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LETTERS

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Norrie disease and peripheral venous insufficiency

Norrie disease (ND) is a rare X linked recessive disorder in which affected males are blind at birth or in early infancy. About one third develop progressive sensorineural deafness. In addition, about 25% of affected males have varying degrees of developmental delay. The ocular findings include bilateral retinal folds, retinal detachment, vitreous haemorrhage, and bilateral retrolental masses consisting of haemorrhagic vascular and glial tissue (vitreoretinal dysplasia).

Histopathological examination of the eyes of an 11 week foetus with ND showed no evidence of primary neuroectodermal maldevelopment of the retina, suggesting that later disordered retinal vascular development may be a more likely disease mechanism.¹

More than 100 different mutations of the ND gene, *NDP*, have been identified.² Germ line mutations in *NDP* have also been identified in X linked familial exudative vitreoretinopathy (FEVR) and in retinopathy of prematurity (ROP). Somatic *NDP* mutations have been implicated in retinal telangiectasis (Coats disease). These findings suggest a role for the Norrie protein in normal retinal angiogenesis. The reported association of ND with peripheral vascular disease in affected males in a large Costa Rican pedigree,³ suggests that *NDP* may also play a role in non-ocular angiogenesis.

We present the second report of Norrie disease associated with peripheral vascular insufficiency, further supporting an angiogenic role for *NDP*.

Case report

A 53 year old man with bilateral congenital glaucoma and vitreoretinal dysplasia underwent ophthalmological review, peripheral vascular examination, and molecular genetic testing. He complained of poor vision since birth. He had undergone an enucleation of his right eye in young adulthood secondary to uncontrolled glaucoma resulting in intractable pain. Vision was hand movement. Anterior segment examination revealed Haab's striae, a shallow anterior chamber

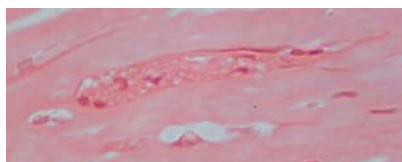


Figure 1 High power photomicrograph of corneal stroma showing a distinct, enlarged nerve bundle.

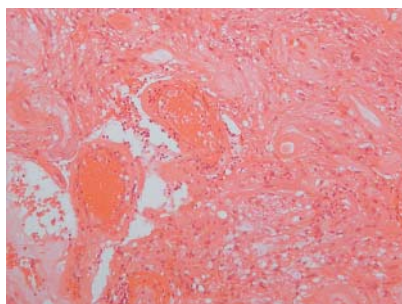


Figure 2 Medium power photomicrograph of markedly disorganised retina with loss of normal architectural features and intense gliosis. Prominent vessels with hyaline walls are present.

and drainage angle dysgenesis. Marked retinal atrophy and optic nerve head calcified drusen had been noted in his left eye before the development of a dense cataract.

He had no evidence of mental retardation. He had sensorineural deafness and had suffered with bilateral lower leg ulceration secondary to peripheral venous insufficiency for over 30 years, necessitating a varicose vein operation at the age of 19 years. Following surgery he has worn support stockings.

A histopathological study of his right eye revealed hypertrophy of corneal nerves (fig 1), a finding which has not been previously reported in association with ND. The ciliary body was seen to be drawn into a preretinal fibrous band at its posterior limit; while the retina had lost its normal architecture and was severely gliotic with cysts and extensive compact lamellar bone formation (fig 2).

The association of congenital glaucoma, vitreoretinal dysplasia, and sensorineural deafness in this male patient raised the possibility of ND. Mutation screening of *NDP* revealed a two base pair deletion in exon 2, resulting in a stop codon and truncation, thereby confirming the clinical suspicion of ND. His two affected maternal uncles were also found to have ND associated with peripheral venous insufficiency and lower leg ulceration.

Comment

These cases represent further evidence of a potential role of *NDP* in vascular development. Mutations in *NDP* have been reported

in several retinal disorders which are characterised by vascular abnormalities, including Coats disease, Stage 5 ROP, and X linked FEVR, suggesting that the protein product of *NDP*, Norrin, may be involved in normal retinal angiogenesis. The association of ND with peripheral venous insufficiency seen in the family reported here and in the Costa Rican pedigree³ suggest that Norrin may also play a role in extraocular angiogenesis.

Further light has been shed on the possible roles of Norrin with the development of an *NDP* knockout mouse model.^{4,5} The retinal vasculature is abnormal by postnatal day 9, with abnormal vessels in the inner retina and few vessels in the outer retina.⁴ The main vasculature of the cochlea, at the stria vascularis, is also abnormal, with eventual loss of two thirds of the vessels. It was therefore proposed that one of the principal functions of Norrin in the ear is to regulate the interaction of the cochlea with its vasculature—further supportive evidence of an important angiogenic role for the Norrie gene.

We present the second report of Norrie disease associated with peripheral vascular disease. This association suggests that *NDP* has an important role in angiogenesis in the eye and other non-ocular tissues.

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Count and size of macular drusen correlated with the parafoveal annular reflex

Age related macular degeneration is one of the most frequently occurring reasons for decreased vision in the elderly population in Western countries.¹ It is divided in a non-exudative form with formation of drusen of the retinal pigment epithelium, and the exudative form with subfoveal chorioretinal neovascularisation and subretinal exudation. Since the subretinal alterations typical for age related macular degeneration may lead to a change in the superficial contour of the retina, it was the aim of this study to evaluate whether the visibility of the macular wall reflex depends on the presence and size of macular drusen as part of age related macular degeneration.

The study included 47 rhesus monkey (*Macaca mulatta*) (77 eyes) for which 60° colour fundus photographs were obtained. Only fundus photographs with the central fundus region fully illuminated were evaluated. The entire study group was divided into eyes of monkeys with unilateral experimental glaucoma (n=36 eyes) or experimental temporary unilateral occlusion of the central retinal artery (n=18), and normal eyes (n=23). The detectability of the parafoveal annular reflex was assessed using a score ranging between "0" for "no parafoveal annular reflex detectable" to "3" for "clear detectability of the parafoveal annular reflex" (figs 1, 2). The reproducibility of the semi-quantitative assessment of the parafoveal annular reflex had been determined in a previous study.² The coefficient of variation for the re-assessment of the ophthalmoscopic detectability of the parafoveal annular reflex was 0.08. The degree of age related macular degeneration was evaluated by counting the number of drusen, separately in the foveal region and in the extrafoveal region within the temporal vascular arcade. The mean size of the drusen was graded into three grades: "1" for very small (30 µm or less) and "3" for very large (larger than 100 µm). The possibility to grade the severity of age related macular degeneration on fundus photographs has already been described in detail previously.³ For assessment of the visibility of the retinal nerve fibre layer, the fundus was divided into eight sectors: temporal inferior, temporal horizontal, temporal superior, superior, nasal superior, nasal horizontal, nasal inferior, and inferior. In each sector, the visibility of the retinal nerve fibre bundles was estimated using a subjective grading ranging from "0" for "no fibre bundles detectable" to "8" for "abundant nerve fibre bundles visible." The technique has already been described in detail.⁴ All eyes included in this study had not undergone any experimental procedure. The study design complied with the National Institutes of Health's as well as the University of Iowa's institutional guidelines for the care and use of laboratory animals, and guidelines of ARVO. All experimental procedures and the fundus photography were performed at Iowa City.

In an univariate statistical analysis, the detectability of the macular wall reflex was significantly and negatively correlated with the number and total area of macular drusen (p=0.05), score of the visibility of the retinal nerve fibre layer as a whole and especially in the temporal horizontal fundus region (p<0.001), and age (p<0.001). A multiple



Figure 1 Fundus photograph of a monkey with clearly visible macular annular reflex in an eye without macular drusen and good visibility of the retinal nerve fibre layer.

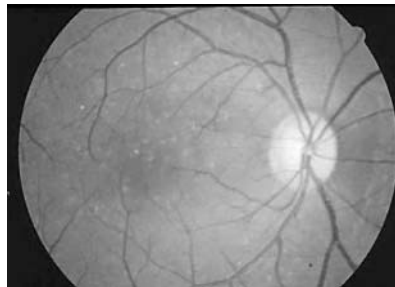


Figure 2 Fundus photograph of a monkey without detectable macular annular reflex in an eye with multiple macular drusen.

linear regression analysis confirmed that the ophthalmoscopic visibility of the macular annular reflex was significantly and negatively correlated with the number and total area of the drusen in the foveal region (p<0.001), visibility of the retinal nerve fibre layer in the temporal fundus region (p<0.001), and age (p=0.01).

The results suggest that the detectability of the macular annular reflex depends on presence and amount of non-exudative age related macular degeneration. It is parallel to other studies in which the visibility of the macular annular reflex decreased with increasing optic nerve damage, presumably because the loss of optic nerve fibres and retinal ganglion cells decreased the height of the macular annular wall and because of that, its ophthalmoscopic visibility.^{2,5} From a clinical point of view, it may suggest that examination of the macular annular reflex may be useful in screening patients for age related macular degeneration. The presence of the macular annular reflex may be taken as hint for the anatomic integrity of the fovea.

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Spontaneous bilateral giant tears of the retinal pigment epithelium

In 1981, Hoskin *et al*¹ described retinal pigment epithelial tears as a newly recognised severe complication of pigment epithelial detachment. Retinal pigment epithelial tears, which may occur either spontaneously or after laser photocoagulation to treat pigment epithelial detachment and choroidal neovascularisation (CNV) in diseases such as age related macular degeneration (AMD), usually cause sudden visual loss at the time of tearing. We report a case of spontaneous bilateral giant tears of the retinal pigment epithelium (RPE).

Case report

A 79 year old woman was referred on 18 January 2002, because of sudden visual loss in the left eye of 2 weeks' duration. In October 2001, the patient had undergone bilateral phacoemulsification and lens implantation by her local ophthalmologist. She had no apparent complications post-operatively, and the postoperative visual acuity (VA) was 20/250 in the right eye and 20/20 in the left eye; however, she noticed sudden decreased vision in the left eye on 3 January 2002, and visited the local ophthalmologist 5 days later.

