Histopathology of birdshot retinochoroidopathy

Birdshot retinochoroidopathy is a chronic posterior segment inflammatory disease with a characteristic clinical presentation and strong correlation with the HLA-A29 antigen. In this report, we describe the histopathological findings in the eye of a patient with this disease.

Clinical presentation

A 49 year old white man was referred to the Proctor Medical Group in 1996 for evaluation of multifocal choroiditis (MFC). This had been an incidental finding on routine examination by his primary ophthalmologist. The patient was bothered by his refractive error, but denied problems with night or colour vision, and did not notice floaters. The patient's past ocular history was notable for myopic correction since childhood. Radial keratotomy (RK) had been performed in both eyes in 1993, with subsequent fluctuations in his refraction. His past medical history was notable for a small cutaneous melanoma removed 5 months before presentation. He had been started on oral prednisone for his MFC before his referral to Proctor.

Best corrected visual acuity was 20/20 in both eyes, and the intraocular pressures were 14 mm Hg. External examination was unremarkable, and the anterior segments showed RK scars and no inflammation. Trace vitreous cell was noted in both eyes. The optic nerve heads appeared pink and healthy, and the vasculature was unremarkable.

Multiple cream-coloured round and oval spots were scattered throughout the posterior poles of both eyes, more prominent nasally (Figs 1A and B). The spots averaged approximately 500 µm in diameter, and were deep to the neural retina. The macula in each eye was flat with appropriate pigmentation. The fundus had a very “blond” appearance consistent with the patient's complexion.

An examination for posterior uveitis included angiotensin converting enzyme (ACE) and lysozyme levels, a purified protein derivative (PPD) test, a chest x-ray, fluorescent treponemal antibody (FTA) titres, and an HLA panel. The only remarkable finding was the presence of the HLA-A29 antigen. The characteristic fundus appearance together with the HLA-A29 antigen indicated the diagnosis of birdshot retinochoroidopathy.

In December, 2001, the patient sustained a myocardial infarction and died. In accordance with the patient's wishes, the right eye was enucleated post mortem and sent to the Hogan Eye Pathology laboratory, University of California San Francisco.

Histopathological evaluation

The corneal scleral rim had been harvested (inadvertently, unaware of the history of RK) by a local eye bank. The globe was submitted in formalin and, lacking the cornea, was grossly distorted. A 4 mm segment of optic nerve was attached. Haematoxylin and eosin staining was used to evaluate the microscopic sections.

The sclera was unremarkable. The anterior segment was markedly distorted as a result of the corneal harvesting, and it was impossible to evaluate the iris and anterior chamber angle. The lens was artefactually luxated. The ciliary body and anterior choroid appeared unremarkable.

Multiple foci of predominantly lymphocytes were located at various levels of the choroid, occasionally occupying the full choroidal thickness, and abutting the choroidal vascular channels (Figs 2A, B, C). Rare plasma cells were seen, and some foci were associated with haemorrhage. A few foci contained epithelioid cells, and there was no necrosis.

The retinal pigment epithelium (RPE) did not appear involved in the underlying choroidal process.
Additional foci of lymphocytes were found surrounding some of the retinal blood vessels (Fig 2D). The neural retina showed no cellular infiltration and appeared normal, although artefactual disorganisation of the photoreceptor outer segments made evaluation of this cell layer inconclusive.

The prelaminar optic nerve head showed an additional lymphocytic focus (Fig 2E), while the remainder of the optic nerve was unremarkable.

**Conclusion**

This study finds that birdshot retinochoroidopathy is characterised by lymphocytic aggregations with their foci in the deep choroid, with additional foci in the optic nerve head and along the retinal vasculature. In all likelihood, the choroidal foci correspond to the fundus spots for which this condition is well known. These histopathological findings are consistent with the angiographic observations in patients with this condition, and may explain the electroretinographic (ERG) changes seen in the advanced stages of this disease.

The characteristic fundus spots, light degree of vitreous inflammation, HLA-A29 antigen, and lack of other contributory laboratory findings strongly support the diagnosis of birdshot choroidopathy in this patient. The HLA-A29 antigen is closely associated with this condition, and this association is so well established that the diagnosis of birdshot is increasingly considered problematic without it.

The histopathological description of our patient's eye contrasts with an earlier report describing the histopathology of a blind, phthisical eye believed to have been affected by birdshot choroidopathy. That eye showed diffuse granulomatous inflammation in the outer retinal layers, with less inflammation in the choroid. Important differences in clinical presentation between our patient and the patient described in that report include: (1) our patient had the HLA-A29 antigen, while the patient in that report did not; (2) our patient's eye was neither blind nor phthisical. In light of these differences, the histopathological findings described in this report are probably more characteristic than those reported earlier for this disease.

The fundus lesions in birdshot choroidopathy did not stand out on fluorescein angiography (FA) in this patient, and lack of fluorescence is not uncommon in this condition, and may represent "very early" phases of the birdshot lesions.

On histopathology, the neural retina, retinal pigment epithelium, and in many areas the choriocapillaris appeared unaffected by the inflammatory process, and could potentially have obscured fluorescence of the deeper structures. Many patients with advanced birdshot show optic nerve head inflammation and diffuse retinal vascular leakage on FA.

Our patient did not have these findings, although his eye did show a small optic nerve head lymphocyte focus and limited retinal perivascular infiltration. It seems likely that these early changes would have become evident on FA eventually if they had had time to advance.

Indocyanine green (ICG) angiography reveals birdshot lesions as hypofluorescent choroidal patches which outnumber those seen clinically. These patches most probably correspond to the deep choroidal lymphocytic foci seen microscopically, which are hypofluorescent because they exclude the surrounding deep choroidal vasculature. Presumably, the lymphocytic foci that characterise this condition must achieve a certain diameter, density, and perhaps inward extension before becoming apparent clinically.

Electroretinogram (ERG) changes characteristic of this disease include a preserved a-wave, with diminished amplitude and increased latency time of the b-wave, suggesting impairment of the inner retina. Retinal vasculopathy (determined angiographically), rather than the extent of RPE/choroidal complex involvement, has also been noted to correlate with electro-oculogram (EOG) changes. One may speculate that the retinal perivascular lymphocytic infiltration seen in this patient progresses, in advanced stages, to inner retinal ischaemia with the observed ERG and EOG manifestations. Electroretinography was not undertaken in our patient because initially this was not essential to the diagnosis, and subsequently the patient did not follow up in our referral centre.

This report of histopathological findings in the eye of a patient with birdshot choroidopathy represents the first such description from an HLA-A29 patient. The microscopically observed changes shed light on what the fundus spots in this condition are composed of, and to some extent explain the angiographic finding in this disease.

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Retinoblastoma and retinal astrocytoma: unusual double tumour in one eye

In the recent literature there is controversy regarding the histopathological origin of retinoblastoma (RB) and retinal astrocytoma (RA). The common origin of both tumours from a multipotential stem cell has been studied in RB cell lines Y-79 and fresh RB material with immunohistological techniques using GFAP (glial fibrillary acid protein), NSE (neuron specific enolase), photoreceptor cell markers (S-100, myelin basic protein), and synaptophysin.

The differentiation between RA and RB and tumour material.

Case report

In a 5 year old girl a divergent strabismus of the right eye was discovered. No family history of RB or phacomatosis was present. Funduscopic examination under anaesthesia showed a central white mass. Nasally inferior in the peripheral retina a second large whiteish mass with vitreous seeding on the top was discerned without abnormal vasculature.

On DNA investigation no mutation in the RBP gene was found with SSCP (single strand conformational polymorphism) technique.

Enucleation was performed within 1 week after the diagnosis RB was established. Histologically, the first, most anterior tumour was largely necrotic, but highly cellular (Fig 1A). Only few islands of vital cells with a central blood vessel were seen. The tumour cells had medium sized nuclei, with a very dense chromatin. The nuclear shape was oval to slightly irregular. Cytoplasm was scanty. There were many apoptotic tumour cells, and mitotic figures and occasional calcifications were present (Fig 1B).

The second and more posteriorly situated tumour was quite different. It showed areas with high cellularity, without necrosis. These high cellular areas were separated by areas of low cellularity, that appeared fibrous, or compact fascicular. Many calcifications were present (Fig 2A). The cells in the cellular areas had fairly small round nuclei (though slightly larger than the neuronal cells in the neighbouring retina), with a finely dispersed, somewhat granular chromatin, and occasional nucleoli. The cells in the compact fascicular areas were more spindle-shaped, but with a similar chromatin pattern. No mitotic or apoptotic figures were found (Fig 2B).

Immunohistochemically, the first, peripheral tumour stained positive for synaptophysin and negative for GFAP and neurofilament. The second, central tumour showed a negative synaptophysin, but showed strong staining for GFAP, especially in compact areas. The cells in the cellular areas only occasionally stained positive for GFAP.

Comment

Both the histology and the immunohistochemistry showed two entirely different tumours, one (the anterior tumour) clearly an RB, largely necrotic. In the second tumour, a glioma, with cellular areas resembling oligodendroglioma, the more compact “fibrous” areas resembled a pilocytic astrocytoma.

As the morphology of the two tumours clearly differed the occurrence of a “seeding” of RB, though theoretically possible, in itself is an unusual sequence of events and is not likely here. The differentiation would have increased the staining intensity for synaptophysin and may even have caused a positive neurofilament staining, but in our case both neuronal markers were negative. Also, the growth pattern of the second tumour with its intermingling of small cells (putative retinocytal) and glial components strongly suggest two different tumours.

However, that does not mean these two tumours cannot be related. We feel this case illustrates the discussion whether RB and RA are two totally different tumours, both originating in the retina, or a transitional form of simultaneous expression of neuronal and glial cells from a germline stem cell.

The differentiation between RA and RB and the possible transitional form derived from the specific glial supporting cells (Mueller cell) were investigated on RB Y-79 cell lines and tumour material.

The view that RBs are neuronal tumours, although sporadic cases may show immunohistochemical signs of partial astrocytic or Mueller's cell differentiation, has been supported by several studies.

In agreement with this finding, Gonzales-Fernandez et al report the in situ expression of photoreceptor and glial cell associated proteins in fresh RB tumour material.

Their data suggest that RB has the histogenetic potential of the immature neural retinal epithelium which can give rise to both photoreceptor and Mueller cell lineages.

These studies suggest that indications for differentiation of RB into a neuronal and a partial glial pathway.

In our opinion it has been demonstrated by many studies that both retinal photosensory cells and Mueller glial cells are derived from a neuroretinal epithelial stem cell, with the
capacity of different expression by immature retinal cells. Perhaps the occurrence of a double tumour, as our case, is therefore not so surprising. However, this case suggests, showing the clinical form of different expression of a germinal retinal neuroectodermal stem cell, that differentiation of immature retinal cells could be a tightly regulated process.

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References

Artefactual uniocular altitudinal visual field defect

Altitudinal visual field defects are commonly associated with ischaemic optic neuropathy and hemibranch artery or vein occlusion. Less commonly, altitudinal visual field defects can be seen in advanced glaucoma. Artefactual visual field defects are not uncommon; however, to our knowledge this is the first reported case of an artefactual uniocular altitudinal visual field defect due to an abnormally sensitive hemifield response with the automated Humphrey perimeter.

Case report

A healthy 61 year old woman was referred to the ophthalmology department by her optician who had noted a visual field defect in her left eye following a routine examination. The patient was asymptomatic and her past ocular history was unremarkable. Initial assessment of the visual field carried out by the optician appeared to show a superior altitudinal field defect in the left eye (Fig 1). Ocular examination revealed 6/6 corrected vision and normal intraocular pressures in either eye. There was no relative afferent pupil defect and both optic discs were healthy. Fundus examination was otherwise unremarkable. Confrontational visual field test failed to show any defect. Goldman visual field testing confirmed normal fields in both eyes. Closer examination of the Humphrey field test carried out by the optician shows the defect to be artefactual.

Comment

Altitudinal visual field defects are most commonly associated with ischaemic optic neuropathy and hemibranch artery or vein occlusion. They can also be seen in patients with glaucoma, chiasmal lesions, and optic nerve lesions such as colobomas. Hysterical or malingered patients and individuals deliberately attempting to mislead the Humphrey machine can manifest visual field defects including altitudinal defects on perimetry. In this reported case the pattern deviation plot initially appears to show a superior altitudinal field defect. However, scrutiny of the threshold sensitivities on the grey scale data reveals that the patient had somehow achieved abnormally high sensitivities in the inferior hemifield only (highest value 50 dB). The threshold sensitivities for the superior hemifield appear normal to slightly high (highest value 37 dB). Hence the pattern deviation defect is not only artefactual but also paradoxical. One can only speculate as to the cause of this artefactual field defect. Patient anxiety often leads to false positive responses and this patient had 67% false positive errors. However, it is curious that this should occur in one hemifield and in one eye only. One must always consider the possibility of either technical problem in stimulus presentation or machine software problems in unexplained or anomalous visual field defects. However, it is difficult to explain the pattern of this visual field defect on the basis of the pattern deviation plot.

