**: 520.
9 Duke-Elder S, Dobree JH. *System of Ophthalmology*. Vol X. London: Henry Kimpton.
10 Murthy KR, Abraham C, Baig SM, Badrinath SS. Eales' disease. *Proc All lnd Ophthalmol Soc* 1977; **33**: 323.
11 Spitzans M, Meyer-Schwickerath GT, Stephen B. Clinical picture of Eales' disease. *Crafes Arch Clin Exp Ophthalmol* 1975; **194**: 73.
12 Elliot AJ. Thirty years observation of patients with Hales' disease. *Am J Ophthalmol* 1975; **80**: 404.
13 Abraham C, Baig SM, Badrinath SS. Eales' disease. *Proc All India Ophthalmol Soc* 1977; **33**: 226.
14 Hussain N, Das T, Mohan Ram LS. Eales' retinopathy. In: Agrarwal A (ed). *Fundus Fluorescein and Indocyanine Green Angiogrpahy*. Slack: Thorofare, NJ, 2008, pp 231–234.
15 Charmis J. On the classification and management of the evolutionary course of Eales' disease. *Trans Ophthalmol Soc UK* 1965; **5**: 157.
16 Das T, Namperumalsamy P. Combined photocoagulation and cryotherapy in treatment of Eales' retinopathy. *Proc All Ind Ophthalmol Soc* 1987; **45**: 108.
17 Kalsi R, Patnaik B. The developing features of phlebitis retinae (a vertical study). *Indian J Ophthalmol* 1979; **27**: 87.
18 Stock W. Retinal haemorrhage due to miliary tuberculosis. *Klin Monatsbl Augenh* 1937; **99**: 367.
19 Gilbert TW. Periphlebitis and endovasculitis of retinal vessels. *Klin M Monalsol Augeuh* 1935; **94**: 335.
20 Awasthi P, Mehrotra ML, Srivastava SN. Ocular conditions in pulmonary tuberculosis patients in India. *Acta XX Concilium Ophthalmologicum* 1966; **1025**.
21 Elliot A. Recurrent intraocular haemorrhage in young adults (Eales' disease). A report of 31 cases. *Trans Am Ophthalmic Soc* 1954; **52**: 811.
22 Donders PC. Eales' disease. *Doc Ophthalmol* 1958; **12**: 1–105.
23 Ashton N. Pathogenesis and aetiology of Eales' disease. *Acta XIX Concilium Ophtlmlmologicum* 1962; 2–28.
24 Muthukkaruppan VR, Rengarajan K, Chakkalath HR, Namperumalsamy P. Immunological status of patients of Eales' disease. *Indian J Med Res* 1989; **90**: 351.
25 Raj N, Krishnamurthy MS, Anantharaman DS. Prevalence of non-specific sensitivity in some parts of India. *Indian J Med Res* 1975; **63**: 1098.
26 Biswas J, Rao NA. Epiretinal membrane in Eales' disease and other vascular retinopathies. *Invest Ophllmlmol Vis Sci* 1990; **31**(Suppl): 369.
27 Badrinath SS, Biswas J, Sharma T, Rao N. Immunophenotyping of inflammatory infiltrates in epiretinal (ERM) and subretinal membrane (SRM) in Eales' disease. *Invest Ophthalmol Vis Sci* 1992; **33**(Suppl): 33.
28 Pratap VB, Mehra MK, Gupta RK. Electrophoretic pattern of serum proteins in Eales' disease. *Indian J Ophthalmol* 1976; **23**: 14.
29 Rengarajan K, Muthukkaruppan VR, Namperumalsamy P. Biochemical analysis of serum proteins from Eales' patients. *Curr Eye Res* 1989; **8**: 1259.
30 Perentes Y, Chan CC, Bovey E, Uffer S, Herbort CP. Massive vascular endothelium growth factor (VEGF) expression in Eales' disease. *Klin Monasbl Augenheilkd* 2002; **219**: 311–314.
31 Angayarkanni N, Selvi R, Pukhraj R, Biswas J, Bhavesh SJ, Tink JT. Ratio of the vitreous vascular endothelial growth factor and pigment epithelial-derived factor in Eales disease. *J Ocul Bio Dis Inform* 2009; **2**: 20–28.
32 Kono T, Yamana Y, Kurimoto S, Inomata H. Histopathology of Eales' disease-retinal vascular changes and proliferation of preretinal membranes. *Acta Soc Ophthalmol Jpn* 1985; **89**: 1001.
33 Biswas J, Badrinath SS, Subramanyam CSV. Microscopic study of vitreous aspirate—a preliminary study. *Trans X Asia-Pacific Acta Ophthalmol* 1985; **664**.
34 Madhavan HN, Therase KL, Gunisha P, Jayanthi U, Biswas J. Polymerase chain reaction for detection of Mycobacterium tuberculosis in epiretinal membrane in Eales' disease. *Invest Ophthalmol Vis Sci* 2000; **41**: 822–825.
35 Pathengay A, Pilli S, Das T. Intravitreal triamcinolone acetonide in Eales' disease: a case report. *Eye* 2005; **19**: 711–713.
36 Ishaq M, Feroze AH, Shahid M, Baig MA, Ameen SS, Feroze SH *et al*. Intravitreal steroids may facilitate treatment of Eales' disease (idiopathic retinal vasculitis): an interventional case series. *Eye* 2007; **21**: 1403–1405.

37 Chanana B, Azad RV, Patwardhan S. Role of intravitreal bevacizumab in the management of Eales' disease. *Int Ophthalmol* 2009; e-pub ahead of print 23 January 2009.
38 Das TP, Namperumalsamy P. *Photocoagulation in Eales' disease. Results of prospective randomised clinical study.* Presented in XXVI Int Cong Ophthalmol, Singapore, 1990.
39 Gopal L, Abraham C. Efficacy of photocoagulation in Eales' disease. *Trans Asia-Pacific Acad* 1985; **10**: 689.
40 Namperumalsamy P, Kelkar AR, Das TP. *Vitreous surgery in Eales' disease-when and why.* Presented in XXVI Ophthalmol, Singapore, 1990.
41 Badrinath SS, Honnatti MR. Vitrectomy in Eales' disease. *Acta Int Cong Ophthalmol* 1982; **24**: 536.