When she presented to our hospital, her VA was 20/200 in right eye and hand movements in the left eye. The intraocular pressure was 18 mm Hg in the right eye and 19 mm Hg in the left eye. The external eye examination, pupillary responses, and results of slit lamp examinations were normal in both eyes except for poor mydriasis. Intraocular lenses were fixed in the capsular bag in both eyes. Results of fundus examination showed bilateral widespread pigment epithelial detachments overlying areas of bare choroid, which measured 7×8 disc diameters in the right eye and 9×10 disc diameters in the left eye, and adjacent sheets of retracted and rolled RPE (fig 1). A fluorescein angiogram of the right eye demonstrated hyperfluorescence of the denuded choroid in the early phase, which lightened slightly in the late phase, that blocked fluorescence corresponding to the retracted RPE, and appeared to have cystoid macular oedema (figs 2, 3). A fluorescein angiogram of the left eye disclosed persistent intense hyperfluorescence of the exposed

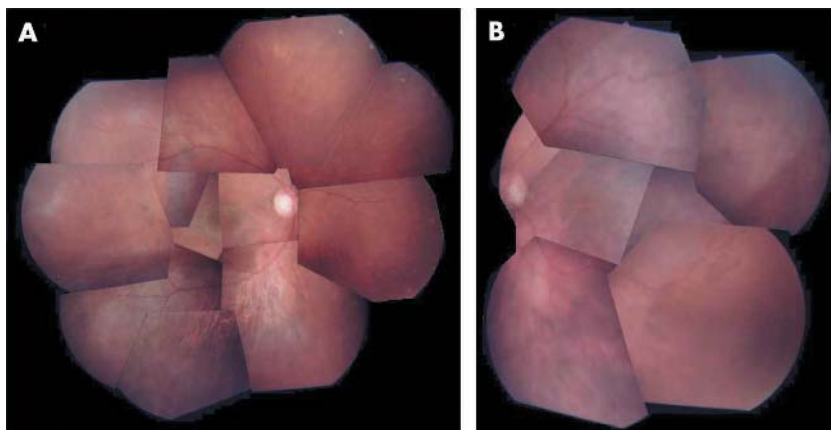


Figure 1 (A) Composite fundus photograph of the right eye. (B) Composite fundus photograph of the left eye. Widespread pigment epithelial detachments overlay areas of bare choroid and adjacent sheets of rolled retinal pigment epithelium.

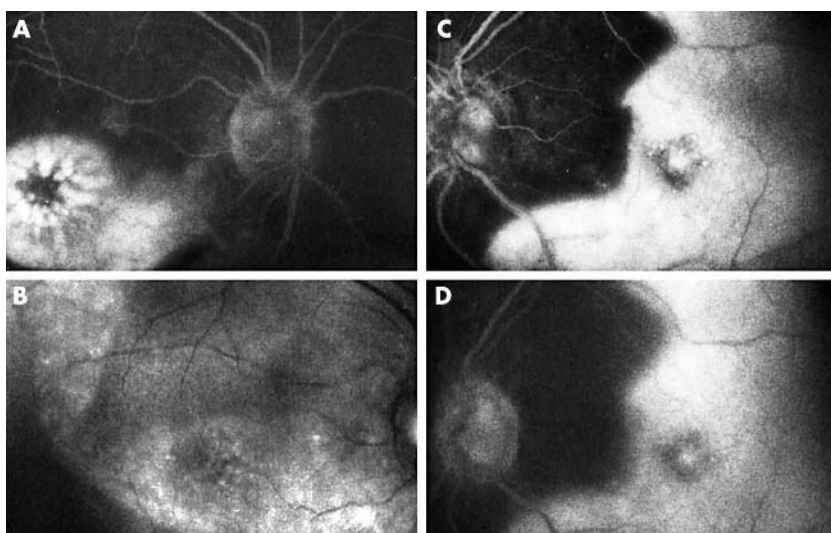


Figure 2 (A) Fluorescein angiogram (FA) of right eye in the early phase. (B) FA of the right eye in the late phase. (C) FA of the left eye in the early phase. (D) FA of the left eye in the late phase. The angiogram of the right eye shows hyperfluorescence of the denuded choroid in the early phase, which lightened slightly in the late phase. The angiogram of the left eye shows persistent intense hyperfluorescence of the choroid.

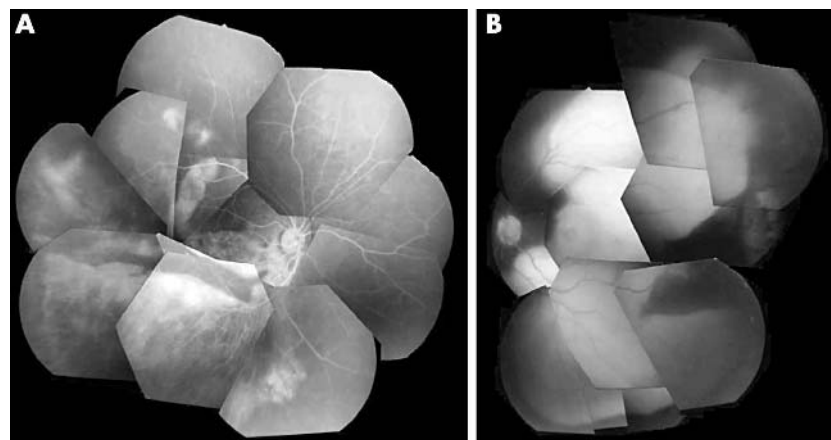


Figure 3 (A) Composite fluorescein angiogram (FA) of the right eye. (B) Composite FA of the left eye. Persistent blocked fluorescence corresponds to the rolled RPE.

choroid, blocked fluorescence consistent with the rolled RPE (figs 2, 3). An indocyanine green (ICG) angiogram of the left eye revealed fluorescence of the large choroidal vessels in the area of the bare choroid and no obvious evidence of CNV. Fundus examination using scanning laser ophthalmoscopy with a diode laser (780 nm) sharply defined the folded RPE (fig 4). From these findings, we diagnosed bilateral tears of the RPE.

Comment

In this case, the fluorescein angiogram showed ill defined light hyperfluorescence in the right eye and well defined intense hyperfluorescence in the left eye, corresponding to the region of the exposed choroid and pigment epithelial detachments. The ICG angiogram of the left eye demonstrated persistent light hyperfluorescence consistent with the bare choroid. On fluorescein angiogram, intense hyperfluorescence was reported in an area of exposed choroid when a RPE tear occurred, and over time the edges were not clearly defined and the fluorescence lightens because of proliferation and infiltration of the pigment epithelial cells on the bare choroid along the margin of the tear.² In an ICG angiogram, it then was reported that hyperfluorescence of an area of exposed choroid in the late phase indicates that the tear may be fresh because of tissue staining in Bruch’s membrane by leakage from the choriocapillaris.² Accordingly, we identified the RPE tears in our patient as an old tear in the right eye and a fresh one in the left eye.

Many reports have been published that a RPE tear is caused by photocoagulation to treat CNV and pigment epithelial detachment in diseases such as AMD because scarring and retraction of the RPE by photocoagulation may result in tangential tractional forces along the RPE that weaken it.¹ Lois *et al*⁴ reported that low intraocular pressure after trabeculectomy causes a RPE tear because of mechanical stress between Bruch’s membrane and the RPE following increased subretinal fluids caused by leakage from the choriocapillaris. There have been no reports that cataract surgery causes a RPE tear, but the possibility that it caused the tear in the left eye in this case cannot be completely excluded. However, in our case, we thought that there was little relation between cataract surgery and the tear, because no complications occurred during surgery and intraocular inflammation after surgery was unremarkable. Although we considered that the RPE in our patient might be weak by nature, there was nothing in the family history or the presence of systematic diseases that affected the connective tissue.

In the present case, the tears measured 7×8 disc diameters in the right eye and 9×10 disc diameters in the left eye. Although the large size of the pigment epithelial detachment might be important in the pathogenesis of RPE tears,⁵ most tears in previous reports were no more than about 5 disc diameters. Accordingly, the tears in this case were much larger compared with previous reports and also bilateral.

In this case, fundus examination using scanning laser ophthalmoscopy with a diode laser defined the folded RPE more sharply than any other examination. It may be useful to observe the rolling shape of the RPE. In conclusion, the possibility that cataract surgery caused the RPE tear in the left eye cannot be completely excluded, but this case

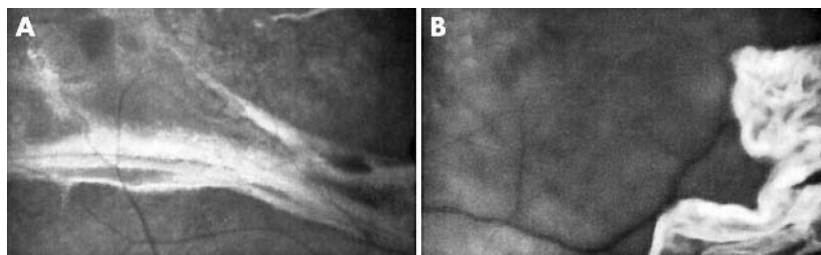


Figure 4 (A) Fundus photograph of the right eye using scanning laser ophthalmoscopy with a diode laser. (B) Fundus photograph of the left eye using scanning laser ophthalmoscopy with a diode laser. The retracted RPE is well defined.

represented a rare report of spontaneous bilateral giant tears.