Figure 1 Humphrey visual field of the left eye showing the "apparent" altitudinal field defect.
of machine failure. This case demonstrates the importance of looking at the pattern deviation in conjunction with the grey scale, threshold sensitivities and interpreting the visual field in the light of other clinical data.

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Bilateral acute anterior uveitis after alendronate

Biphosphonates are increasingly being used for the prevention and treatment of osteoporosis in women where hormone replacement therapy is contraindicated. Alendronate (Fosamax) is a potent aminobiphosphonate that reduces bone resorption and increases bone mass and therefore reduces the incidence of fractures in postmenopausal women with osteoporosis. The most common adverse effects are upper gastrointestinal, including dysphagia, heartburn, oesophagitis, and oesophageal strictures. We report a case of bilateral acute anterior uveitis following the use of alendronate (once weekly 70 mg tablet). This is the first reported case of bilateral acute anterior uveitis associated with alendronate.

Case report

A 57 year old woman had been taking oral alendronate 10 mg daily for a year without experiencing any eye problems. To simplify the method she was on “weekly” biphosphonate therapy consisting of a single weekly dose of 70 mg. Two days after the first dose she developed a painful red left eye and was seen by an ophthalmologist in Russia. She was diagnosed with left kerato-iritis and was prescribed topical atropine, dexamethasone and ciprofloxacin, and oral azithromycin. On her return to England 3 months later, she was noted to have bilateral acute anterior uveitis. The patient had no history of Sjogren’s syndrome, rheumatoid arthritis, lupus, or any other systemic disease or family history for blindness or glaucoma. She had not had conjunctivitis or keratoconjunctivitis sicca previously. The only objective finding was bilateral iris hyperemia. Treatment with topical and oral corticosteroids and topical cycloplegics resulted in resolution of the acute anterior uveitis in both eyes. Subsequent tapering of prednisolone was uneventful.

References


Effect of a YAG laser iridotomy on intraocular pressure in pigmentary glaucoma

Pigmentary glaucoma (PG) is characterised by the liberation of pigment from the iris pigment epithelium and its deposition on various anterior segment structures. The accumulation of pigment in the aqueous outflow system can result in an increase in intraocular pressure (IOP) and eventual glaucoma. Campbel1 proposed that mechanical rubbing between the concave posterior iris surface and the zonular bundles is responsible for the release of pigment granules from the iris pigment epithelium. Laser iridotomy was proposed to eliminate the reverse papillary block mechanism of pigment dispersion syndrome (PDS). Using ultrasound biomicroscopy (UBM) laser iridotomy has been shown to alter the iris configuration in PDS patients.13 However, the effect of a laser iridotomy on IOP in PG is not clear. Here we present a case of PG with active pigment release, in which substantially lower IOPs were achieved over a period following a yttrium-aluminium-garnet (YAG) laser iridotomy.

Case report

A 36 year old male patient was referred from an optometrist for high IOPs and visual field loss in 29 January 2001. We saw this young man on 6 February 2001, who has a personal and family history of blindness, diabetes, and glaucoma. He was only a recent sufferer of a systemic disease or family history for blindness or glaucoma. The only medication taken was Proppecia for treating hair loss for the past 1½ years. His visual acuity was 20/20 in the right eye and 20/20 in the left eye. IOPs were 54 mm Hg in the right eye and 52 mm Hg in the left eye by application. Slit lamp examination revealed grade 4 anterior chamber angles with hyperemia, spindles; anterior chambers that were very deep with 3+ pigment debris; and irides demonstrating radial transillumination defects and posterior bowing. Gonioscopy revealed grade 4 anterior chamber angles with very heavy trabecular meshwork pigmentation and a Sampaiolesi’s line in both eyes. Fundus examination showed cup-disc ratios of 0.5 bilaterally.

Combination timolol/trusopt and brimonidine were started in both eyes to lower the pressure. UBM examination on 9 March (Fig 1A) demonstrated posterior iris bowing and a relatively large zone of iris deposit. A YAG laser iridotomy was performed in the right eye 1 week afterwards and UBM examination showed a planar iris configuration following the laser iridotomy (Fig 1B). IOPs were 32 mm Hg in both eyes immediately before the laser. Three days later, IOPs were 17 mm Hg in the right eye and 34 mm Hg in the left. Examination revealed no anterior chamber pigment debris in the right eye and persistent pigment debris in the left. A YAG laser iridotomy was performed in the left eye on 16 March. One week later, IOPs were 25 mm Hg in the right and 18 mm Hg in the left with no pigment debris in the anterior chambers of both eyes. IOPs remained in the 20s in both eyes for several weeks. However, the IOP had risen to 28 mm Hg in the right eye and 24 mm Hg in the left on 4 April and beta-blockers were added to the glaucoma regimens of both eyes. Four months after laser therapy, the IOPs were 21 mm Hg in the right and 22 mm Hg in the left. On 4 September the IOPs were 27 mm Hg in the right eye and 25 mm Hg in the left eye. To prevent further increase in his IOP and optic nerve damage, Ahmed valve implantation combined with mitomycin C application was performed in the right eye on 16 November. Subconjunctival injections of...
5-fluorouracil were given weekly for 6 weeks after the operation. Two months postoperatively, IOPs were 24 mm Hg in the right eye and 30 mm Hg in the left with only the left eye receiving glaucoma therapy. Filtering surgery is planned for the left eye.

Comment

In PDS, the accumulation of pigment can overwhelm the aqueous outflow system, causing trabecular occlusion and collapse, and an increase in IOP. An iridotomy may be effective in stabilizing the iridium configuration by reducing the IOP gradient between the anterior and the posterior chamber. Consequently, there would be a lower chance of iridocornical contact and pigment release. Using UBM, Potash et al. and Lagreze and Funk showed the presence of iris concavity and iridocorneal contact in PDS patients and demonstrated that laser iridotomy can restore a normal iris configuration. It has been suggested that an iridotomy might reduce the incidence of ocular hypertension in eyes affected by PDS.

The ideal initial approach to treat PAG is to eliminate the source of IOP elevation. Before YAG laser iridotomy, our patient had shown posterior iris bowing and constant pigment release, demonstrated by the 3+ pigment debris in the anterior chamber. After YAG laser iridotomy, he no longer had pigment debris in the anterior chamber. The iris moved forward to the planar position, which was clearly demonstrated by UBM imaging. The true mechanism for the pressure lowering is unknown. The iridotomy may reduce the pressure by ending the chronic irritation (and consequent inflammation) to the iris from the zonular rubbing and from the iris being stretched in the bowed position. Another possibility is that aqueous suppression has a role in the temporary improvement of IOP shortly following the iridotomy. A further mechanism may be that phagocytosis by the trabecular meshwork cells cleared much of the remaining pigment granules in the inter-trabecular spaces. This may have temporarily reduced the outflow obstruction and lowered the IOPs. Our patient had shown lower IOPs for a short period following YAG laser iridotomy. In young patients who show constant active pigment release, laser iridotomy seems to have an effect on the short term IOP control and may have possible long term benefits.

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Reference


Rhodotorula rubra endophthalmitis in an HIV positive patient

Rhodotorula species are imperfect basidiomycetous yeasts belonging to the family Cryptococcaceae and are widespread throughout nature.1 In many clinical situations Rhodotorula spp are considered a contaminant, but when identified in normally sterile sources such as blood, cerebrospinal fluid and vitreous the cultures are significant for myotic infection.2 Human disease is extremely rare with Rhodotorula spp but opportunistic cases of endocarditis, septicaemia, meningitis, verruculosis, and peritonitis are reported in the literature.3 Ocular infections include chronic dacryocystitis, keratitis,4 chronic postoperative endophthalmitis,5 and corneal lamellar graft infection.6 It is becoming increasingly important to clinically recognise and possibly treat such opportunistic organisms as an increasing number of patients are immuno-compromised by either iatrogenic or disease related causes. Immuno-compromised status, indwelling catheters, recent surgery of trauma, and injecting drug use appear to be the major factors leading to infection.7,8 This report presents a case of endogenous Rhodotorula rubra infection in an HIV positive male.

Case report

A 26 year old man was referred to the Ottawa Eye Institute by the infectious disease department with a 6 week history of floaters and a 2 week history of minor pain, tearing, injection, and decreasing vision in the right eye. Vision had declined to hand movements 1 week before examination. He was systemically asymptomatic, afebrile, and had no localising symptoms.

Past medical history was significant for injecting drug use, a diagnosis of HIV with concomitant lung abscess in 1991, and osteomyelitis of the L3 vertebrae in 1999. He had no previous ocular history. He was taking 95 mg of methadone daily and denied use of antiretroviral medications. He has an 11 pack year smoking history and denied alcohol use.

Review of systems disclosed multiple track marks on both arms, but was otherwise unremarkable. Best corrected visual acuity was hand movements in the right eye and 20/20 in the left eye. Four plus cells were present in the anterior chamber and vitreous cavity of the right eye. Multiple superior retinal vessel supplies were present. The patient refused vitrectomy at this time. Blood cultures, urine cultures, and chest x ray were normal. The patient was discharged home with close monitoring. He was partially compliant with a home remote and stereo eye chart regimen.

Cultures of the vitreous aspirate grew Rhodotorula rubra on the fifth day after culture and the specimen was sent to the provincial laboratory for confirmation. The patient showed no improvement clinically. A second vitrectomy was performed because of concern about dissemination of fungus systemically.

Comment

Endogenous endophthalmitis accounts for 2–15% of all endophthalmitis cases and fungi account for over half of all cases.9 Fungaemia leads to metastatic seeding of organisms in the choroid and subsequent intraocular infection, although in many cases the patient is systemically asymptomatic and blood cultures may be negative. Bilateral involvement is present in 25% of cases.10 Despite current antibiotic therapy and surgical advances the prognosis for patients with endogenous endophthalmitis remains disappointing because of factors such as organism virulence, compromised host status, and delay in diagnosis.11 The best treatment regimen is unresolved with reports of amphotericin B.
5-fluorocytosine, and a combination of both medications with or without vitrectomy. Despite aggressive medical and surgical management our patient was eventually offered enucleation as the eye had no light perception and was a possible nidus for infection. Future investigations into prevention, optimal diagnostic techniques, and appropriate management are needed.

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Ultrasound biomicroscopy: “fisherman’s tale”

Ultrasound biomicroscopy (UBM) has been proved to be a valuable investigative tool in the evaluation of suspected anterior segment ocular foreign bodies. This is especially so in cases involving small, non-metallic objects and where the foreign body is not visible by slit lamp biomicroscopic examination or where a clear history of trauma is not forthcoming.

Case report
A 51 year old fisherman presented to the ophthalmic casualty department with a 2 week history of localised discomfort and redness on the temporal aspect of his right eye. He had no significant ophthalmic history and did not give a history of trauma.

Slit lamp examination of the anterior segment was unremarkable on the left side and revealed an inflamed nodular mass on the temporal aspect of the right sclera (Fig 1).

There was no visible foreign body or conjunctival tear in that region. At this point the suspected clinical diagnoses included inflammatory nodular scleritis and a lymphoma or other neoplastic mass. The patient was referred to the ophthalmic ultrasound clinic for UBM (Fig 2).

UBM revealed a high reflectivity discrete echo source (arrow) embedded deep in the sclera, surrounded by a low reflective mass (granuloma).

The appearance was consistent with a foreign body and, on direct questioning, the patient admitted to possible injury while filleting fish on his boat. An excisional biopsy was performed under local anaesthesia. Post-operative recovery was uneventful on a topical regimen of Betnesol-N eye ointment four times daily for 2 weeks; the patient’s symptoms ceased after that.

Serial sectional and histopathological examinations were carried out. This revealed a florid foreign body granulomatous reaction directed against some degenerate material of animal origin. In several levels a barbed cellular structure highly suggestive of a fishscale was seen (Fig 3).

Comment
UBM is a high resolution ultrasound using high frequency transducers (50–100 MHz) that was developed by Pavlin et al in 1990. It is a non-specific imaging technique that allows a highly magnified image of the anterior segment to be obtained. It is capable of producing images in the living human eye to a depth of approximately 4 mm at an axial and lateral resolution approaching 20 μm.

The high resolution provided by this technique combined with its non-invasive and non-ionising nature make UBM a very attractive investigative method in the evaluation of suspected anterior segment foreign bodies.

This is so even when no clearcut history of trauma is forthcoming as evidenced by this fisherman’s tale and the fact that UBM has been used successfully in the past to demonstrate ocular surface and intraocular foreign bodies.

In this case UBM enabled us to obtain sub-surface images of the conjunctiva and sclera at the area of interest that was not possible with slit lamp biomicroscopy. It actually influenced management by raising the suspicion of a foreign body and justifying an excisional biopsy and its subsequent deeper histological sectioning when, clinically, a provisional diagnosis of conjunctival lymphoma or another neoplasm was being pursued that would not have necessarily been treated by an excisional biopsy.

We recommend the use of UBM in some cases of suspected foreign bodies in the sub-surfaces of the conjunctiva and sclera when the nature and extent of the lesion is in doubt.

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References

Rapid improvement of chronic interstitial keratitis with acitretin

Acitretin, a synthetic retinoid, which regulates the proliferation, differentiation, and keratinisation of epidermal cells, is usually used to treat severe psoriasis or ichthyosis. The main side effects are teratogenesis and mucocutaneous forms of xerosis such as chelitis and blepharoconjunctivitis. The biological effects of acitretin in non-epidermal cell lines, and
especially those derived from ocular tissues, could explain the beneficial actions of acitretin in diseases other than skin disorders. We report a drastic improvement in tuberculosis related interstitial keratitis in a patient treated with acitretin for severe psoriasis.

Case report
A 21 year old Moroccan man was referred to our ophthalmology department in 1992 with severe chronic bilateral interstitial keratitis associated with skin lesions. Initial examination revealed epidermal lesions clinically and histologically consistent with pustular psoriasis. The patient also had a history of tuberculosis, with likely onset at age 3 months and first treatment at age 7 years, with isoniazid, rifampicin, and streptomycin. Visual acuity was 20/400 in both eyes. Slit lamp examination revealed confluent interstitial opacities in both corneas, hindering examination of the anterior and posterior segments of the eyes. From 1992 to 1997, successive treatment courses with calcipotriol, psoralene, plus ultraviolet A irradiation and methotrexate for the skin lesions failed to improve the ocular lesions, and neither did steroid therapy given to control systemic signs of inflammation. The lesions, and neither did steroid therapy given to control systemic signs of inflammation. The left eye became blind to periods of ocular inflammation during exacerbations of the skin disease. Another two corneal grafts were attempted in the left eye during the subsequent 3 years, with poor long term results. The left eye became blind and painful and was removed. Surgery was not attempted on the right eye.

In 1998, treatment was started with acitretin (30 mg/day for 1 month, then 20 mg/day) because of a relapse of the skin disease. Within 1 month acuity in the right eye had improved to 20/100 and there was a marked improvement in corneal interstitial opacities (see Fig 1). For the first time in 6 years, detailed examination of the anterior and posterior segments of the eye was possible. Synchiae were observed from the iris to the lens, together with posterior opacities in the lens, likely secondary to previous episodes of ocular inflammation. The aspect of the retina was normal. Two years after the onset of acitretin treatment, the right cornea remains clear.

Comment
Both the rapid improvement in the interstitial keratitis following acitretin introduction for this patient’s skin lesions, and the fact that none of the previous treatments for the psoriasis had improved the ocular lesions, strongly suggest that acitretin may be beneficial in some patients with severe interstitial keratitis threatening corneal opacities. This may be explained by the activity of acitretin on corneal cells, as suggested by experimental studies and by a case report of acitretin related keratoconus. Further laboratory studies and clinical trials are needed to determine whether the adverse effects of acitretin are offset by its beneficial action in chronic interstitial keratitis.

Peripheral retinochoroidal anastomosis after central retinal vein occlusion
Central retinal vein occlusion (CRVO) may lead to the spontaneous formation of shunt vessels running over the optic nerve head. This may contribute to improve retinal venous drainage. The occurrence of shunt vessels elsewhere in the fundus in these patients has not been reported yet. We report here a case of retinochoroidal venous anastomosis through a peripheral chorioretinal scar that revealed itself after the occurrence of CRVO, suggesting that elevated retinal venous pressure triggered the creation of the venous bypass.

Case report
A 70 year old man presented in our department with loss of vision in the left eye which had started 2 months previously. At presentation, visual acuity was 20/200. Fundus examination showed the presence of dilated veins and scattered haemorrhages in four retinal quadrants associated with macular oedema. In addition, in the superotemporal area a large atrophic chorioretinal scar underlying the superotemporal retinal vein was present (Fig 1, left). The patient had no history of eye trauma, inflammation, or photocoagulation. Fluorescein angiography showed that within the scar there was no detectable connection between the arterial and choroidal circulations (Fig 1, right). At a control examination 1 month later, the superotemporal vein overlying the scar was interrupted (Fig 2, left). ICG videoangiography demonstrated that the superotemporal retinal vein was anastomosed to the underlying choroidal vein, with drainage of upstream but not downstream venous blood (Fig 2, right). At that time, rubecious irides was present, associated with widespread capillary non-perfusion. Retinal panphotocoagulation was performed which led to regression of rubecious. Final visual acuity was 20/200.

Comment
Shunt vessels over the disc are frequently observed after CRVO. They are possibly caused by the elevation in capillary pressure that dilates pre-existent retino-opticociliary capillaries. Shunt vessels occurring outside of the disc have been reported in association to a chorioretinal scar, but to our knowledge not during CRVO. In our case, pre-existing

References
retinochoroidal anastomosis or choroidal new vessels may have been present within the scar before CRVO until the increased retinal venous pressure due to CRVO increased the retinochoroidal flow through the scar. However, on the first fluorescein angiogram, there is no evidence of pre-existing anastomosis or new vessels. We therefore cannot conclude on the precise mechanism relying the anastomosis to the CRVO. The anastomosis did not appear to have significantly impacted upstream or downstream venous drainage. Moreover, there was occlusion of the venous segment downstream of the anastomosis site. This indicates, as observed after laser induced chorioretinal anastomosis, that anterograde and retrograde drainage is not always present together in the anastomosis site. This may be because a higher difference in pressure between retinal and choroidal veins is needed to promote retrograde drainage.

The authors have no proprietary interest in the present study.

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References

Loss of myelinated retinal nerve fibres in diabetic retinopathy

Myelinated retinal nerve fibres usually remain unchanged but loss of myelin can occur either from primary demyelination (for example, optic neuritis) or secondary to retinal ganglion cell damage. We present a case of extensive loss of myelinated retinal nerve fibres as a result of progressive diabetic retinopathy. To our knowledge, this is a rare observation.

Case report
A 64 year old African-American woman with diabetes mellitus for 11 years, hypertension for 5 years, and hypercholesterolaemia presented, after being lost to follow up, with progressive blurred vision in both eyes. There was no history of glaucoma, laser treatment, or any other significant medical or neurological disease. Visual acuity was counting fingers in the right eye and 20/400 in the left eye. The pupillary examination, gonioscopy, and applanation tonometry were normal. A moderate nuclear sclerosis was present. Funduscopy examination revealed severe proliferative diabetic retinopathy with vitreous haemorrhages in both eyes. The left eye had peripapillary myelinated retinal nerve fibres (Fig 1) with partially cicatricial retinal neovascularisation and low lying tractional retinal detachments along the superotemporal and inferotemporal arcades. There was diffuse macular oedema with cystoid changes. Fundus photographs taken 6 earlier years revealed severe non-proliferative diabetic retinopathy with macular oedema in both eyes and much more extensive peripapillary myelinated nerve fibres of the left eye (Fig 2).

The area of myelinated retinal nerve fibres had markedly decreased allowing visualisation of the previously obscured retinal vessels and optic disc margin. The loss of myelinated retinal nerve fibres was more pronounced at the superior and inferior disc margins corresponding to the areas of tractional retinal detachment.

Comment
Myelinated retinal nerve fibres are usually benign, developmental abnormalities found on routine examination. They occur when myelinisation of the optic nerve continues beyond the lamina cribrosa to involve the retinal nerve fibres. On fundoscopy, they typically appear as a solitary white or grey-white striated patch which follows the nerve fibre layer. In a series of 1986 consecutive necropsies the incidence of myelinated retinal nerve fibres was found to be 0.98%.

Myelinated retinal nerve fibres usually remain unchanged. Loss of myelin can occur either from primary demyelination—for example, in optic neuritis or secondary to retinal ganglion cell damage. The latter can be caused by ischaemia, inflammation, degeneration, or compression anywhere along the path of the retinal ganglion cell from the inner retinal layer to the lateral geniculate body. Reported examples involving inner retinal ischaemia as a cause of myelinated retinal nerve fibre loss include branch retinal artery occlusion and central retinal artery occlusion. In diabetic retinopathy, ischaemic changes occur in the inner retina, leading to damage to the ganglion cell and atrophy of the nerve fibre layer. This is the mechanism responsible for the loss of myelinated retinal nerve fibres in our patient. Retinal tractional retinal detachment, usually a late complication of diabetic retinopathy, most likely contributed to the atrophy. Ischaemic damage to the retinal nerve fibres is common in early diabetic retinopathy. Chihara et al. using retinal nerve fibre layer photographs, found retinal nerve fibre layer defects to be common in eyes with diabetic retinopathy. We report the observation that inner retinal ischaemia secondary to diabetic retinopathy can result in the loss of myelin in the myelinated retinal nerve fibres.

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References
Microscopic fragmentation of ophthalmic surgical sponge spears used for delivery of antiproliferative agents in glaucoma filtering surgery

Trabeculectomy remains the standard surgical glaucoma procedure against which other procedures are measured. The incidence of failure of trabeculectomy in higher risk cases can be reduced with the use of the adjuvant antiproliferative agents 5-fluorouracil and mitomycin C. The standard method of delivery of these adjuvant agents to the surgical site is via several small pieces of microsurgical sponge spear.

A recent change in our practice in augmented trabeculectomy has been to use cut pieces of polyvinyl alcohol (PVA) sponge, instead of cut pieces of cellulose sponge for antiproliferative agent delivery to the surgical site. This change in practice was because the PVA sponges seemed to be less friable after cutting than the cellulose sponges, and less likely to leave remnants behind after removal. We carried out this study to try to confirm these suspicions. In addition, we wanted to assess whether residual microfragments of different sponge surgical spears routinely used for blood and fluid absorption during glaucoma drainage surgery are left behind.

Materials, methods, results

Four different microsurgical sponge spears were assessed: two brands of cellulose ophthalmic spears (Cellulose Spears, Eyetec Ophthalmic Products, Altomed Ltd, UK and Visispear Eye Sponge, Visitec, Becton Dickinson and Company, USA), one brand of PVA ophthalmic spear (PVA Spears, Eyetec Ophthalmic Products, Altomed Ltd, UK), and one brand of reprocessed PVA ophthalmic LASIK spear (Lasik Spear Classic, Eyetec Ophthalmic Products, Altomed Ltd, UK).

Each type of sponge spear was cut with sharp scissors into small fragments, which were then soaked in 5-fluorouracil 25 mg/ml or mitomycin C 0.2 mg/ml. Fresh cadaveric pig eyes were prepared with a fornix based conjunctival flap as if for trabeculectomy. In each eye, four antiproliferative agent soaked sponge fragments were placed with non-toothed forceps for 4 minutes on the scleral bed beneath the fornix based conjunctival flap. The sponges were removed with non-toothed forceps, and the subconjunctival space was irrigated with 10 ml balanced salt solution. The sclera and conjunctiva were fixed and processed for microscopic examination.

We also assessed whether the whole microsurgical sponge spears used for intraoperative blood and fluid absorption leave behind any microfragments. The same four types of sponge spear were each used to wipe away balanced salt solution on fresh cadaveric pig sclera, prepared with half thickness scleral incisions to simulate initial creation of a scleral flap in glaucoma drainage surgery. The sclera and conjunctiva were fixed and processed for microscopic examination.

Before processing the cadaveric pig eyes, it was found that cellulose sponge was identifiable by microscopy by its birefringence in plain polarised light. PVA and reprocessed PVA were found to stain with periodic acid Schiff (PAS) (Fig 1). The observer of the microscopy slides was blind as to which sponge spear had been used in each case.