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Ocular findings as a presenting sign of hydroa vacciniforme

Hydroa vacciniforme (HV) is an unusual photosensitivity disease of unknown aetiology which starts in childhood and is characterised by vesiculopapular eruptions on the exposed area of the body.^{1,2} Ocular manifestations of this disease are uncommon but can include conjunctivitis, vesicular eruptions of the conjunctiva and cornea that resemble phlyctenular keratoconjunctivitis,³ corneal infiltration with vascularisation,⁴ and keratouveitis.^{5,6} However, no cases of HV have been reported in the ophthalmic literature in over 40 years, and in contrast with previously reported cases, to our knowledge, this is the first case of a patient with HV who presented initially only with ocular findings.

Case report

A 6 year old Indian boy was referred to the Proctor Foundation with a 3 month history of recurrent, self resolving episodes of redness, pain, and photophobia in his right eye associated with a "bump" on his temporal conjunctiva. Aside from an episode of "cold sores" on his lips 2 weeks before his presentation, he had no cutaneous complaints.

On examination, visual acuity was 20/20 right eye and 20/25 left eye. The conjunctiva of the right eye was injected temporally, and the inferotemporal cornea had a faint anterior and diffuse deep stromal haze with vessels, consistent with an interstitial keratitis. The patient was given a presumed diagnosis of phlyctenular keratoconjunctivitis and treated with topical corticosteroid drops. Three months later, his symptoms returned in association with a vesicular crusting reaction of his lower lip and upper ears. A conjunctival scraping was obtained for polymerase chain reaction testing, and a purified protein derivative (PPD) and chest x ray were ordered to rule out herpes simplex virus and *Mycobacterium tuberculosis*, respectively, as causative aetiologies of the patient's findings. The tests yielded negative results.

Twenty three months after his initial presentation, the patient returned with an acute, unilateral, granulomatous, anterior uveitis in the left eye and vesicular crusting of his lips and upper ears. The uveitis responded to treatment with topical corticosteroid drops. Serological testing for varicella zoster virus IgG, toxoplasma IgG, erythrocyte sedimentation rate (ESR), angiotensin converting enzyme (ACE), lysozyme, rapid

plasma reagin (RPR), and fluorescent treponema antibody absorption (FTA-abs) test were all negative.

Six months later, the patient returned with red eyes and vesicular skin lesions of his ears (fig 1A), lips (fig 1B), arms, and fingers. Slit lamp examination revealed a sclerokeratitis temporally in both eyes (fig 1C and D). Both corneas were slightly oedematous temporally with deep stromal vessels. There was also a mild iritis in the left eye. Oral prednisone was started to treat a possible systemic inflammatory cause for his sclerokeratitis, and a papulovesicular lesion of the ear was biopsied. Serological testing for ANA, ANCA, anti-SNA, anti-SS-A, anti-RNP, and anti-Smith was performed; all results were negative.

Histopathological examination of the biopsied lesion revealed an epidermotropic lymphoid infiltrate with focal epithelial necrosis consistent with the diagnosis of hydroa vacciniforme (fig 2A). The infiltrate was of T cell lineage, confirmed by immunoperoxidase staining, with diffuse expression of CD3 (fig 2B); scattered CD8 positive lymphocytes were present (fig 2C). In situ hybridisation identified the presence of Epstein-Barr virus encoded small nuclear RNA in a minority (~10%) of the lymphocytes present, suggesting the diagnosis of a hydroa vacciniforme-like lymphoproliferative disorder (fig 2D). Genotypic analysis via a polymerase chain reaction method revealed no evidence of a clonal rearrangement of T cell receptor genes.

The patient was treated for hydroa vacciniforme with oral prednisone, ganciclovir, and precautions about ultraviolet light exposure. Since starting therapy for hydroa vacciniforme, he has not had any flares of ocular inflammation, and he has only suffered one episode of dermal inflammation. At the last follow up visit, 40 months after his initial presentation, the patient demonstrated no ocular inflammation, and his best spectacle corrected visual acuity was 20/20 both eyes. He is currently being maintained on ganciclovir therapy. The patient's parents

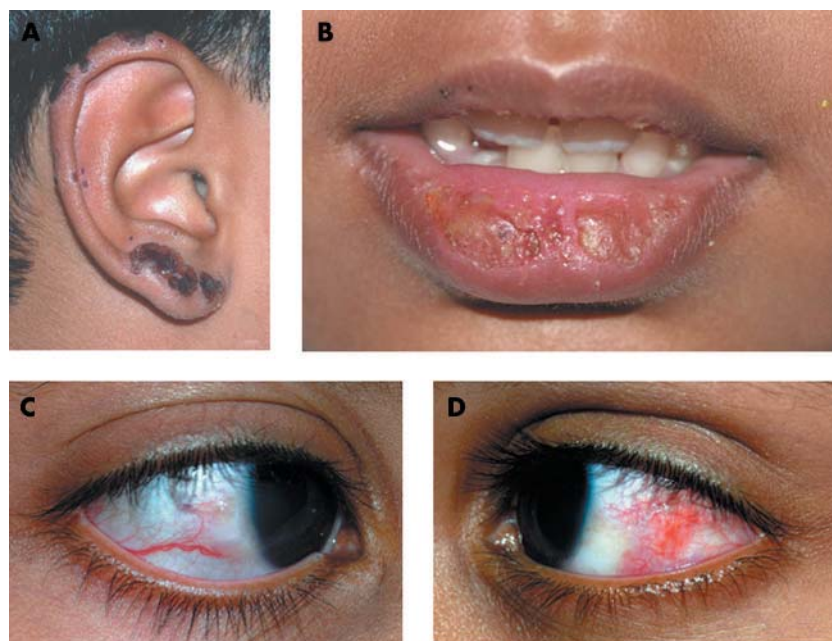


Figure 1 Hydroa vacciniforme lesions on the left ear (A) and lower lip (B). Sclerokeratitis temporally in right (C) and left (D) eyes.

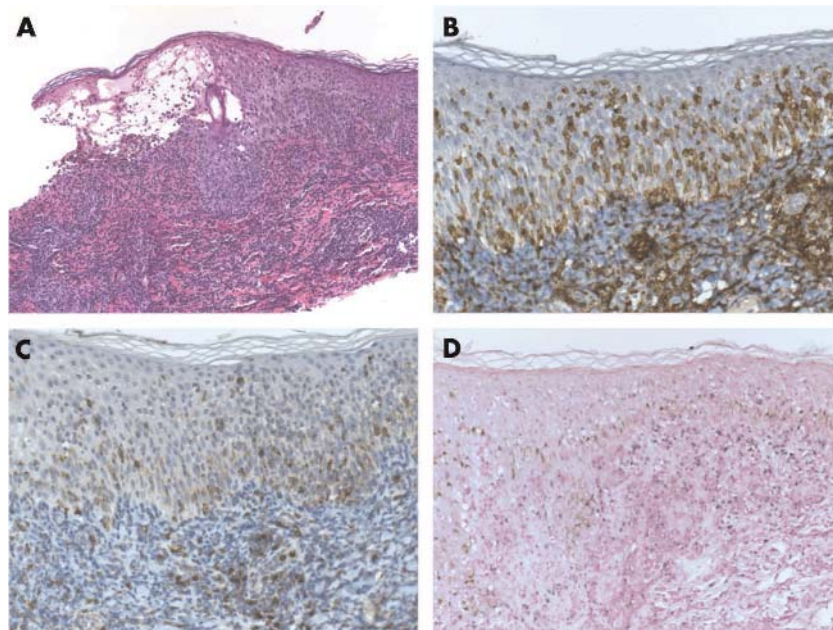


Figure 2 (A) Dense infiltration of lymphoid cells with epidermal necrosis consistent with hydroa vacciniforme (haematoxylin and eosin, original magnification $\times 40$). (B) Immunoperoxidase staining demonstrating diffuse expression of CD3 (original magnification $\times 100$). (C) Immunoperoxidase staining demonstrating scattered staining for CD8 (original magnification $\times 100$). The immunoperoxidase chromagen in (B) and (C) is diaminobenzidine (DAB) with a haematoxylin counterstain. Appropriate positive and negative control staining was also observed (data not shown). (D) In situ hybridisation demonstrating the presence of Epstein-Barr virus encoded small nuclear RNA transcripts in a minority of the lymphocytes (original magnification $\times 100$). The antisense probe in this preparation shows dark black nuclear staining in positive cells, while the sense (control) probe demonstrated no nuclear labelling (data not shown). The counterstain is nuclear fast red.

deny recalling a history of Epstein-Barr virus (EBV) infection in the past.

Comment

Hydroa vacciniforme was initially described by Bazin in 1862,⁷ and the estimated prevalence of this disease is at least 0.34 cases per 100 000.⁸ Patients typically present with vesicles or bullae on an erythematous base that occur primarily on light exposed body areas and develop within several days of sun exposure. With time, these lesions become progressively necrotic and ultimately heal with varioliform scars.⁹

Although laboratory testing has revealed no haematological, biochemical, or immunological abnormalities in affected patients, recent investigations have found that the cutaneous lesions of hydroa vacciniforme are associated with latent infection with the EBV,^{1-2,10} and in situ hybridisation confirmed the presence of EBV RNA synthesis in our patient's skin lesions.

Although many dermatologists recognise that EBV associated hydroa vacciniforme-like skin lesions may have malignant potential, it is not yet clear whether this disease is inflammatory or neoplastic.¹⁰ Iwatsuki and associates² have recently reported that three of their six patients with atypical hydroa vacciniforme progressed to overt haematological neoplasms 2–14 years after onset of their cutaneous findings. Chen and associates¹¹ subsequently reported a patient with a CD8+ cutaneous T cell lymphoma that presented with, rather than progressed from, hydroa vacciniforme-like skin lesions. Together, these reports suggest that hydroa

vacciniforme may not only progress from a smouldering stage to a lymphoid malignancy, but that it could itself be a lymphoid neoplasm. Therefore, our patient may be at increased risk for the development of an EBV related lymphoma, for which he will be monitored closely.