In four repeated experiments, cut pieces of both brands of cellulose microsurgical sponge
sponges left behind microfragments at the conjunctiva-sclera interface, when soaked with 5-fluorouracil or with mitomycin C (Fig 2). The PVA ophthalmic sponges and the reprocessed PVA ophthalmic sponges did not leave behind any microfragments, whether soaked with 5-fluorouracil or mitomycin C. When whole sponge sponges were used for fluid absorption, none of the four types of microsurgical sponge spear left any microfragments behind on the scleral bed. Full results are shown in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Sponge absorption</th>
<th>Sponge pieces</th>
<th>Sponge pieces</th>
<th>Whole fluid</th>
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<tbody>
<tr>
<td>Cellulose sponges, Eyetec</td>
<td>+</td>
<td></td>
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</tr>
<tr>
<td>Visspeare eye sponge, Viscitec (cellulose)</td>
<td>+</td>
<td></td>
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<tr>
<td>PVA sponges, Eyetec</td>
<td></td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Laski Spear Classic, Eyetec (reprocessed PVA)</td>
<td></td>
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Comment

This study demonstrates that in cadaveric porcine eyes cut pieces of cellulose sponge used for antiproliferative agent delivery in glaucoma filtering surgery leave behind microfragments at the conjunctiva-sclera interface. Cut pieces of sponge soaked in 5-fluorouracil or mitomycin C will not leave behind microfragments. This is in keeping with the marketing claims for PVA sponges. Antiproliferative agent delivery in trabeculectomy is safe when soaked in antiproliferative agents.

Antiproliferative agent delivery to the surgical site in trabeculectomy aims to reduce fibrosis, thereby promoting a functioning filtering bleb. Retained microfragments of antiproliferative soaked cellulose sponge at the surgical site may adversely affect the surgical outcome. Cellulose sponge can be regarded as a slowly degradable material. The time needed for the total disappearance of cellulose sponge from subconjunctival tissue in rats is longer than 60 weeks. Cellulose is also known to be capable of initiating a foreign body reaction in the peritoneal cavity, retained cellulose can lead to a foreign body granuloma and intestinal obstruction. Cutting of cellulose sponges, to provide smaller fragments for antiproliferative agent delivery, that is responsible for leaving friable cellulose edges.

Three times postoperatively, the vitreous haemorrhage resolved almost completely. The intraocular pressure was normal without drugs. Three weeks postoperatively, the vitreous haemorrhage resolved almost completely. The intraocular pressure was normal without drugs. Three months postoperatively, BCVA was 6/12 with a closed macular hole and significant decrease of central scotoma in the left eye.

**Case 2**

A 65 year old man with essential hypertension presented with mild cataract and ERM with disturbing metamorphopsia in the left eye. BCVA was 6/12 and 6/18 in the right and left eye, respectively. PPV and removal of ERM with ICG stained ILM was performed. The periooperative course was uneventful. On the sixth postoperative day, the patient returned after she had bumped her head gently against a table. Significant vitreous haemorrhage was found. Ultrasonography revealed no retinal detachment. On the 12th postoperative day, a haemolytic glaucoma occurred with an intraocular pressure of 55 mm Hg, which was successfully controlled by a combination of systemic and topical antiglaucomatous drugs. Three weeks postoperatively, the vitreous haemorrhage resolved almost completely. The intraocular pressure was normal without drugs. Three months postoperatively, BCVA was 6/12 with no recurrence of ERM and significant improvement of metamorphopsia in the left eye.

**Vision threatening vitreous haemorrhage after internal limiting membrane peeling in macular surgeries**

Indocyanine green (ICG) dye has been used to stain the retinal internal limiting membrane (ILM) and facilitate its removal in macular hole and epiretinal membrane (ERM) surgeries. In our previous study, removal of ICG stained ILM around idiopathic macular hole was confirmed with histology. Here we report two (3.6%) cases of vision threatening vitreous haemorrhage out of a prospective consecutive series of 55 cases operated by one surgeon with ICG assisted ILM removal. We suspect that ILM peeling may expose the already compromised superficial retinal vessels in hyperensive patients, and trauma may precipitate a significant vitreous haemorrhage. Limiting the areas of ILM peeling, avoidance of trauma, and adequate control of essential hypertension may decrease the chance of such complication.

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References

Liposarcoma of the orbit presenting as an enlarged medial rectus muscle on CT scan

Primary orbital liposarcoma is extremely rare in the orbit. Only a few published cases have included imaging studies, showing findings varying from well defined, homogeneous lesions of soft tissue density to heterogeneous masses containing fat.1 We report one patient who presented with painless proptosis and double vision and had an enlargement of the medial rectus muscle on computed tomography (CT) as the sole initial imaging finding.

Case report

A 75 year old man presented with a 3 month history of painless diplopia and protrusion of the left eye. His medical history revealed only diabetes mellitus. On ophthalmic examination his visual acuity was 6/6 in the right eye and 6/9 in the left eye. There was a reddish tumoral growth in the medial canthus of the left eye, right above the insertion of the medial rectus muscle below the conjunctiva. The left eye was dislocated laterally and anteriorly, with 2 mm of propotss, limitation of adduction, elevation, and depression. A CT scan was obtained and revealed marked enlargement of the medial rectus muscle throughout its extension, with enhancement after intravenous contrast administration (Fig 1). Extensive laboratory investigation including thyroid hormones and TSH was normal except for diabetes. A trial of oral prednisone (80 mg/day) was introduced for 1 week without any improvement in his condition and therefore a transconjunctival biopsy of the lesion was performed. It revealed a pleomorphic liposarcoma and a radical tumour removal was indicated. The patient was reluctant to accept it and returned only 2 months later when there was marked enlargement of the tumour. A repeat CT scan revealed that the tumour extended to the orbital fat and was now a heterogeneous lesion with central hypodense areas circumscribed by hyperdense, contrast enhancing areas (Fig 2).

The patient underwent orbital exenteration followed by skin graft of the orbital cavity and postoperative orbital irradiation. There was complete removal of the tumour that was restricted to the orbit. The patient remained free of tumour for the following 6 years, when she died as a result of systemic complications after a femur fracture.

Comment

Despite the large amount of adipose tissue in the orbit, primary orbital liposarcomas are extremely rare, with only 27 cases previously reported.2–5 Metastatic orbital liposarcomas are also extremely rare with only a few cases documented in the literature.6 When liposarcoma occur in the orbit there is no specific pattern of involvement and the tumour presents marked diversity of clinical presentations. Our patient presented initially with a tumour restricted to the medial rectus muscle with a radiological appearance very similar to the metastatic liposarcoma reported by Fezza and Sinard.7 Contrary to their case, however, our patient did not have any history of systemic disease and did not develop tumour elsewhere in the body in a 6 year follow up period. Although preferential involvement of one extracocular muscle has been documented,8 to our knowledge none of the previously described cases of primary orbital liposarcoma was restricted to the extraocular muscle as in our case.

Although the differential diagnosis of extracocular muscle enlargement is extensive and includes Graves’ orbitopathy, myositis, carotid cavernous fistula, lymphoma, metastatic tumours, etc, our case shows that physicians should include a liposarcoma in differential diagnosis of patients in which the clinical and laboratory findings are not in accordance with other more common causes of extraocular muscle enlargement.

Concentration of intravitreally injected triamcinolone acetonide in intraocular silicone oil

For decades, corticosteroids have been known to reduce inflammation and, depending on their concentration, to suppress proliferation of cells. Applied either locally or systemically, steroids have consequently been used for treatment of various oculair diseases. Often, however, the intraocular concentrations of cortisone were not sufficiently high, or the systemic side effects were too pronounced, to effectively treat the ocular disorder. Taking into account that the eye comprises only 0.01% of the whole body volume, and considering that for achieving high concentrations of a drug at its site of action it is best to apply it directly into the region of requested action, Machemer and other researchers studied the possibility of injecting cortisone directly into the eye. Clinical studies have correspondingly revealed that a single intraocular injection of triamcinolone acetonide may be a therapeutic option as adjunctive treatment of exudative age related macular degeneration, diabetic cystoid macular oedema, and proliferative diabetic retinopathy.9,10

It has been unknown so far, how long after a single intravitreal injection, clinically detectable concentrations of triamcinolone acetonide are available in the eye. Postmortem topographic findings of patients who received an intravitreal injection of triamcinolone acetonide suggest that triamcinolone acetonide crystals remain visible in the eye up to 6 months after the injection.11 The aim of this study was, therefore, to assess the concentration of triamcinolone acetonide in silicone oil samples removed from patients who had previously undergone pars plana vitrectomy with silicone oil endotamponade.
Case report
The study included three patients (one woman, two men) with a mean age of 57.7 (SD 5.4) years. They had undergone pars plana vitrectomy with silicone oil endotamponade as treatment of proliferative vitreoretinopathy (n=2) or diabetic vitreoretinopathy (n=1). At the end of surgery, 25 mg of triamcinolone acetonide was injected into the silicone oil bubble. Silicone oil was removed 2, 5, and 8 months, respectively, after the instillation, and the concentrations of triamcinolone acetonide were determined.

The concentration of triamcinolone acetonide was 3 µg/kg silicone oil in the silicone oil sample removed from the eye which had undergone pars plana vitrectomy 4 months before the oil removal, and in which the retina remained attached after the release of silicone oil. Concentration of triamcinolone acetonide was 61 µg/kg silicone oil in the sample removed 7 months after the instillation into the eye in which the retina was attached before the silicone oil removal, in which, however, the retina re-detached within 1 week after removal of the oil. In the sample which was removed 8 months after instillation, concentration of triamcinolone acetonide was 11 µg/kg silicone oil. In that eye, the retina was partially detached before the removal of the silicone oil, and the eye underwent a second pars plana vitrectomy.

Proprietary interest: none.

References
2 Machemer R. Five cases in which a depot steroid (hydrocortisone acetate and methylprednisolone acetate) was injected into the eye. Retina 1996;16:166–7.

Focal limbal stem cell deficiency corresponding to an iris coloboma
When the stem cells population is destroyed or their supporting stromal environment is dysfunctional, limbal stem cell deficiency (LSCD) manifests. Clinically, LSCD carries the hallmark of conjunctivalisation—that is, the corneal surface is covered by ingrowing conjunctival epithelium containing goblet cells. Conjunctivalisation is invariably associated with the destruction of the basement membrane, emergence of superficial neovascularisation, scarring, and diminished visual acuity. 3

Corneal diseases associated with LSCD can be subdivided into two major categories. 4 In the first category, limbal epithelial stem cells have been previously destroyed by a known or recognisable insult. The second category is characterised by a gradual loss of the stem cell population without a known or identifiable factor. In this second category, the limbal stromal environment, so called niche, is presumably affected progressively by different aetiologies including aniridia. 5 Although iris coloboma has been noted to be associated with corneal surface abnormalities, 6 7 no report appears to confirm if this developmental abnormality is also associated with LSCD. Here we report one such case, which manifested focal LSCD in the same area of iris coloboma.

Comment
The results suggest that detectable concentrations of triamcinolone acetonide can be found in intraocular silicone oil samples up to 8 months after its instillation. Future studies may evaluate which factors, besides the time interval after its injection, may be responsible for the varying concentration of triamcinolone acetonide.

Proprietary interest: None.

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References
2 Machemer R. Five cases in which a depot steroid (hydrocortisone acetate and methylprednisolone acetate) was injected into the eye. Retina 1996;16:166–7.

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Comment
Previously, Soong and Raizman 8 reported four patients with iris coloboma that were accompanied by corneal changes. Here, for the first time, we demonstrate that these corneal changes may represent or eventually evolve into a state of LSCD by the use of impression cytology disclosing the hallmark of conjunctivalisation. 3 These abnormal epithelial changes were associated with corneal epithelial erosion adjacent to an irregular migratory epithelium with late fluorescein staining, and superficial peripheral corneal vascularisation. Other known aetiologies for partial limbal deficiencies were excluded. The strong anatomical correlation of focal LSCD in the region of iris coloboma resembles what has been reported in patients with aniridia in which total LSCD is found invariably in eyes lacking the development of the entire iris. 9 In aniridia, these abnormal corneal changes develop as early as the first decade of age and progressed rapidly to total conjunctivalisation. 3 Mutations in the Pax6 gene are associated with a wide range of ocular abnormalities including anophthalmos, aniridia, and various anterior segments anomalies with peripheral vascularisation. 3 A reduction of Pax6 activity in heterozygotes for Pax6 mutation results in mice with aniridia and nanophthalmos in the knockout mice. 10 11 We thus speculate that a less severe alteration of Pax6 might have a role in the ocular surface changes observed in coloboma. Such a similarity between iris coloboma and Pax6 mutation prompts us to speculate that these two diseases might share the same underlying pathogenesis. This interpretation strengthens our hypothesis that deficiency in the iris development is accompanied by the abnormality of the limbal stroma that is vital to the support of limbal epithelial stem cells. Future studies dissecting into this correlation will help unravel the secrecy concerning the regulation of limbal epithelial stem cells.

Proprietary interest: None.