Ocular involvement secondary to hydroa vacciniforme is uncommon and typically occurs coincidentally with an outbreak on the face.³ Occasionally, ocular findings occur at a later time than cutaneous findings, which may be the result of the protection afforded by the eyelids.⁴ Although his later ocular findings occurred simultaneously with facial lesions of hydroa vacciniforme, in the very beginning, our patient manifested only ocular symptoms and findings, including an interstitial keratitis. To our knowledge, this is the first case of hydroa vacciniforme in which ocular findings preceded the onset of cutaneous lesions. Therefore, based on our report, the differential diagnosis for interstitial keratitis in young children should include hydroa vacciniforme.

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An unusual strategy for fixation in a patient with bilateral advanced age related macular disease

Patients with central scotomas must use peripheral retina in place of the damaged fovea. Many patients exhibit a "preferred" retinal locus (PRL) for fixation.^{1–4} Previous studies have only described monocular fixation behaviour. This case report describes a patient who successfully uses a novel strategy of observing with two non-corresponding PRLs in different eyes for different tasks.

Case report

A 78 year man attended the clinic with a 7 year history of exudative age related macular disease (AMD) in the right eye and an 18 month history of exudative AMD in the left eye. The patient reported using his right eye for distance vision and his left eye for reading. He covered the contralateral eye for both tasks. He has no history of amblyopia. As a young man, the patient used his right eye for rifle shooting. He is right handed.

On fundus examination, both eyes show disciform scars at the macula, with a larger lesion in the right eye. Best corrected visual acuity was 0.92 logMAR (6/48) in the right eye and 0.60 logMAR (6/24) in the left. Contrast sensitivity, measured using a Pelli-Robson chart, was 1.05 log units in each eye.

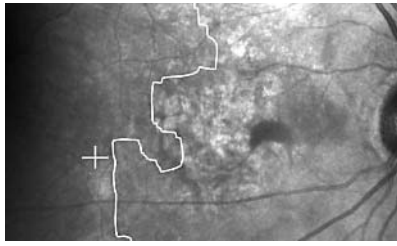


Figure 1 Scanning laser ophthalmoscope image of the right eye. White cross shows fixation centre, white line shows perimeter of dense scotoma.

With optical correction (using hyperocular lenses) reading speed was 85 words/minute, using the left eye. "Fluent" reading can be defined as being faster than 80 words/minute.³

Fixation behaviour was measured for each eye using a scanning laser ophthalmoscope (SLO). The patient was asked to observe a cross-shaped target of height 2.5° for a period of 10 seconds. Fixation stability was assessed during this task by calculation of the bivariate contour ellipse area (BCEA).⁶ The BCEA is a measure of the area of an ellipse which encompasses a given proportion of fixation points (in this case, 68%). Smaller BCEA values correspond to more precise fixation. BCEA values were 14 900 minutes of arc² for the right eye and 5360 minutes of arc² for the left. BCEA values for normally sighted observers are typically around 450 minutes of arc².⁷

The size of the dense scotoma was measured using SLO microperimetry, with stimuli being Goldmann III size targets of 200 cd/m² presented for 200 ms.⁸ Digitised SLO images were recorded (figs 1 and 2).

Comment

The left eye had better distance visual acuity, a smaller dense scotoma and a less peripheral, more stable PRL than the right eye. It is unsurprising that this patient uses this eye for reading. Unexpectedly, he found his right eye (which has poorer distance visual acuity) to be of more use for navigation and other distance tasks. Such visual behaviour can not be explained on the basis of the retinal lesions. It is assumed that the previous dominance of this patient's right eye must play a part in determining which eye is preferred for distance vision. Examination of the SLO images shows a large area of healthy retina adjacent to the PRL in the right



Figure 2 Scanning laser ophthalmoscope image of the left eye. White cross shows fixation centre, white line shows perimeter of dense scotoma.

eye whereas in the left eye the PRL is constrained by the optic disc and the macular lesion.

Although the PRLs are in the same quadrant of retina in each eye, the PRL in the right eye is further away from the previously normal fovea than that in the left. The fact that the patient covers his better seeing left eye while looking to the distance reinforces the fact that these loci are not in corresponding retinal locations. On detailed questioning, the patient cited the greatest difficulty with his vision being for wiring a plug or setting a combination lock on a suitcase: tasks requiring good binocular function.

This patient's behaviour suggests that for distance vision, a large "window" of functioning retina is of more use than a smaller region of retina with better visual acuity. It also indicates that it is possible to use different, non-corresponding preferred retinal loci in each eye for different tasks. It is not straightforward to predict which retinal location, or even which eye, patients will use from clinical features alone.

This patient has selected different PRLs for near and distance vision to partially ameliorate the symptoms of his macular disease. Although unable to perform detailed binocular tasks, he is able to navigate successfully, to read correspondence, and to remain independent.

Acknowledgements

The authors thank Jenni Turner for referring the patient to us and the patient for his enthusiastic cooperation in the writing of this case report. MDC is supported by Guide Dogs for the Blind Association ophthalmic research grant 2000–29a. SAK is supported by a Colin Kunkler Memorial Fellowship.

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MAILBOX

Potential complications of phakic IOLs

I read with interest the case report of Ashraff *et al.*,¹ where a posterior chamber phakic intraocular lens (PCPIOL) was used in a pseudophakic eye with axial myopia and pseudoexfoliation for the management of anisometropia. I would like to highlight a potential problem in such eyes: dislocation of PCPIOL into the vitreous cavity.

PCPIOLs are inserted blindly behind the iris and, depending on the design, allow their haptics to rest at the structures of the posterior chamber or float in it. Ultrasound biomicroscopy (UBM) identified haptic-zonules contact and lens rotation for the implantable contact lens (ICL)² and the phakic refractive lens (PRL),³ although these PCPIOLs are intended to fixate at the ciliary sulcus and float in the posterior chamber respectively. Because of this potential haptic-zonules contact and lens rotation of PCPIOLs the entire zonular apparatus should be intact and healthy.

Pseudoexfoliation is characterised by progressive zonular disruption and axial myopia by zonular weakness and both conditions may lead to zonular defects. Although phakodonesis and iridodonesis may point towards zonular insufficiency, those signs may be absent in a number of eyes with occult zonular defects as shown in UBM studies.⁴ Such zonular defects may result in spontaneous dislocation of the PCPIOL into the vitreous cavity. Two cases have been described already where PCPIOLs dislocated into the vitreous cavity through such defects. Kaya *et al.*⁵ reported a case of dislocation of a silicone PCPIOL into the vitreous cavity following mild head injury 3 weeks postoperatively in a highly myopic eye (–19 DS). Another case of dislocation of a myopic PRL into the vitreous cavity has been reported by the European Clinical Trial with PRL group (Philipson B. PRL (phakic posterior chamber IOL)—the 12 month results of the European clinical trial. Presented at the XXI Congress of the ESCRS-Munich 2003). I have recently reported a case of spontaneous dislocation of a PRL into the vitreous cavity in a young healthy female with high myopia 2 months postoperatively (spherical equivalent –19.5 D).⁶

The reported cases stress the importance of health and integrity of zonular apparatus in the long term stability of PCPIOLs. Since pseudoexfoliation is a progressive disease that may lead to progressive zonular disruption and spontaneous IOL-bag dislocation into the vitreous cavity even many years after cataract surgery,⁷ I think that PCPIOLs should not be used in pseudophakic eyes with pseudoexfoliation.

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BOOK REVIEW

ABC of Eyes, 4th ed.

P T Khaw, P Shah, A R Elkington. London: BMJ Publishing Group, 2004, pp 93; £25. ISBN 0 7279 1659 9.

The *ABC of Eyes* by consultant ophthalmologist P Shah and professors P T Khaw and A R Elkington and is now one of the most well established introductory textbooks to ophthalmology. Using a symptom based approach that characterises the ABC series, this book comprehensively covers all of the most common complaints in ophthalmology. It owes its success to its renowned simplicity and straightforward explanations, which appeal to the wider audience of readers who are not experts in the field. The fourth edition has been fully updated with an accompanying CD-Rom for those who prefer e-books to printed ones. This new edition continues to describe the ABCs of eyes with superb accomplishment.

The contents of the book begin with an introductory chapter that takes the reader through history taking and examination techniques in ophthalmology, specifying what may be achieved without the use of specialised equipment and when to refer to a

specialist. The following chapters describe the diagnosis and management of essential topics like the red eye, trauma, glaucoma, squints, and cataracts. New chapters have been added to this fourth edition—on age related macular degeneration and the global impact of eye disease. Summary tables provide a quick and concise reference to the main text and tip boxes give useful hints that draw from the authors' wealth of clinical experience. Clinical signs are well illustrated by colour photographs. Complicated microsurgical techniques and physiological mechanisms are effectively explained using clear and understandable diagrams.

The main strength of the book is the authors' ability to describe complex concepts in simple accessible terms for the professional and the layperson. Since I first used this textbook as a medical student, each successive edition has been improved on and updated without any loss of clarity. This latest edition includes important recent advances in ophthalmology, such as photodynamic therapy for age related macular degeneration. With its comprehensive list of support organisations for those affected by visual impairment in the United Kingdom, this book is also a useful resource for practising ophthalmologists and the general public alike. The authors have also considered the global impact of visual impairment and blindness in their new chapter, a topic that is rapidly gaining increasing recognition with the World Health Organization's "Vision 2020: the right to sight" initiative to eliminate avoidable blindness by 2020. As a basic reference text to ophthalmology, there is isn't a topic left uncovered, but this is not a practical manual to help the layperson manage eye disease themselves. Instead, the authors rightly recommend referral to an eye specialist where appropriate.

I have no doubt that there will be future editions of the *ABC of Eyes* and that the book will continue to maintain its popularity. There is future scope in developing the accompanying CD into a more interactive tool—for example, as an aid to diagnosis.

Overall, this book deserves to be on the shelves of every junior doctor, GP, nurse, and member of the public with an interest in ophthalmology.

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NOTICES

4th International Congress on Autoimmunity

The 4th International Congress on Autoimmunity will take place 3–7 November 2004 in Budapest, Hungary. The deadline for the receipt of abstracts is 20 June 2004. Further details: Kenes International Global Congress Organisers and Association Management Services, 17 Rue du Cendrier, PO Box 1726, CH-1211 Geneva 1, Switzerland (tel: +41 22 908 0488; fax: +41 22 732 2850; email: autoim04@kenes.com; website: www.kenes.com/autoim2004).

Ophthalmic Anesthesia Society

The 18th Annual Meeting of the Ophthalmic Anesthesia Society will be held on 1 – 3 October 2004 in Chicago, USA. For further details: Ophthalmic Anesthesia Society (OAS), 793-A Foothill Blvd, PMB #119, San Luis Obispo, CA 93405 USA (tel: 001 805 534 0300; fax: 001 805 534 9030; email: info@eyeanesthesia.org; website: www.eyeanesthesia.org).

Glaucoma Society Silver Jubilee Meeting 2004

The Silver Jubilee Meeting and Dinner for the Glaucoma Society will be held on 3 December 2004 at the Royal College of Physicians in Regents Park, London. The meeting will take place between 8.30am and 5pm and the dinner will be held between 6.30pm and 10pm. For further information, please contact: Janet Flowers, Administrator, 29 Quarry Hill, Grays, Essex, RM17 5BT (tel: 01375 383172; e-mail: glausoc@ukeire.freeseve.co.uk).

Amsterdam Retina Debate

The Amsterdam Retina Debate will be held on 10 December 2004 at the Academic Medical Centre, Amsterdam, The Netherlands. For further information, please contact: Nicolaes Tulp Institute; tel: +31 20 566 8585; fax: +31 20 696 3228; email: retinadebate@amc.uva.nl

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LETTERS

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Disappearance of eyelid xanthelasma following oral simvastatin (Zocor)

The major risk factors for coronary heart disease include smoking, elevated blood pressure, and elevated serum cholesterol.¹ Risk reduction starts with identification of those at risk and then alteration of factors such as discontinuation of smoking, lowering of blood pressure, and reduction of serum cholesterol. Patients who should have blood cholesterol testing include those with family history of premature coronary heart disease or hyperlipidaemia, personal history of coronary heart disease, or clinical evidence of elevated lipids with features of xanthelasma, corneal arcus under age 50 years, and cutaneous xanthomas at any age.¹ Two of the latter clinical features are ophthalmic and detection relies on the ophthalmologist.

Xanthelasma appear as multiple yellow placoid lesions in the periocular skin and represent a concentration of lipocytes in the dermis.² There are numerous methods to manage the cosmetic appearance of xanthelasma, which typically involves surgical excision or laser ablation.³ We report a novel approach to management using oral cholesterol lowering medication and patience.

Case report

In 1992, a 68 year old male smoker with a history of hypertension and elevated serum cholesterol was referred for evaluation of a newly diagnosed iris mass. On examination, the visual acuity was 20/20 in both eyes. The mass was diagnosed as a benign iris naevus and observation was advised. Coincidental bilateral medial canthal and upper and lower eyelid xanthelasma were detected (fig 1A). The largest xanthelasma measured 16 mm in diameter. Observation was advised with tentative plan for surgical excision in the future. The patient was advised to continue his antihypertensive medications and anticholesterol medication (oral simvastatin (Zocor) 20 mg once daily). At the 6 month follow up the iris nevus was stable and the xanthelasma persisted. Yearly examinations were advised. The patient did not return for 10 years. Surprisingly, the xanthelasma had

completely resolved, leaving no clinical trace of subcutaneous lipid (fig 1B). He continued on his medications and serum cholesterol was normal.

Comment

In the Lipids Research Clinics Program Prevalence Study, xanthelasma and corneal arcus were associated with increased levels of serum cholesterol and low density lipoprotein cholesterol (LDL-C), especially in young males.⁴ People with either lesion had increased odds of having type IIa dyslipoproteinaemia. Adjusted odds ratios for ischaemic heart disease in participants with xanthelasma and corneal arcus were generally increased. The study concluded that the clinical findings of xanthelasma or corneal arcus, especially in young people, helped to identify those with plasma lipoprotein abnormalities.⁴

Management of patients with elevated LDL-C include both low cholesterol diet and cholesterol lowering medications, the most popular of which are the statins. There are currently five statin drugs on the market in the United States and these include lovastatin (Mevacor, Altacor), simvastatin (Zocor), pravastatin (Pravachol), fluvastatin (Lescol), and atorvastatin (Lipitor). The major effect of these medications is to lower LDL-C by slowing down the production of cholesterol and by increasing the liver's ability to metabolise the LDL-C in the blood. Statins reduce LDL-C by approximately 40% and produce a modest increase in high density lipoprotein-cholesterol (HDL-C). These medications are given daily in the evening to take

advantage of the fact that the body makes more cholesterol at night. Statins reduce measured blood LDL-C within 4–6 weeks. In a study of 20 536 patients, this resulted in long term reduction in coronary heart disease, stroke, and mortality.⁵

Simvastatin is derived synthetically from a fermentation product of *Aspergillus terreus*. Simvastatin is hydrolysed to an inhibitor of an enzyme responsible for cholesterol synthesis. In the Multicenter Anti-Atheroma Study, simvastatin slowed the progression of atherosclerosis, measured by vascular stenosis diameter on angiography, and decreased significantly the development of new lesions.⁶

To our knowledge, there have been no previous reports on the effect of statins on eyelid xanthelasma. A PubMed search for keywords "statin and xanthelasma" and simvastatin and xanthelasma" yielded no relevant publications. The management of eyelid xanthelasma includes surgical excision, microsurgical inverted peeling, laser inverted resurfacing, photovaporisation using carbon dioxide laser, and application of bichloroacetic acid. Patients with the highest recurrence rate are those with elevated cholesterol. These local treatments do not address possible systemic associations. By observations in this report, we suggest that serum cholesterol be evaluated and if elevated, oral statin combined with dietary cholesterol restriction might result in resolution of xanthelasma over time, but, more importantly, reduction of patient cardiac risk.

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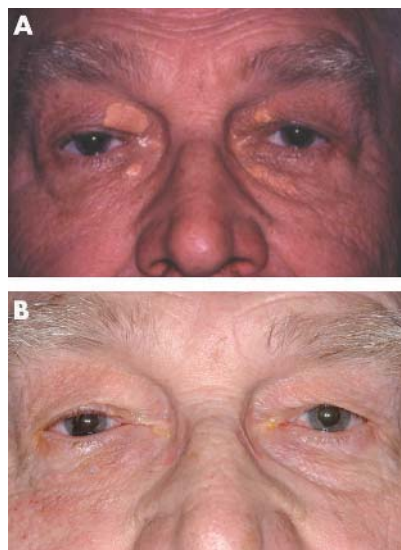


Figure 1 A 68 year old man with hypertension and elevated cholesterol and bilateral upper and lower eyelid xanthelasma. He was on oral simvastatin for hypercholesterolaemia. (A) January 1992. At presentation, the multifocal yellow xanthelasma are noted. (B) April 2002. After 10 years lost to ophthalmic follow up, the patient returned with complete resolution of xanthelasma.

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New onset diplopia: 14 years after retinal detachment surgery with a hydrogel scleral buckle

In 1979, the hydrogel explant (Miragel, Waltham, MA, USA) was introduced as a scleral buckling material in the surgical management of retinal detachment.¹ It was widely used in the 1980s and early 1990s as it was initially believed to be well tolerated, less prone to infection, and easy to manipulate.² However, long term complications related to swelling and fragmentation of the explant have been reported over recent years,^{3–6} resulting in discontinuation of its use in 1995.

Case report

A 36 year old healthy man presented on 2003 with symptoms of mild right ocular discomfort. Past ocular history included a right retinal detachment repair 14 years previously, using a 907 (3×5 mm) Miragel scleral buckle (Miragel, Medical Instruments Research Associates, Waltham, MA, USA), sutured to the inferior sclera. On examination, visual acuity was 20/120 right and 20/20 left. There was no diplopia or limitation of eye movements. What was thought to be a small conjunctival cyst was noted inferiorly but, otherwise, the ocular examination was unremarkable and the retina was secure.

A year later (2004), he presented with increasing marked right ocular discomfort and diplopia in all fields. His visual acuity was unchanged, but there was marked restriction of elevation and reduction in adduction of the right eye and binocular diplopia in all fields of gaze. A tense swelling of the inferior conjunctiva was noted (fig 1, top), intraocular pressure was normal, and the retina was flat with a moderate anterior buckle effect. Computed tomography (CT) (fig 1, bottom) demonstrated a right orbital circumferential soft tissue mass surrounding the lower half of the globe with a small area of calcification. The initial diagnosis was a postoperative giant conjunctival cyst and the patient underwent surgery.

Intraoperatively, exploration revealed no conjunctival cyst, but a large encapsulated scleral buckle. The explant was friable, gel-like, and translucent, but could be removed in one piece (fig 2). A 3 mm diameter area of scleral thinning associated with calcification was found underlying the buckle inferotemporally. At 1 month follow up the patient was asymptomatic with no diplopia, unrestricted extraocular movements, and the retina was flat.

Comment

Hydrogel explants are composed of a low molecular weight hydrophilic material that is water permeable. These explants have a tendency to absorb water over the years and increase dramatically in size. The resulting complications range from a non-tender subconjunctival mass to intraocular or external extrusion.^{3–6} The long time lapse from buckle surgery may result in a high misdiagnosis rate. Kearney *et al*⁶ reported 17 eyes of



Figure 1 Top: Clinical photograph of the right eye showing bulging of the inferior fornix. Bottom: Coronal computed tomographic scan showing a circumferential soft tissue mass surrounding lower half of the globe and a small area of calcification on the inferotemporal sclera.

patients with complications related to hydrogel explant swelling. In nine cases the initial diagnosis was incorrect, being mainly Graves' disease, idiopathic orbital fibrosis, and a subconjunctival inclusion cyst.