Case report
In 1988, a 38 year old male patient was referred for evaluation of a peripheral vascularisation in his right eye and a persistent epithelial defect in the left eye after two previous failed penetrating keratoplasties. At that time, an inferonasal iris coloboma associated with regional peripheral superficial vascularisation, and mild corneal haze was noted in the right eye, which also had a past history of amblyopia with a best corrected visual acuity of 20/200. Impression cytology performed then did not show any evidence of conjunctivalisation in the right eye. The left eye has received three additional penetrating keratoplasties (two for inadventent blunt trauma leading to wound dehiscence) and with a contact lens he could see 20/10.

In 2002, he presented with a complaint of progressive foreign body sensation and redness in his right eye. Slit lamp examination revealed a central corneal epithelial defect and peripheral superficial corneal vascularisation located in the same quadrant where an iris coloboma was present (Fig 1A). An irregular epithelium in a migratory pattern was noted in the affected corneal quadrant, where late fluorescein staining was also found (Fig 1B). Repeat impression cytology confirmed the presence of conjunctival epithelial cells and goblet cells on the peripheral cornea of this region, supporting the diagnosis of focal LSCD (Fig 1C).

Comment
Previously, Soong and Raizman 8 reported four patients with iris coloboma that were accompanied by corneal changes. Here, for the first time, we demonstrate that these corneal changes may represent or eventually evolve into a state of LSCD by the use of impression cytology disclosing the hallmark of conjunctivalisation. 3 These abnormal epithelial changes were associated with corneal epithelial erosion adjacent to an irregular migratory epithelium with late fluorescein staining, and superficial peripheral corneal vascularisation. Other known aetiologies for partial limbal deficiencies were excluded. The strong anatomical correlation of focal LSCD in the region of iris coloboma resembles what has been reported in patients with aniridia in which total LSCD is found invariably in eyes lacking the development of the entire iris. 9 In aniridia, these abnormal corneal changes develop as early as the first decade of age and progressed rapidly to total conjunctivalisation. 3 Mutations in the Pax6 gene are associated with a wide range of ocular abnormalities including anophthalmos, aniridia, and various anterior segments anomalies with peripheral vascularisation. 3 A reduction of Pax6 activity in heterozygotes for Pax6 mutation results in mice with aniridia and nanophthalmos in the knockout mice. 10 11 We thus speculate that a less severe alteration of Pax6 might have a role in the ocular surface changes observed in coloboma. Such a similarity between iris coloboma and Pax6 mutation prompts us to speculate that these two diseases might share the same underlying pathogenesis. This interpretation strengthens our hypothesis that deficiency in the iris development is accompanied by the abnormality of the limbal stroma that is vital to the support of limbal epithelial stem cells. Future studies dissecting into this correlation will help unravel the secrecy concerning the regulation of limbal epithelial stem cells.

Proprietary interest: None.
Novel nonsense mutation (Tyr44stop) of the Norrie disease gene in a Japanese family

Norrie disease (ND) is an X-linked genetic disorder causing bilateral blindness in early infancy because of severely dysplastic retinas. The major disease phenotype is a retrolental mass caused by undifferentiated, proliferated vitreous, and retina, accompanied by maldeveloped anterior segment, leading to atrophy of the eyeball. A certain number of patients show psychomotor retardation or hearing impairment as part of a multisystem disorder. After the identification of the gene for ND, various types of pathological mutations have been documented in different ethnic groups. Phenotype-genotype evaluation has clarified that a mutation in the ND gene may also be responsible for a separate clinical entity, exudative vitreoretinopathy, retinopathy of prematurity, or unclassified retinal dysplasia. The clinical distinction between sporadic ND and bilateral persistent proliferative primary vitreous (PPHV) can be difficult.

We report a novel truncating mutation of the ND gene in a Japanese family, in whom the proband was initially diagnosed with a sporadic form of PPHP.

Case report

The proband (patient 1) was the first son of non-consanguineous parents. He was born in 1993 with full term uneventful delivery and his mother noticed bilateral leucocoria 2 weeks after birth. An ophthalmologist suggested a severe case of PPHP in both eyes, and the patient underwent vitreous surgery on the right eye at 4 months of age because of the haemorrhage behind the lens. The patient was then referred to our hospital. He had normal psychomotor development and normal hearing ability. Pupils were not responsive to light and the visual acuity was no light perception in both eyes. The corneal diameter was 4 mm right eye and 9 mm left eye and band-shaped keratopathy was present in both eyes. A vascularised retrolental fibrous mass was barely visible behind the hazy lens accompanied by posterior synechiae in each eye. Ultrasonography showed a funnel-shaped retrolental mass in each eye. Scopotic electroradiograms were non-recordable. Visual evoked potential measurements revealed tentative P100 wave forms in both eyes. Eyeballs showed a gradual shrinkage in subsequent follow up studies to 7 years of age.

The parents and their second son were healthy with normal vision. The other family members had lived long in the Osaka area, Japan. According to the statements from the parents, the first child at 15 months of age had normal vision. At this phase, patient 1 was thus diagnosed as a sporadic, severe form of bilateral PPHP.

In 2000, the third son (patient 2) was born at full term with uneventful delivery. The parents noticed bilateral leucocoria at birth. On examination at 6 days of age, the pupils were not responsive to light. Corneal diameters were 9 mm in both eyes. Each eye had a clear media but showed a vascularised retrolental whitish-yellow mass with ectropion uveas and posterior synechiae. Ultrasonography showed a funnel-shaped retrolental mass in each eye with axial lengths of 16 mm in both eyes. Magnetic resonance imaging revealed a more detailed feature of the retrolental masses (Fig 1). Results of electroradiograms and visual evoked potential measurements were similar to those of patient 1. During the subsequent follow up period, the eyeballs of patient 2 showed a gradual shrinkage and he remained unremarkable in neurological or ophthalmological studies.

We obtained peripheral blood with informed consent and analysed DNA samples of patient 2, his mother, and 100 normal controls, for mutations in the ND gene. One female and three male sporadic patients with bilateral PPHP were examined simultaneously as pathological controls. Patient 1 was not accessible for the molecular genetic examination. The coding exons of the ND gene were amplified according to the published data. Sense and antisense nucleotide sequencing of the amplicons was directly determined by dye terminator autosequencing. Patient 2 had a hemizygous mutation at Tyr 44 of the ND gene—namely, an insertion of adenine (TAT to TAAT) that creates a premature terminator (Ochre) to predict elimination of the subsequent amino acids of the ND protein (Fig 2). His mother had the normal and mutant types of the gene, which was expected for heterozygotes of the disease. On the other hand, four patients with bilateral PPHP and 100 normal controls showed only wild type sequences of the relevant gene.

Comment

In Japanese families, ND gene mutations have been identified at the initiation codon (Met to Val) and codon 95 (Cys to Arg). This Japanese family shows a novel nonsense mutation (Tyr44stop) of the ND gene in a manner expected for an X-linked genetic disease. This is the fourth Japanese family with ND in whom mutations of the ND gene were identified. We are unaware of previous reports of this mutation and could find no reference to it in a computerised search utilising Online Mendelian Inheritance in Man (OMIM) or the Cardiff Human Gene Mutation Database (HGMD). Among 60 types of ND gene mutations in the literature, seven nonsense mutations are located at Ser 29, Ser 57, Ser 73, Arg 109, Cys 110, Cys 126, and Cys 128, with typical clinical features of ND. In the manner similar to these mutations, Tyr44stop in the present report presumably eliminates subsequent amino acid peptide when the gene is expressed. It is therefore likely that the present mutation has a strong effect leading to the ND phenotype.

The proband (patient 1) in the present family had been diagnosed as a sporadic form of PPHP.
of bilateral PHPV until the third male offspring (patient 2) was born blind. Magnetic resonance imaging may be superior in demonstrating the retrolental masses to computed tomography imaging or ultrasonography. Magnetic resonance imaging in patient 2 clarified a detailed feature of the intraocular abnormalities including retrolental masses, abnormal lenses, elongated ciliary processes, and microphthalmic eyes. This type of morphological appearance would not be inconsistent with PHPV. It is technically difficult to distinguish ND from PHPV with undefined aetiology especially in sporadic cases and the diagnostic confusion could be overcome by molecular genetic assessments. ND gene analysis has contributed the clinical diagnosis of a simplex patient with either ND or PHPV. However, two sporadic patients with bilateral PHPV were negative for mutations in the ND gene.

In our series of sporadic patients with bilateral PHPV, we could not find any abnormalities in the ND gene. Thus, the frequency of ND gene mutation is very low in PHPV populations. The molecular genetic assessment of the ND gene enables us to make early diagnosis and give useful information for the genetic counselling.

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Primary monophasic synovial sarcoma of the conjunctiva

Synovial sarcoma is a malignant mesenchymal tumour, which makes up to 10% of all soft tissue sarcomas. It most often affects younger adults and is commonly found in periaricular sites of the extremities. It may occur at other locations, including head and neck, heart, abdominal wall, mediastinum, and lung. Synovial sarcomas of the head and neck are rare, making up only 10% of all synovial sarcomas, and typically localising to the hypopharynx or parapharyngeal space. We report a first case of primary monophasic synovial sarcoma of the conjunctiva in a 29 year old man with no significant medical history, who developed an enlarging conjunctival lesion at the medial canthus of the right eye.

Case report

A 29 year old man presented with a 4 month history of a growth in the conjunctiva at the medial canthus of the right eye. Gross appearance was of a pink, fleshy, soft tumour, 10 mm in diameter, with a prominent feeding blood vessel (Fig 1). There was no significant past history, in particular, no apparent risk factors for acquired immunodeficiency or history of previous orbital irradiation. Ophthalmic examination showed no visual deficit. Computed tomography (CT) scan showed no deep extension of the mass. General examination and CT staging of potential primary and metastatic tumour sites showed this to be a solitary lesion.

At surgery the tumour was found to be adherent to the medial rectus muscle and was excised with close margins. Excision was microscopically complete, and the appearance was of a 1 cm diameter soft tissue lesion, vascular and without necrosis. Histology showed a spindle cell tumour with collagen bundles and frequent vessels in the stroma (Fig 2). Immunohistochemistry showed widespread EMA staining and scattered keratin positive cells. Stain for CD-99 and bcl-2 was positive. These are characteristic features of a monophasic synovial sarcoma. Stain for S-100 was also positive, which is a feature observed in one of these tumours. Blocks were referred to an international sarcoma pathology reference centre.

Comment

There has been a significant recent rise in the reporting of ocular and ocular adnexal sarcomas. Most cases are associated with acquired immunodeficiency syndrome (AIDS), and irradiation of the orbits of children with hereditary retinoblastoma.

Adult Kaposi’s sarcoma and childhood leiomyosarcoma are increased more than 10 000 fold with AIDS.1 Hereditary retinoblastoma shows increased risk of sarcomas in the path of radiotherapy beam, especially if the patient is irradiated below 1 year of age.2 Synovial sarcoma is not of synovial origin, but is thought to be derived from as yet unknown multipotent stem cells capable of differentiating into mesenchymal and/or epithelial structures. It may be biphasic (consisting of epithelial cells admixed with spindle cells) or monophasic (spindle cells with little or no evidence of epithelial differentiation). Synovial sarcoma is associated with the chromosome translocation t(x;18)(p11.2;q12.1) causing a transcribed fusion product of two genes, SYT and SSX, or SSX1 and SSX4. SYT may be confirmed by fluorescence in situ hybridisation (FISH) or polymerase chain reaction (RT-PCR).3 Although primary orbital synovial sarcoma,4 and primary biphasic synovial sarcoma of the orbit5 have been reported, we can identify no cases of a primary monophasic synovial sarcoma presenting as a conjunctival tumour. Other soft tissue sarcomas may present as a primary tumour of the conjunctiva, including malignant fibrous histiocytoma of the conjunctiva,6 and primary conjunctival rhabdomyosarcoma.7 Benign leiomyoma of the caruncle8 and leiomyosarcoma of the conjunctiva have been reported,9 as has conjunctival liposarcoma.10 Complete surgical excision is the only curative option for adult soft tissue sarcomas. Adjuvant postoperative radiotherapy may reduce the risk of local relapse. Paediatric soft tissue sarcomas may respond to cytotoxic chemotherapy, but this is unusual in adult lesions. For soft tissue sarcoma of the conjunctiva, surgical adjuvant treatment with superficial radiotherapy (strontium-90) has been reported.7 Although rare, primary synovial sarcoma should be considered in the differential diagnosis of conjunctival masses.

Acknowledgements

We thank Professor C D M Fletcher, director of surgical pathology, Brigham and Women’s Hospital, Boston, MA, USA for his advice.
In England group I drivers should be able to read a standard number plate at 20.5 metres in a good light using both eyes with correction worn if necessary. They should also have a binocular field of 120 degrees along the horizontal with no significant defect within 20 degrees of fixation in any direction. This should be tested with an Esterman binocular field test. Recent guidelines from the Driver and Vehicle Licensing Agency (DVLA) have changed with regard to visual field interpretation, allowing small areas of field loss within these areas to qualify for a pass for group I licence holders. In particular, patients with static long term field defects, particularly those who have a safe driving history who would previously have failed to meet the field requirements, may still be considered for a licence.