In our case, there was a profound increase in the explant volume during a 14 year period. The resulting diplopia and restriction of extraocular movement as well as the clinical evaluation mimicked a giant orbital inclusion cyst. The correct diagnosis was only made intraoperatively. Scleral thinning and necrosis as seen in our case has been reported previously,⁷ resulting in intraoperative vitre-

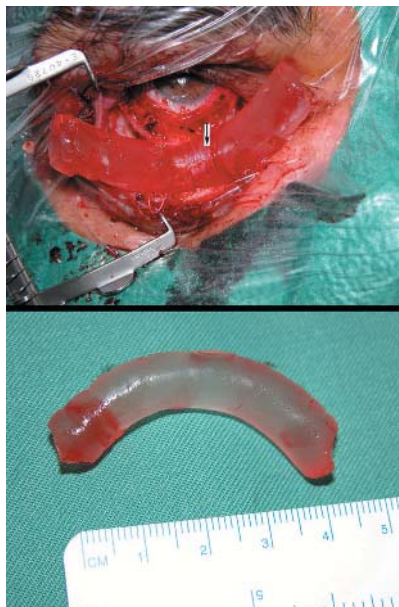


Figure 2 Top: Intraoperative photograph showing the swollen hydrogel buckle under the inferior rectus muscle (arrow). Bottom: The hydrogel buckle after removal.

ous leak after removal of the expanded explant.⁸ In our patient, there was an area of thinned sclera, but the surrounding calcification and the early removal of the explant prevented vitreous leak.

It is important to note that patients who have undergone scleral buckling with hydrogel explants before 1995 are at risk of developing this complication. Symptoms of progressive diplopia, pain, and restriction of extraocular muscle movement in these patients should also raise the possibility of explant expansion. The assistance of a retinal surgeon may sometimes be required because of the increased risk of scleral thinning and leakage of liquid vitreous intraoperatively.

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Inverse globe retraction syndrome complicating recurrent pterygium

Often larger and more aggressive than the original lesion, recurrent pterygia can cause visual symptoms that are most often secondary to their mechanical effects on the cornea.¹ We report a case of inverse globe retraction syndrome (that is, retraction during abduction) due to the restrictive effect of a recurrent pterygium and the management of this complication.

Case report

A 28 year old man without a medical history or ocular symptoms underwent pterygium excision in his left eye with a superotemporal conjunctival autograft and intraoperative mitomycin C. Three weeks postoperatively, he noted a feeling of pressure in the left eye

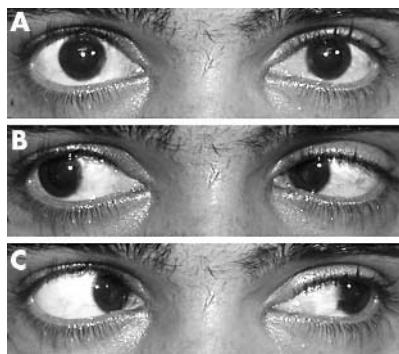


Figure 1 The patient's appearance at presentation in (A) primary gaze, (B) right gaze, (C) left gaze. There is relative enophthalmos in the left eye that increases during left gaze. During right gaze, adduction in the left eye occurs with less effort than abduction in the right eye.

and diplopia during left gaze. Two months postoperatively he presented to us and his ophthalmic examination was significant for the following—left eye: 2 mm enophthalmos relative to right eye, recurrence of the pterygium, globe retraction during left gaze secondary to a leash effect from the recurrent pterygium, and minimal abduction deficiency (fig 1). One month later, his examination was stable and surgery was scheduled. Intraoperatively forced ductions showed -1 (on a scale of 1 to 4) limitation of abduction in the left eye. The left eye was positioned in abduction and a 6 mm vertical incision was made in the nasal conjunctival 3 mm posterior to the limbus. A 5×6 mm graft of amniotic membrane (locally procured and kept frozen before use) was sutured in the resultant gap in the conjunctiva using 9-0 Vicryl suture after the conjunctival edges were undermined. Two months following this procedure, the patient's feeling of pressure was relieved and there is neither diplopia nor globe retraction during left gaze (fig 2).

Comment

Inverse globe retraction syndrome is rare.²⁻⁵ It has been reported as being caused by medial

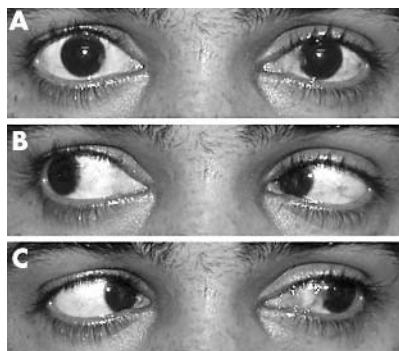


Figure 2 The patient's appearance 6 weeks after amniotic membrane placement in (A) primary gaze, (B) right gaze, (C) left gaze. There is no longer globe retraction left eye during left gaze. During right gaze, adduction in the left eye occurs with effort similar to that needed for abduction in the right eye.

rectus abnormality,² innervational misdirection,³ and secondary to restriction from traumatic tissue capture in the medial orbital wall.^{4,5} The current case demonstrates another cause for the syndrome, globe retraction as a result of a leash effect from aggressive pterygium recurrence. The risk of pterygium recurrence after initial pterygium removal is minimised by the technique of conjunctival autograft with adjunctive mitomycin C⁶; however, because aggressive recurrence is still possible initial pterygium surgery should only be performed for patients with significant cosmetic and/or functional concerns. For the management of inverse globe retraction syndrome complicating recurrent pterygium in this case, the use of amniotic membrane as a tissue spacer permitted excellent functional improvement.

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Seeing is not believing

We describe a case of posterior cortical atrophy presenting with progressive visuo-perceptual and visuospatial difficulties, but with no abnormalities on standard ophthalmological examination.

Case report

The patient, a 53 year old right handed woman, with well controlled primary generalised epilepsy, presented to her optometrist with a 1 year history of deterioration in vision. She had particular difficulties with walking downstairs and following text while reading. She could read 6/12+2 RE (with -0.75/-0.25×90 correction) and 6/12+3 (with -0.75 correction) LE. With +2.25 correction she could read N5 slowly with each eye. On subsequent ophthalmological review no significant abnormality was found on examination and no specific diagnosis was made.

Over the following months her vision deteriorated. She reported difficulties following a line while writing and was unable to tell when a glass was full when pouring a drink. Her husband thought that she was unable to see things in her peripheral vision. This culminated in her crashing her car. She did not have any memory difficulties, she had

preserved insight, and there had been no change in personality.

On admission to our unit her visual acuity was 6/18 RE and 6/12 LE with the above correction. She was able to read slowly at N5 corrected with each eye but was unable to name any of the Ishihara plate numbers including the test plate, despite being able to name the colours, trace the outline of the numbers with her finger, and read numbers in normal print. Confrontation visual fields were essentially full although she was slow to recognise objects in her peripheral visual fields owing to an apparent narrowing of attention to foveal vision and had optic ataxia, in that she was unable to localise in space, by pointing, objects placed in her peripheral visual fields. On Goldmann perimetry her visual fields appeared somewhat constricted, probably related to her difficulties with attention, but, importantly, no hemianopia was demonstrated (fig 1). Pupillary responses were normal as was fundal examination. On eye movement testing she had broken smooth pursuit eye movements, although she was able to generate voluntary saccades. The rest of the neurological examination was unremarkable.

Her mini-mental state examination score was 28/30. She had some deficits in verbal abstract reasoning and made occasional phonemic errors in speech. She had mild dyscalculia and dyspraxia, but she was able to differentiate left from right and name body parts. She had mild memory impairment, although these were mainly in tasks requiring visual input. She demonstrated simultanagnosia in that she was unable to see the whole of a picture and only described parts of it.

On testing with the cortical vision screening test¹ she passed the hue discrimination test, the word reading test, face perception test, the crowding test of letter reading and was able to detect the presence of a circle in the shape detection test but was unsure what to say if it was not present. On the symbol

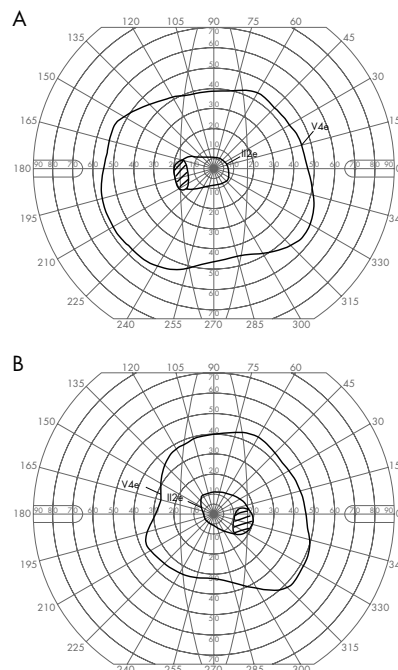


Figure 1 Goldmann perimetry (V4e and II2e).

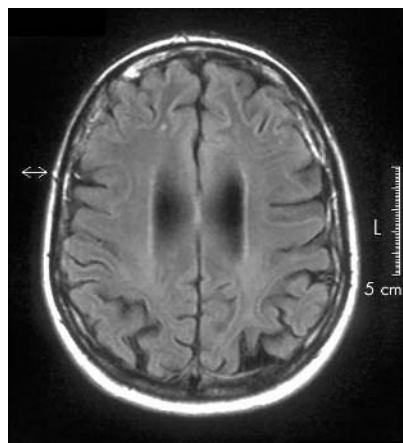


Figure 2 FLAIR MRI demonstrating mainly posterior cortical atrophy.

acuity test her Snellen equivalent was 6/18 with each eye, despite being able to read text at N5, which suggested that she had more difficulty in identifying shapes than words. She failed tests of shape discrimination and size discrimination to indicate bilateral occipital dysfunction and also failed tests of scattered dot counting and fragmented numbers to indicate right parietal dysfunction.