This prospective clinic based audit is the first to use the licence plate test at 20.5 metres rather than a Snellen chart to quantify the size of the problem in a typical ophthalmology clinic in a district general hospital. The use of a number plate is important since Snellen acuity is known to be a poor predictor of an individual's ability to meet the required visual standard for driving; this is probably because of the differing symbol format, lighting levels, and other conditions involved.

### Participants and methods

In all, 156 consecutive patients were reviewed prospectively in general ophthalmology clinics with subspecialty interests in glaucoma and diabetes. All patients were asked if they held a group I (private car) or group II (large goods vehicle or passenger carrying vehicles) licence. Patients were tested in good light with a standard number plate (letters 79.4 mm high) at 20.5 metres using both eyes with their glasses if worn. They were given two attempts to read the number plate. Patients who were felt to be at risk of failing the field regulations (typically on the basis of monocular field tests for glaucoma or patients who had had bilateral panretinal photocoagulation) were asked to have an Esterman binocular field test. The notes of all patients who failed to achieve the visual standard for driving were reviewed and the patients were asked if they had ever been told not to drive before.

### Results

A total of 156 patients were asked if they held a driving licence. Of these, 66 (average age 63.6, range 30–83, 52/66 male) held a group I driving licence, only two patients held a group II licence. Eleven patients (average age 72, range 62–81) who held a licence failed to meet the driving standard (Table 1).

One of the group II patients failed the test on acuity but was due to surrender his licence in the next few months as he was retiring and had already ceased driving.

None of these patients had been told not to drive previously although the notes indicated vision (less than or equal to 6/18 in each eye) or field loss at the previous visit which should have made it clear that it was unlikely that these patients would be legally fit to drive in four of the cases. There was no documentation on whether these patients drove or had been advised not to in any of their notes. Three of the 11 patients had already ceased driving because they no longer felt confident enough but had retained their licences.

Nine of 11 patients failed to meet the driving standard because of poor visual acuity with two patients failing because of glaucomatous field loss. The new fields requirements would not have allowed either of these two patients to pass.

### Conclusion

A total of 42% of patients seen in a busy eye clinic still held a driving licence and these 7% did not fulfil the legal criteria to drive (7% of all patients seen). None of them had been informed previously that they should give up their licences despite evidence that at least 41/11 would have been unfit to drive from measurements made at a previous visit. Men were much more likely than women to be driving with inadequate vision (91% of those failing the driving standard in this study) and most of them were over the age of 70 years.

All patients should be asked if they drive or not and this should be recorded in the notes. If vision is inadequate for driving the notes should contain a statement that the patient has been informed of this and a letter sent to the general practitioner. This is particularly important from a medicolegal point of view since in one study half of the patients informed that they should surrender their licences continued to drive. Doctors should remain aware that they have a responsibility to alert patients that they should stop driving and that the patient should inform the DVLA. If the doctor does not inform these patients they may be liable to litigation should an accident occur. It may be worth pointing out to those patients who do not inform the DVLA of their poor eyesight that driving with inadequate vision may jeopardise insurance cover, as this may persuade many of them to stop driving.

As previously reported the Snellen acuities did not correspond well with the ability to read a number plate. Ideally all eye clinics should have a number plate which can be viewed in good light from 20.5 metres for use when advice about driving is given. Unfortunately some number plates are easier to read than others and a “good light” is not defined in law so the test is not standardised. Although it is easy for a policeman to perform the test at the side of the road it is not a very reliable means of visual assessment particularly in equivocal cases and better standards would be helpful.

Most people in this study failed the test due to poor acuity rather than an inadequate field. It is possible that a few more people would have made it clear that it was unlikely that these patients would be legally fit to drive if the new fields requirements were standardised. It is unlikely that the new more lenient field requirements will have a significant impact on the number of people seen in each clinic who drive illegally.

Whether these patients actually pose a significant risk to themselves or other road users is debatable; drivers with poor acuity appear to drive more carefully to compensate. However drivers with binocular field defects have

### Table 1

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In Table 1 the group II licence holder is debatable; drivers with poor acuity appear to drive more carefully to compensate. However drivers with binocular field defects have
been estimated to have twice the normal rate of driving accidents in some studies. What is worrying is that patients who attend an eye clinic seem unlikely to have been spontaneously warned to stop driving and doctors should be more aware of their role in protecting both their patients and society from road traffic accidents.

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Idiopathic parafoveal telangiectasis associated with a foveal pseudovitelliform lesion

Idiopathic parafoveal telangiectasis (IPT) and basal laminar drusen with pseudovitelliform lesions are both uncommon ocular findings. Gass classified parafoveal telangiectasis into several groups. Group 2 is characterised by bilateral acquired parafoveal telangiectasis that usually becomes clinically apparent later in life, in the fifth and sixth decade. The zones of telangiectasis tend to be symmetric and measure up to one disc diameter, with preferential involvement of the temporal parafoveal region. Typical findings are minimal retinal oedema, “right angle” veins, which drain the telangiectatic areas, underlying retinal pigment epithelial (RPE) alterations and superficial retinal refractile deposits. Gass has also described the development of a small, foveal yellow pseudovitelliform lesion in some patients, but no associated basal laminar drusen were noted. Abnormal blood glucose metabolism may play a part in the development of IPT. Basal laminar or cuticular drusen are focal thickenings of the basement membrane of the RPE. Although they are sometimes difficult to detect on clinical examination, these basal laminar drusen present a striking fluorescein angiographic picture of innumerable uniform, small, slightly raised, hyperfluorescent nodules. Patients with basal laminar drusen may develop a yellowish exudative macular detachment (“pseudovitelliform lesion”) that may resemble the foveal lesion characteristic of Best’s vitelliform dystrophy. In some cases, the yellow material may gravitate to the inferior part of the detachment, producing a “pseudohypopyon” appearance. Typically, the pseudovitelliform material shows progressive staining with fluorescein dye during the course of the angiogram.

This case report describes the presence of these two relatively uncommon conditions in the same eye of one patient. To the best of our knowledge, there is no previously reported case of simultaneous presentation of basal laminar drusen with pseudovitelliform lesion and parafoveal telangiectasis in one eye.

Case report

A 48 year old white woman presented for refraction with no other complaints. Around the age of 10, she presented with ptosis and a dilated pupil on the right eye and was diagnosed with a third nerve palsy. A examination ultimately revealed a craniopharyngioma for which she underwent resection. She did not receive any postoperative radiation treatment. Since the surgery, she has continued to have persistent ocular motility problems in the right eye. She also felt that her vision has been poor, though stable, since the time of the surgery in the right eye. No other ocular findings were reported at that time.

After the surgery, she developed secondary panhypopituitarism for which she received hormone replacement therapy. A recent fasting blood sugar was normal, and diabetes was ruled out by her primary care physician. Her current medications include hormone replacement therapy (for the panhypopituitarism), consisting of prednisone 5 mg/day, levothyroxine sodium, desmopressin acetate, conjugated oestrogens, and medroxyprogesterone. Her family history was notable for cataract and diabetes mellitus. She has a 14 pack year smoking history, but quit 18 years ago.

On examination, best corrected visual acuity measured 20/40 in the right eye and 20/20 in the left eye. Visual fields were full to confrontation in both eyes. She had a non-reactive pupil on the right, but, by reverse testing, she did not have an afferent pupillary defect. She had marked limitation of movements of the right eye, particularly depression, elevation, and adduction. Abduction was also mildly reduced. Extraocular movements of the left eye were full. She had approximately 30 prism dioptries of exotropia of the right eye in primary position. Colour vision was 14 out of 14 in each eye, although somewhat slower on the right side.

External eye examination was within normal limits. Slit lamp examination disclosed trace nuclear opacities bilaterally. Contact lens biomicroscopy showed a cup-disc ratio of 0.3.

Figure 1  (A) Fundus photograph of the right eye. The pseudovitelliform lesion is seen in the centre of the fovea (long arrow). Crystalline changes (short arrows) and temporal paracentral parafoveal telangiectasis (arrowhead) are also present. (B) Fundus photograph of the left eye. Multiple basal laminar drusen are seen. No pseudovitelliform lesion, telangiectatic vessels, or crystalline deposits can be observed.

Figure 2  (A) Early frame of a fluorescein angiogram. Subtle telangiectatic vessels are seen temporal to the foveal avascular zone in the right eye. Early fluorescein from multiple basal laminar drusen is observed deep to the retina. An area of blocked fluorescence is noted in the foveal centre corresponding to the pseudovitelliform lesion noted clinically. (B) Late frame of the same angiogram shows diffuse intraretinal leakage around the foveal avascular zone and staining of clusters of drusen.
in each eye. Both eyes showed evidence of numerous basal laminar hard drusen (best seen with indirect illumination), which formed typical clusters in numerous areas. There was no evidence of a pseudovitelliform lesion on the left. On the right side, there was a central yellowish lesion deep to the retina, which was consistent with a pseudovitelliform lesion. In addition, she appeared to have fine telangiectatic capillaries in the parafoveal retina most prominent temporally. The parafoveal retina was mildly thickened, and had a slight greyish sheen. Crystalline changes were also observed in the superficial retina (Fig 1).

A fluorescein angiogram was obtained transiting the right eye. The transit revealed telangiectasia of the parafoveal capillaries (most prominent temporally) with intraretinal leakage from these capillaries in later frames (Fig 2). The dye did not accumulate in cystoid spaces. There was no disc hyperfluorescence. Blocked fluorescence was observed under the fovea, corresponding to the pseudovitelliform lesion noted clinically. There was also punctate hyperfluorescence associated with the numerous basal laminar drusen present in both eyes (Figs 2A and 3). No evidence of telangiectasia or at least no evidence of leakage from telangiectatic capillaries was evident in the left eye (Fig 3).

Comment

This 48 year old woman with evidence of basal laminar drusen in both eyes and a vitelliform lesion in the right eye also has parafoveal telangiectasia in the same right eye.

She does not have any history of radiation treatment and she does not have diabetes. In addition, the distribution of telangiectatic capillaries and retinal leakage does not conform to the distribution of a branch retinal vein occlusion. Thus, the most likely explanation for the central vascular changes in the right eye is idiopathic parafoveal telangiectasia. Most of the patients with acquired IPT (group 2A according to Gass classification) present with bilateral disease. However, some patients present with unilateral disease and some may present with asymmetric lesions and develop IPT in the other eye later in life.1,2 Our patient had typical findings including RPE changes, mild thickening of the retina, greyish sheen, characteristic crystalline deposits, and a typical fluorescein angiogram.3 Gass also noted that IPT could sometimes be associated with a yellow central spot. He described five patients in group 2A that had such a spot, 100–300 µm in diameter in the centre of the foveal region.1 The pseudovitelliform lesion in our patient, however, did not resemble the lesions described by Gass. Gass identified a yellow precipitate within the retinal layers. Our patient’s lesion was deep to the retina and had the typical appearance of lesions associated with basal laminar drusen.4

In addition, our patient, unlike those described by Gass, had clusters of basal laminar drusen, seen both clinically and angiographically.

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Bilateral serous macular detachment in a patient with anaemic retinopathy secondary to gall bladder cancer

Various ocular complications of anaemia including hard exudates, cottonwool patches, frame-shaped haemorrhages, and Roth spots, have been documented as anaemic retinopathy for many years. In addition, it has been reported that retinal venous tortuosity is directly related to severity of anaemia.1 However, bilateral serous macular detachment has never been reported to be complications with anaemic retinopathy. Bilateral serous detachment of the macula has been reported in some patients with systemic or ocular disorders, including lymphoma,2 leukaemia, Vogt-Koyanagi-Harada syndrome, age related macular degeneration, and idiopathic central chorioretinopathy (ICSC).3,4 ICSC demonstrates central serous sensory detachments associated with leaks at the level of the retinal pigment epithelium. The classic features of ICSC are well known; this condition most commonly affects young or middle aged men between 30 and 50 years of age, occurs unilaterally and frequently in patients who have had a preceding stressful event, and has good visual prognosis.5 We describe an anaemic cancer patient with bilateral serous macular detachment similar to ICSC. We are unaware of other published reports similar to this case.

Case report

A 69 year old man admitted to the Kesennum county hospital presented with mildly decreased vision and micropsia 1 week. Ocular history was unremarkable. Medical history was notable for gall bladder cancer diagnosed 2 months before presentation, for which the patient underwent surgery 6 weeks before presentation, and for anaemia. His haemoglobin had fallen to 8.0 g/dl secondarily to the cancer 5 months before presentation. On consultation, his haemoglobin was 11.0 g/dl. The histological examination of the tumour showed undifferentiated carcinoma of the gall bladder.

Upon ophthalmological examination, best corrected visual acuity was 0.4 in the left eye and 0.6 in the right, intraocular pressure was right eye 12 and left eye 14. Slit lamp examinations revealed no evidence of anterior chamber or vitreous inflammation in either eye. Both

Figure 3 Late frame of a fluorescein angiogram of the left eye shows punctate hyperfluorescence associated with numerous basal laminar drusen. There is no evidence of telangiectasia or retinal vascular leakage.

Figure 1 (Top) Colour photographs of (top left) right and (top right) left eyes show serous macular retinal detachment and multiple intraretinal haemorrhages including several Roth spots and mild venous dilation. (Bottom) Fluorescein angiography photographs of (bottom left) right and (bottom right) left eyes show bilateral round subretinal pools at the macula.
fundi showed serous macular retinal detachment and multiple intraretinal haemorrhages including several Boss spots and mild venous dilatation (Fig 1, top). In both eyes, fluorescein angiography revealed macular leakage in the early phases and round subretinal pools in the late phases (Fig 1, bottom).

We observed the patient conservatively and, 1 week later, his visual acuity recovered by one line in both eyes. Furthermore, his visual function was recovering gradually without any particular therapy such as systemic steroid treatment. Two months after his first visit to our department, best corrected visual acuity was 1.0 in both eyes. Fundi were almost normal except for several vanishing intraretinal haemorrhages. Bilateral serous macular detachment disappeared completely and fluorescein angiography showed no macular leakage and no subretinal pools (Fig 2, bottom). However, his anaemia was still unimproved at the time.

Comment

Bilateral central serous detachment similar to CSC was resolved and vision recovered spontaneously, but the patient’s anaemia did not improve. Although the pathogenesis of the bilateral serous macular detachment is unclear and histological proof is lacking in our case, pigment epithelial cell dysfunction of the bilateral macula and disruption of the blood-retinal barrier may occur as a result of anaemia or an idiopathic phenomenon. A case of bilateral serous retinal detachment resembling central serous chorioretinopathy (CSC) was reported to follow cervical steroid injection for treatment of chronic upper back pain. No drugs given to the patient in our department or the surgery department are known to cause serous macular detachment. This case highlights two points: that anae-
imic retinopathy from cancer is rarely compli-
cated with bilateral serous macular detach-
ment, which causes the patient moderate visual loss; and that a good return of vision may be possible spontaneously even if anae-
imia does not improve.

Proprietary interests, none.

Figure 2  (Top) Colour photographs of (top left) right and (top right) left eyes appear almost normal except for several vanishing intraretinal haemorrhages. (Bottom) Fluorescein angiographic photographs of (bottom left) right and (bottom right) left eyes show no macular leakage and no subretinal pools.

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Choroidal detachment induced by dorzolamide 20 years after cataract surgery

One case of choroidal detachment induced by topical dorzolamide after filtration surgery has been reported.1 We would like to report a case of a patient with uveal hypertension (OH), treated with topical timolol and dor-
zolamide who developed a choroidal detach-
ment 20 years after cataract surgery.

Case report

A 70 year old white woman with a 12 year history of OH was treated effectively (in-
traocular pressure was 15 mm Hg in both eyes) by topical timolol 0.5 % once daily. She also had a 20 year history of bilateral extracapsular cataract extraction with no postoperative complications and no history of choroidal effusion or choroidal detachment. In February 2002, she was examined for a routine follow up. Her corrected visual acuity and intraocular pressure (IOP) were 6/10 and 22 mm Hg in both eyes. She was switched from timolol 0.5 % to twice daily topical combina-
tion of timolol 0.5 % and chlorhydrate dorzolamide 2%. Five days later, she came to the emergency department with headaches and ocular pain. Her corrected visual acuity was 6/10 in the right eye and 3/10 in the left eye. Her IOP was 25 mm Hg in the right and 35 mm Hg in the left eye. She had a bilateral angle closure. Ocular examination showed a bilateral choroidal detachment that was con-
firmed by an oculic echography. The topical combination of timolol and chlorhydrate dorzolamide was discontinued and 0.5% topical timolol once daily associated with 1% topical rimexolone four times daily were started. Five days later she was examined for follow up. Her corrected visual acuity and intraocular pres-
sure were 6/10 and 16 mm Hg, the choroidal detachment and the functional symptoms had resolved in both eyes.

Comment

Selecting an appropriate pharmacological intervention for a patient with OH can reduce IOP by decreasing aqueous humour produc-
tion by the ciliary processes—for example, carbonic anhydrase (CA) inhibitors. Because of their efficacy, the β adrenergic blockers are the example, timolol, is the gold standard com-
pared with the other treatment. Dorzolamide may be used topically in addition to a β adrenergic blocker if the IOP cannot be reduced. In addition, dorzolamide can be used to prevent OH in patients undergoing cataract surgery. The predominant isoenzyme of CA in ciliary processes is isoenzyme II for which dorzolamide has a great affinity. The pres-
umed mechanism is a slowing of bicarbo-
nate ion formation, which reduces sodium and fluid transport, resulting in lower in-
traocular pressure.

Considered to have few systemic side effects, dorzolamide may be associated with keratitis,1 corneal oedema,2 and periorbital dermatitis.3 A combination of dorzolamide and timolol has also been associated with conjunctival hyperaemia and eye itching, blepharitis, eye oedema, foreign body sensa-
tion, lens opacity, and vitreous detachment. Other cases of choroidal detachment after filter-
ing surgery linked to oral and topical CA inhibitors have been reported. However, to the best of our knowledge, this is the first case of choroidal detachment after filtration surgery. The mechanism of choroidal detachment with dorzolamide is probably due to hypotony caused by the reduction of intraocular pressure by the combination of timolol and dorzolamide.1 This mechanism has been mentioned in cases of choroidal detachment caused by latanoprost, a prostaglandin analogue used topically to reduce IOP, reported by Marques after filtration surgery. Another case of choroidal detachment has been reported in a patient who underwent left extracapsular cataract extraction with topi-
cally latanoprost prescribed immediately postoperatively.

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Ocular surgery, even if there is a history, seems to increase the risk of choroidal detachment when used as a pharmacological aqueous humour suppressant therapy—for example, dorzolamide or the combination of timolol and dorzolamide.

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Astigmatism and the analysis of its surgical correction

Thank you for the opportunity to reply to the letter from Alpins concerning our recent article in the BJO.

Noel Alpins is a widely respected contributor to many international meetings, having written comprehensively on the use of astigmatism vector analysis. His software program ASSORT is widely used for the planning of refractive surgery and provides many derived indices (transformations) from the vector analysis of both refractive and topographic astigmatism. Although the derived indices are summary measures, we have argued that their usefulness for statistical analysis is limited.

This is because the perception of astigmatism is a psychophysical phenomenon altered by the orientation of the axis of astigmatism (the power meridians of the cornea and crystalline lens) and other factors. Unfortunately, the perceptual response means that the measurement of the axis of astigmatism (which is with an arbitrary 180° scale) is non-linear in outcome terms, as related to visual acuity outcome. Astigmatism obliquity is the least desirable outcome but this is separated into two on the scale “with the rule” astigmatism (WTR), which is generally the most desirable outcome. Oblique astigmatism also separates the two groups “against the rule” astigmatism (ATR) from the WTR astigmatism. Developments of vector analysis so far have not resolved this issue of non-linearity of the axis of astigmatism compared with the visual outcome. Alpins recognised the relative value of WTR astigmatism and described how to plan refractive corrections using this principle (his Fig 10a) (reference 33 in our article). We suggested the WTR transformation would help eliminate the problem of divided oblique and WTR astigmatism, but this makes the use of vector analysis difficult and does result in data compression.

We agree that our understanding of astigmatism is incomplete. With over 4000 responses to a search for astigmatism on PubMed, there is much to know and yet still unknown. The references cited in the article were simply representative or illustrative of the arguments discussed in the article.

By way of apology, the correct reference for the “surgical error” (originally given as reference 34) in Figure 7, equation 20, and the relevant text page 1311 should in fact be reference 70, Alpins’s first article on vector analysis of both refractive and topographic astigmatism. The surgical error is the arithmetic result of the operative cylinder producing a 90° astigmatism (or the TIA) not cited in our article. The surgical emphasis is best directed towards the “difference vector” (which is a mathematically precise and absolute measure of the surgical error) Unfortunately does not address the problem of non-linearity (that is, the relative value in terms of visual acuity outcome) so is not useful as a summary measure of the outcome. However the difference may be useful in understanding the effects of the surgery (that is, as a process measure) and for deriving the “index of success.”

Alpins describes the SIA “torque” effect with reference to the preoperative axis of astigmatism (or the TIA) not cited in our article. Torque needs to be distinguished from the effect of rotation of the corrective cylinder that is derived from the postoperative astigmatism value. Unfortunately, our discussion on the optical decomposition did not clearly state that the 45° polar value is derived from the postoperative result, thus correctly describing the rotation effect (as discussed with the obliquely crossed cylinder effects). We apologise for creating some confusion with the “torque” effect.

We agree that the healing response is connected to the surgical process; however, healing is a very individual response. Vector analysis in terms of the SIA can only reflect the surgical process. Although a “vector” could be used to represent the measurement of the healing response at any point in time, it may not be representative of the healing responses at other times because the healing process is continuous. Furthermore, an individual’s response may not be well represented by the aggregate or mean vectorial response, as discussed, as it is not always the non-linearity problem of the separation of the oblique and ATR astigmatism axis values (see reference 104 in our article).

In his early article (reference 33) Alpins discusses surgical treatment planning combining the topographic astigmatism values with the refractive values to produce an optimal corneal curvature. Alpins suggests that the surgical emphasis is best directed towards a WTR result when there is a disparity between the values requiring some residual astigmatism after surgery. Without recognising Javal’s rule, Alpins, none the less, has ascribed a better relative value to ATR astigmatism suggesting that optimal treatment planning be based on this psychophysical phenomenon. As we stated “only using keratometric data for the planning of refractive surgery” would create a problem otherwise.

It is understandable that Alpins feels that the concepts presented in our article are in conflict with some of his own, but these do not diminish the value of vector analysis as a process measure, particularly for individual cases. It is the use of vector analysis as an outcome measure relative to the visual acuity that was critically evaluated by our article.

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References


Autologous serum in epithelial defects: reply

Mukerji and colleagues have criticised several aspects of our study and justified their views with unrepresentative quotations from the literature.¹

Choice of time period before an epithelial defect can be described as “persistent”

There is no accepted definition of persistent epithelial defect (PED) that includes a time period. We favour the definition given in one text “when the epithelium fails to regrow over a defect within the expected time course.”² For the purpose of a study the time course must be specified. Mukerji et al prefer 2 weeks,² whereas in another recent paper 10 days was chosen with the proviso that the study treatment could start earlier if there was progression or perforation.³ The penalty for patients at high risk of corneal melt, in the presence of a persistent defect, is substantial. In our study 2/13 patients had an epithelial defect for less than 2 weeks before inclusion in the study. Mukerji et al can ignore the data from these patients if they wish.

Washout period with preservative-free artificial tears

No “washout period” was used in this study, as we were trying to identify whether serum would have an additional effect on epithelial healing over preservative-free artificial tears and conventional therapy in patients with severe ocular surface disease. We were not trying to compare the efficacy of serum against preservative-free lubricants in healing Peds. Conventional therapy was continued as serum alone could not fully address all the ocular surface problems, including aqueous tear deficiency and eyelid trauma, so that giving serum without continuing the other treatments may have caused harm to some of the patients. Other studies have adopted similar protocols with a PED defined as a defect that persisted “despite conventional treatment such as artificial tears or extended wear contact lenses” with no washout period or that lowered by a reduction in the 10 day wash out period if corneal ulceration progressed.⁴ In a clinical study some ethics committees may not condone the treatment of persistent defects without non-preserved antibiotic prophylaxis against bacterial keratitis.

Keratoplasty patients being treated without waiting for the corneal epithelial defect to heal by itself

The authors state both failed previous grafts because of corneal perforation resulting from Peds and one patient had recurrent epithelial breakdown, responding to the re-introduction of serum drops, after their initial withdrawal. We thought that for some readers, this might be useful data to add to this descriptive study.