Blood tests and cerebrospinal fluid examination were both normal. Magnetic resonance imaging demonstrated cerebral atrophy most marked in the both posterior parietal and occipital lobes (fig 2). A diagnosis of posterior cortical atrophy was made.

Comment

This woman therefore presented with progressive visuoperceptual and visuospatial difficulties, but had no abnormalities on ophthalmological examination. She had some features of Balint's syndrome (that is, simultanagnosia and optic ataxia)² and other cognitive deficits. Her poor distance visual acuity may have been related to her poor visuospatial ability, given her good, albeit slow, near vision. Her inability to recognise any of the Ishihara plates, with otherwise normal colour vision, is probably a reflection of her other visuoperceptual difficulties, which has been reported before in similar

patients,³ although difficulty with figure-ground discrimination cannot be excluded.

Posterior cortical atrophy is a clinical and radiological diagnosis based upon the presence of occipitoparietal abnormalities with initially preserved occipitotemporal (face and colour recognition) and anterior cerebral function.^{4,5} It is thought to be as a result of Alzheimer's disease, in most cases,^{5,6} although the syndrome has been described with other pathologies—for example, sub-cortical gliosis, Creutzfeldt-Jakob disease, and progressive multifocal leukoencephalopathy.^{5,7} Although it is rare, it should be suspected in any patient presenting with visuoperceptual or visuospatial difficulties in the absence of any signs on standard ophthalmological examination. Screening tests for higher visual function deficits can then be employed.^{1,6,8}

The corollary of this is that a patient with an established diagnosis of dementia should be tested for disorders of higher visual function, because a patient with otherwise mild cognitive deficits may still be driving.⁶

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Radial optic neurotomy in combined cilioretinal artery and central retinal vein occlusion

Combined cilioretinal artery and central retinal vein occlusion (CRVO) is a rare clinical finding, first described by Oosterhuis.¹ The pathogenesis of this condition is not well established and remains controversial. Most reports postulate that the initial CRVO causes an elevation of the intraluminal capillary pressure and induces a consecutively reduced perfusion pressure at the arterial side. Since the perfusion pressure of the cilioretinal artery is lower than the central artery, it becomes relatively occluded.^{2–4} Recently Opremcak *et al* described radial optic neurotomy (RON) involving pars plana vitrectomy (PPV) and radial incision of the optic nerve to treat CRVO.⁵ We report this new surgical approach in a patient with combined cilioretinal artery occlusion and CRVO.

Case report

A healthy 64 year old woman complained of unilaterally blurred vision for the past 3 days. Her visual acuity (VA) was 20/200 in the right eye (RE) and 20/20 in the left eye (LE). The anterior segment in both eyes was unremarkable on slit lamp examination. Fundus examination RE demonstrated a whitening of the macula corresponding to an area supplied by an cilioretinal artery. The retinal veins were dilated, accompanied by adjacent retinal haemorrhages (fig 1A). The fundus of the left eye appeared normal. Fluorescein angiography (FA) RE revealed a delayed arteriovenous (AV) perfusion time of 13 seconds. Systemic evaluation of the patient did not reveal any general disease. Although treated systemically with corticosteroids⁶ and low dose heparin for 4 weeks, she developed CRVO with severe disc oedema, extensive dilatation of the retinal veins, radial orientated intraretinal haemorrhages, and cotton wool spots (fig 1B). On FA there was a reduced perfusion time of the cilioretinal artery in addition to the typical



Figure 1 Colour fundus photography of the right eye. (A) 3 days after decrease of VA. A whitening of the macula corresponding to an area supplied by the cilioretinal artery (white arrow) can be seen. The retinal veins appear dilated and sparse retinal haemorrhages are visible. (B) 1 day preoperatively. The cilioretinal artery appears with reduced diameter (white arrow), typical picture of CRVO with disc oedema without visible disc margin, extensive dilatation of the retinal veins, radial orientated intraretinal haemorrhages, and several cotton wool spots are present. (C) 10 weeks postoperatively. The optic disc appear with sharp margin, the diameter of the retinal veins are similar to those of the left eye. Chorioretinal whitening at the 2 and 4 o'clock position at the disc margin indicate the location, direction, and length of the radial cuts by RON (white arrows). Remaining signs of the CRVO, including retinal haemorrhages or macular oedema have vanished. The cilioretinal artery appears with physiological diameter.

signs of CRVO (fig 2A). Based on positive results of RON in CRVO, we offered this treatment to our patient. After she signed an informed consent, RON was performed with two radial cuts at the nasal edge of the optic disc. After 2 days disc oedema was significantly reduced with sharp visible disc margins. Two months postoperatively the retinal haemorrhages, cotton wool spots, and disc oedema resolved and her VA improved to 20/25 RE (fig 1C). FA demonstrated a physiological AV perfusion time of less than 3 seconds and no signs of an occluded cilioretinal artery (fig 2B).

Comment

Combined cilioretinal artery occlusion and CRVO are discussed as a separate clinical entity in the literature,¹⁻⁴ and its treatment by RON has not been described. Opremcak *et al* postulated that a surgical decompression of the optic disc and scleral ring by RON may contribute to an improved venous perfusion in CRVO. Our patient demonstrated additional signs of an arterial occlusion with delayed filling of the cilioretinal artery in the macula, which may induce permanent functional loss. The underlying pathomechanism of CRVO remain unknown, current discussion leans towards an intraluminal occlusion by a thrombus, increased extravascular pressure, or a combination of both as possible causes.⁷ In addition the therapeutic effect of RON is also questionable. It remains unclear as to whether RON causes a decompression of the optic disc increasing the ocular blood flow or

induces the formation of new chorioretinal shunt vessel.⁸ In our case the goal of RON was to reduce the capillary pressure, therefore increasing the perfusion in the cilioretinal artery and thus improving central vision. Patients with combined occlusive AV disease may benefit from RON by improving their haemodynamic perfusion pressure, retinal anatomy, and consecutive central visual function.

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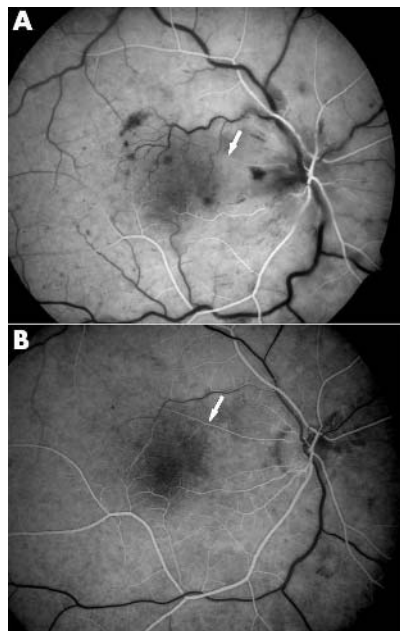


Figure 2 Fluorescein angiography of the right eye. (A) Preoperative, arterial phase (14 seconds after dye injection). A delayed filling of the cilioretinal artery becomes apparent (white arrow). The macular area supplied by the cilioretinal artery appear hypofluorescent as a result of retinal thickening. (B) 10 weeks postoperatively, arterial phase (14 seconds after dye injection). The filling of the cilioretinal artery occurs at 13 seconds and appears similar to the central retinal artery. There are no signs of non-perfused areas or ischaemia.

MAILBOX

Value based medicine

In a fine recent editorial, Drs Melissa and Gary Brown raised issues at the nexus of health policy and clinical science.¹ As utility assessment is relatively new to the visual sciences, understanding both the assumptions behind this work and the consequences of relaxing those assumptions is essential for the conduct of high quality research and appropriate interpretation of the results.

The use of community elicited utilities (that is, including people without the disease in the elicitation study) in economic evaluation should be given more than minimal consideration. Economic evaluations are intended to inform health policy makers by assessing the value society places on the cure or prevention of disease. Community based

utilities typically reflect larger estimates of utility loss than those elicited from patients and result in a more favourable analysis of the cost effectiveness of preventive interventions than those relying on patient elicited utilities.² At the same time, estimating community elicited utilities requires the development of easily understood scenarios to assist community members in understanding life with the disease,³ after leading investigators prefer to rely on patient elicited utilities. Rather than dismiss the community elicited approach, economic evaluation in ophthalmology would be greatly facilitated by development of a catalogue of community elicited utilities related to old disease developed through the standard gamble or time trade-off methods or responses to health status questionnaires that include algorithms to estimate health utilities.

While the Browns caution against the use of functionally based health related quality of life instruments (for example, the NEI-VFQ) in economic evaluation, we would like to offer an alternative explanation for this concern. Most disease specific instruments are based in psychometric theory and designed to measure change in the patient's self reported health status in investigator defined domains.⁴ Domain scores do not reflect the importance the respondent assigns to the activities, but scoring algorithms developed by the instrument designer. The result is a metric that is often meaningful to clinicians but does not reflect the value the patient or society places on the health state. This limits generalisability across disease groups, as well as investigators' ability to comment on the most efficient method to screen for, or treat, an ophthalmic condition affecting multiple areas of physical, mental, or emotional function.

Finally, the standard gamble elicitation method should not be dismissed off handedly. More frequent use of the time trade-off reflects the method's intuitive appeal rather than theoretical superiority. As opposed to the time trade-off in which the anchor event (typically, death, blindness, etc) occurs in the future, in the standard gamble the event is immediate. This provides an estimate of the person's risk preference unconfounded by time. The time trade-off consistently results in higher estimates of utility loss than the standard gamble,^{5,6} potentially resulting in an overestimation of the cost-effectiveness of treatment or prevention.

We hope that our comments will help future work to be pragmatic and theoretically sound. This is necessary if we are to properly characterise the appropriateness of our methods as well as the value of our findings.

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Authors' reply

We thank Drs Kymes and Frick for their excellent letter regarding utility analysis as a health related quality of life instrument. We agree that the use of primarily function based quality of life instruments such as the NEI-VFQ-25 may result in missing many important variables in the quality of life arena, as well as limit applicability across all diseases.¹ In contrast, preference based quality of life instruments, such as utility analysis, are applicable across all diseases and encompass all variables that comprise quality of life, as well as the weighting of those variables. Of great additional importance is the fact that preference based instruments can be used in healthcare economic analyses, especially utility analysis, while most function based instruments have not been successfully used.^{1,2}

Concerning the use of time trade-off and standard gamble utility analysis, we have found that the time trade-off methodology is easier for patients to comprehend and also is more sensitive to milder health states since there is risk aversion to the consequence of immediate death associated with the standard gamble variant.^{1,2} Froberg and Kane³ have also shown that the time trade-off method of utility has greater test-retest reliability, intra-rater reliability and inter-rater reliability than standard gamble methodology. In our experience, time trade-off utilities generally demonstrate better construct validity⁴ and a wider range between pre-intervention and post-intervention values than standard gamble utilities, thus resulting in more favourable cost utility analysis, rather than less favourable analyses.

With regard to quality of life respondents, we remain firm in our adherence to the fact that a basic pillar of value based medicine is the use of utility values obtained from respondents with a health state in question.^{1,2} We have found that utility value diminution in patients who actually have age related macular degeneration ranges from 103% to 750% greater than the decrement estimated by treating ophthalmologists for the same condition.^{4,5} This has been noted as well for non-ophthalmological health states.⁶

We respectfully disagree that community utility values generally overestimate the degree to which a disease decreases quality of life. In contrast, we and others⁴⁻⁹ have noted that community and provider participants asked to evaluate the quality of life associated with a health state using utility value analysis generally underestimate the decrement in quality of life compared to

patients with that health state. In essence, patients who have lived with a health state are those best able to ascertain the quality of life associated with that health state. And it is usually worse than others imagine.

In conclusion, we thank Kymes and Frick for their interest and comments and look forward to additional awareness in the arena of value based medicine. As increasing numbers of those who allocate healthcare resources become aware that value based medicine allows for higher quality care (by incorporating quality of life parameters that evidence based primary clinical trials often ignore) and the most efficient use of resources, it will have a considerably greater role in the delivery of cost effective, quality healthcare. When that takes place, all will benefit.

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Cystoid macular oedema with trypan blue use

We read with interest the article by Gouws *et al*¹ on the apparent increased incidence of cystoid macular oedema (CMO) in phacoemulsification patients when trypan blue was used to stain the anterior capsule.

Trypan blue has been commonly used in both anterior and posterior segment surgeries.²⁻⁴ If trypan blue does cause macular toxicity, its risks should theoretically be higher when used in posterior segment surgeries. However, studies on the use of trypan blue, both in the anterior^{2,3} and

posterior^{4,5} segments, did not show apparent toxicity.

Thus, it would be appreciated if the authors could clarify whether other potential confounders were assessed in their study, including: (1) other causes of CMO such as diabetes, uveitis, and prostaglandin use; (2) operating time since phototoxicity from the operative microscope⁶ is a risk factor for CMO development. It appears that only operations for patients in group B were performed by one surgeon, if operations for patients in group A (with trypan blue use) were done by trainees, the operative time is expected to be longer; (3) whether all patients received a fundus examination with dilated pupil after the operation. If these were only performed in patients with suboptimal visual acuities, the incidence of CMO may be underestimated.

Finally, we concur with the authors' view that we should try all means in terms of minimising any theoretical toxicities of trypan blue. It is our routine to actively remove trypan blue with the bimanual irrigation aspiration system as soon as the anterior capsule has been stained. It is very effective and the potential toxicities may be reduced.

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Authors' reply

We thank Lam *et al* for their interest. In response to their comments, as stated in the article and demonstrated in figures 1B and C, the effect persists when co-morbidity such as diabetes is removed.

Both groups' surgery was performed by the same surgeon who did not have juniors attached to the list.

Not all patients had dilated fundus examination postoperatively. Clinically significant cystoid macular oedema (CMO) is unlikely in patients with visual acuities of 6/12 or better, although subclinical CMO can be demonstrated in up to 20% with fluorescein angiography.¹

This retrospective study on a unique cohort of patients provided us with the opportunity to demonstrate a potential side effect with the use of trypan blue. A prospective trial is required to control for all the variables and confirm or refute our findings.

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BOOK REVIEW

The History of Moorfields Eye Hospital, Volume III

Ed Peter K Leaver. London: Royal Society of Medicine Press Ltd, 2004, pp 360; £30. ISBN 1-85315-580-2.

Like John Mortimer's book of a similar title this third volume of the history of Moorfields Eye Hospital is an affectionate but critical look back at the hospital that has been a major influence in many ophthalmologists' training and subsequent practice. The volume is written in a positive upbeat style but also describes some of the faults and difficulties that have beset it in the past four decades. In a complex organisation such as a hospital there are inevitable inefficiencies and problems with personalities but the author has wisely stuck to the facts and has plotted the course of the management of the hospital in a very readable way; he has sensibly avoided petty confrontations and offers a lucid outline of the course of Britain's flagship ophthalmic hospital.

The two previous histories of Moorfields described times past when ophthalmic practice changed only gradually and political upheaval was minor. The current author has been in the unique position of being involved with Moorfields throughout the 40 years he describes. Given the turmoil, both professional and managerial, that has engulfed the delivery of health care during this period he was fortunate that many of the individuals involved with the hospital were available for interview, thus providing first hand accounts of the good and bad times that affected the hospital. The various chapters outline lucidly the clinical and political changes of the time; Moorfields represents in microcosm all the influences to which NHS consultants of all

disciplines have been subjected. One special feature of the period described is that it also covers the first 40 years following the foundation of the Institute of Ophthalmology and the not always easy relationship between the hospital and the institute is recorded both openly and tactfully.

The book comprises a number of chapters outlining the various aspects of the hospital development—for example, clinical, managerial, financial, etc. The first chapter is an overview involving all aspects of the hospital during the 40 years from 1963 to 2003. It provides a concise synopsis of all the forces bearing on the hospital; not only clinical but also in terms of research, teaching, and political upheaval. Indeed, for those younger ophthalmologists entering the profession at the present time this chapter gives a concise overview of those political influences that have shaped the lives of the NHS and its staff during recent decades.

As the author points out in his preface the subsequent chapters take up the issues raised in the first chapter and analyse them in more detail. If one, therefore, picks up the book and reads it cover to cover there is a strong repetitive element but it was not really the author's intention that the book should be necessarily read in this way. Each of the later chapters is written in a stand alone fashion dealing with clinical progress, academic development, research, management, and finance so that some repetition is inevitable. The major characters in the story of Moorfields development are given due weight; particularly Professor Barrie Jones, under whose influence Moorfields progressed from a rather slow moving organisation to the establishment of all the subspecialist services we know today.

Apart from rather a large number of nautical metaphors such as "calm waters," "stormy seas," and a few petty errors of detail, such as dates, this volume is a good read, particularly if approached as the author intended. He himself has made major contributions to the standing of Moorfields Eye Hospital and the book is written in the typically clear and polished style, reminiscent of his own scientific contributions.

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NOTICES

Worldwide clinical trials for new technique for early detection of eye disease

A unique new non-invasive technique for high resolution optical imaging of the eye is receiving global acclaim. By combining two high-resolution imaging technologies, the new technique provides doctors with 3-D images of the retina, macula and the optic nerve.

For more information, contact the Media Office on 01227 823581/823100 or email MediaOffice@kent.ac.uk News releases can also be found at: <http://www.kent.ac.uk/news>

Trachoma control

The latest issue of Community Eye Health (No 52) discusses new developments in the control of trachoma. For further information please contact: Journal of Community Eye Health, International Resource Centre, International Centre for Eye Health, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK (tel: +44 (0)20 7612 7964; email: Anita.Shah@lshtm.ac.uk; online edition: www.jceh.co.uk). Annual subscription (4 issues) UK £28/US\$45. Free to developing country applicants.

EVER 2005 meeting

This will take place on 5-8 October 2005 in Vilamoura, Portugal. For further details please contact: Christy Lacroix, EVER Secretary, Kapucijnenvoer 33, B-3000 Leuven, Belgium (tel: +32 (0)16 233 849; fax +32 (0)16 234 097; email: ever@skynet.be).

World Ophthalmology Congress 2006 – Brazil

The World Ophthalmology Congress (which is replacing the International Congress of Ophthalmology) is meeting in February 2006 in Brazil.

For further information on the congress and committees, scientific program and coordinators of different areas are available at the congress website www.ophthalmology2006.com.br

CORRECTIONS

doi: 10.1136/bjo.2005.42556corr1

In the letter entitled, Norrie disease and peripheral venous insufficiency (*Br J Ophthalmol* 2004;88:1475) the ordering of the authors was incorrect. The correct order is Michaelides M, Luthert PJ, Cooling R, Firth H, Moore AT. The journal apologises for this error.

doi: 10.1136/bjo.2005.58032corr1

Owing to an author error the name of one of the authors of the paper entitled, Long term effect on IOP of a stainless steel glaucoma drainage implant (Ex-PRESS) in combined surgery with phacoemulsification, which appeared in the April issue of the journal (*Br J Ophthalmol* 2005;89:423-9) was omitted (S Gandolfi). The author list should be C Traverso, F De Feo, A Messas-Kapal, P Denis, S Levartovsky, E Sellem, F Badalà, Z Zagorski, A Bron, S Gandolfi, M Belkin. S Gandolfi is at the Clinica Oculistica, University of Parma, Italy.