The rationale behind the use of 100% serum when previous studies have proved the efficacy of a 20% solution

The previous study Mukerji et al quote is, like ours and all the other studies on this subject, a descriptive study and no more proves that serum drops at 20% work than does our own with 50% and 100%. Other studies, all uncontrolled, have used from 20%–30% serum for both persistent defect and dry eye. All these studies use empirical regimens for serum concentration and dosing frequency. Unlike Mukerji et al, we have some patients (one reported in the study) who prefer 100% serum to 50%. Mukerji et al are probably also unknowingly studying demonstrating that 100% serum is less toxic than 50% serum to cultured corneal epithelial cells;⁵ this provides some laboratory data to support the use of 100% serum. Lastly, the manufacture of 100% serum requires less handling so reducing the risk of contamination.

The use of the slit lamp micrometer

Mukerji et al have missed the point that the treatment end point was closure of the defect, for which their proposed technique is inappropriate, rather than rate of closure, for which it would be ideal. The deficiencies in our study are not the points that Mukerji et al have made but the fact that it was uncontrolled. The study was planned as a randomised controlled trial but could not be delivered such for the reasons alluded to in the last paragraph. These regulatory problems are being overcome in the United Kingdom. We should all hope to see randomised treatment trials carried out in this area as we await laboratory studies necessary to support the clinical application of serum.

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References


Sclera substitutes: a cautionary note

In their article in the BJO,³ Mehta and Franks provide a valuable and timely review of the use of human sclera in ophthalmic surgery. The article was prompted by the implications of using human sclera in the light of the as yet unquantified risk of iatrogenic transmission of variant Creutzfeldt-Jakob disease (vCJD).

The authors list a number of alternatives to sclera, including dura mater. While they point out that the surgical use of dura mater has itself resulted in a significant number of cases of transmission of classic CJD, it is also stated that a commercial preparation of dura mater, treated to reduce the risk of vCJD transmission, is available. In the United Kingdom, the Medical Devices Agency (MDA) withdrew the licences issued under the Surgical Materials Act 1971 for the two available commercial preparations of dura mater in 1991 and 1992, respectively. According to the MDA, no products containing human dura mater are currently licensed for clinical use in the United Kingdom. It is clearly necessary to recommend use of an unlicensed product whatever claims have been made about its preparation. It should be noted that individuals who have received dura mater allografts are excluded from subsequently donating tissues for transplantation.² Finally, it would be important to know whether any ophthalmic surgeons in the United Kingdom have in fact used preparations of dura mater since 1992 as further guidance may need to be sought.

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Preoperative management in cataract surgery for high myopes

We enjoyed reading the recent series of papers by Seward et al which illustrate some management issues for a high myope (approximately −12D) presenting with bilateral cataract.¹ Packard recommends preoperative fundal assessment and prophylactic treatment if necessary while Allen advocates a retinal opinion before discussing the risks of cataract surgery with the patient. The accompanying overview by Seward stresses the need for retinal opinion, and we are told that the patient received prophylactic laser treatment to a peripheral round break before cataract surgery. It is not routine in our hospital to obtain a retinal opinion high myopes before cataract surgery and the evidence for prophylactic treatment of asymptomatic retinal breaks and lattice degeneration is not good. With the assistance of the American Academy of Ophthalmology preferred practice pattern retinal panel, Wilkinson conducted an extensive literature search on this topic, reviewing all relevant papers in the English language over the preceding 35 years.² His conclusion was that, based on the basis of good quality (level 1) data, only symptomatic retinal tears warranted routine prophylactic treatment. Lesser quality (level 2) evidence also indicated that treatment was not required for lattice degeneration in asymptomatic myopic eyes, and only rarely indicated for asymptomatic atrophic holes in phakic eyes. He also highlighted the best published (level 2) evidence for prophylactic treatment of fellow eyes.
following retinal detachment, which indicates that the benefit of treating lattice degeneration is modest at best and of no value in eyes with more than 6 dioptres of myopia or with more than 6 clock hours of lattice degeneration.

As evidence based medicine quite rightly gains importance in our clinical decision making, it is pertinent to question some of the traditional treatment options which have been handed down to us. We feel that this otherwise excellent overview of the problems of cataract surgery in myopia has not satisfactorily discussed the question of prophylactic retinal treatment and has, perhaps unwittingly, advocated the continued use of an ineffectual clinical practice.

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References

Amniotic membrane transplantation

We read with keen interest the article by Espana et al on the use of amniotic membrane transplantation (AMT) for ocular surface reconstruction after exision of large neoplasia.

We firmly endorse their view that AMT is rapidly evolving as a viable option in the management of a wide spectrum of ocular surface disorders because of a multitude of beneficial properties that it possesses. However, we would like to clarify a few misgivings in some crucial areas of concern.

As the authors have aptly emphasised total eradication of tumour cells from the ocular surface is essential for successful treatment and recurrence rates. To achieve this objective, in our own clinical experience and in the literature, frozen section controlled excision (FSCE) of the tumour, combined with the single freeze-thaw cycle of cryotherapy is now a recognised, accepted technique in a majority of centres across the world.1,2 It has been reported to achieve very effective tumour control and reduce recurrence rates from as high as 24–50% to a negligible 4.5%.1 It is especially useful in patients with conjunctival malignant melanoma where lack of pigmentation may not always be indicative of a tumour free margin. Although the authors have reported a relatively low recurrence rate of 10% in cases of conjunctival intra epithelial neoplasia (CIN) even without this technique, we strongly feel that FSCE should only be used when dealing with such lesions.

Secondly, it is our considered opinion that in case tumour excision is being carried out on the basis of clinical parameters alone, without confirmation with FSCE, a double freeze-thaw cycle of cryotherapy (in contrast to the single freeze-thaw cycle used in this study) is advisable.1 Moreover, leaving a clinically assessed tumour free margin of 3–4 mm, as described, may not be safe enough and it may be more prudent to leave a healthy margin of at least 5 mm, even at the cost of sacrificing a bit of extra normal tissue, thereby gaining a lower probability of tumour recurrence and patient morbidity in the bargain.

Finally, we would like to say that the results achieved by the authors are commendable by any standards and indicate a really meticulous surgical technique and painstaking follow-up.

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Surgical endoscopic dacryocystorhinostomy

We have read the thought provoking article by Ying and Hardman-Lea on their experience with surgical endoscopic dacryocystorhinostomy (DCR).1 We appreciate the success rates achieved by them, which are among the highest in endonasal lacrimal surgery and compare well with the results of external DCR in most centres of the world. We would like to discuss some relevant issues and seek clarifications about certain controversial areas.

The authors have admirably described their surgical technique for negotiating nasolacrimal duct (NLD) as well as common canicular obstructions.1 However, they have not mentioned the technique they employed in tackling more proximal blocks—i.e., those involving the upper, lower, or both canaliculi in their group of such patients (13 cases).

Undoubtedly, these obstructions are the most difficult to treat and various surgical and laser assisted treatments have been described in the literature, with variable success rates.

A detailed elucidation of how the authors approached the individual lacrimal canaliculi from the endonasal route to relieve the obstruction will be extremely valuable to the readers as a whole, and to dacryologists in particular.

Silicone stents have become an almost universal procedure in lacrimal surgery for enhancing success rates in cases with relatively poor prognosis. However, we would like to express reservations about keeping the stent in situ permanently, as described by the authors in proximal canicular obstructions. Most of the previous studies have recommended placement of the stent for a period ranging from 6 months to 1 year. Although silicone stents are absolutely inert and usually harmless, on prolonged placement they can act as a nidus for granuloma formation and infection, leading to failure of the lacrimal procedure in the long run. Moreover, inadvertent traction to the nasal end can result in slitting of the puncta and cheese wiring of the canalicular complex, whereas gradual ascent in the nasal cavity can lead to prolapse of the tube at the medial canthus.1 So, in our opinion, the time period of stent placement should be optimised and permanent placement could have long term deleterious effects.

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Sclerectomy with collagen implant

Tan and Hitchings should be commended on attempting to tackle the issue of sclerectomy with collagen implant.1 Nevertheless we do feel that their fundamental points and principal arguments merit reconsideration.

The authors state categorically that “long term outcomes do not exit for the newer non-penetrating surgery technique” when, in fact, long term (43.2 months (SD 14.3)) results for deep sclerectomy with collagen implant have been published some time ago.1 The study provided a qualified success rate of 14.8% and the complete success rate of 61.9% after 60 months (survival analysis), with a mean IOP at end of follow up of 11.8 (SD 3) mm Hg. The study reported no surgical induced cataract in the whole series of 105 patients.

The authors, unfortunately, failed to cite a landmark study1 comparing deep sclerectomy without an implant with trabeculectomy in the two eyes of the same patient in a prospective randomised fashion. At 12 months mean IOP reduction was 12.3 (4.2) mm Hg (sclerectomy) versus 14.1 (6.4) mm Hg (trabeculectomy) (p = 0.15), and an IOP ≤21 mm Hg was achieved in 36% of 37 eyes (94.9%) (p = 0.9), respectively. The authors of this study concluded that deep sclerectomy might provide comparable IOP reduction with fewer complications in the management of primary open angle glaucoma.

Furthermore, the authors cite a study by Gandolfi (personal communication) suppos-edly providing evidence that “trabeculectomy produces lower and better sustained IOP control than either viscoanastomosis or deep sclerectomy.” The authors fail to mention however, that in this particular study postoperative YAG goniotomies were considered as a failure criterion. Excluding gonipuncture from the success criteria would easily be
Acanthamoeba and disinfecting contact lens solutions

I read with interest the article by Itti et al on the susceptibility of Acanthamoeba to a multipurpose disinfecting contact lens solution and two hydrogen peroxide systems. The association between Acanthamoeba keratitis and contact lens wear is now firmly established. Thus, the use of contact lens disinfecting solutions effective at killing Acanthamoeba organisms is important in preventing corneal infections. I would like to make a few comments on this article.

The standard methods for testing disinfecting solutions against Acanthamoeba presents a critical problem when sensitivity assays are set up. The authors say that 1 ml of disinfectant per well was applied in 24 wells plate, but the amount of suspension distributed in each well is missing. PHMB (0.0005%) was found to be ineffective against A. castellanii and A. lenticulata cysts after 8 hours' exposure. This is not surprising. Indeed, at concentrations (0.5–15 µg/ml) used in commercial contact lens solutions, PHMB is almost ineffective against amoeba cysts. PHMB concentrations ranging from 45–90 µg/ml are required to eradicate Acanthamoeba cysts in under 1 hour of exposure.

The authors observed that a step 3% H2O2 system as a safe disinfectant for Acanthamoeba was ineffective against the cysts of a corneal isolate of A. castellanii after 9 hours' exposure. Silvany et al reported similar results. Because the catalyst is present from the very beginning of the disinfection step, the H2O2 is neutralised long before any disinfection can occur. Therefore, adequate exposure time before neutralisation is crucial.

The authors also found that a step 0.6% H2O2 system was effective against A. castellanii and A. hatchetti cysts after 8 hours' exposure. However, Zanetti et al observed that an equivalent dilution of 3% H2O2 was ineffective against the cysts of a corneal isolate of A. castellanii after 9 hours' exposure. These variations in susceptibility may depend on inherent strain differences. Therefore, unlike the authors, I would not recommend the step wise 0.6% H2O2 system as a safe disinfectant against Acanthamoeba. From previous data, I suggest that the following measures should result in less contact lens case and contact lens contamination, thereby possibly reducing the risk of microbial keratitis.

- Naturally: wash hands before handling contact lenses
- Use “one day” disposable contact lenses
- If other types are preferred: Use a two step 3% H2O2 system and neutralise after 9 hours' exposure (overnight)
- Replace the contact lens case regularly (preferably every 2 weeks).

References
Squamous cell carcinoma of the conjunctiva

The article by McKelvie et al is especially noteworthy as it highlights a number of interesting observations.

In the first instance, the authors highlight that conjunctival squamous cell carcinoma (SCC) is not as uncommon worldwide as reported earlier. Recurrence of ocular surface squamous neoplasia (OSSN) is common, with significantly increased risk for older patients, large size, high proliferation index (Ki-67 score), and positive surgical margins (total recurrence being 27%). For control of local disease, exenteration may be the answer. The larger the diameter of the mass, the more accurate is the clinical diagnosis. A high proliferation index increases the predictability of recurrences and serial impression cytology is an extremely useful tool for early detection of recurrences.

Intraocular, corneal and/or corneoscleral invasion, and death due to metastasis are the other important findings.

We have been working in this field since 1977 and managed a large number of eyes at two tertiary eye care centres of developing countries (All India Institute of Medical Sciences, India; 86 in 22 years, BP Koirala Institute of Health Sciences, Nepal; seven in 2 years). We would like to comment on a few aspects that have been reported by the authors.

We are in agreement with the authors that SCC is not uncommon, which is true even in our part of the world. From the histopathological analysis revealing involvement of the margins in a few cases, it is not clear whether the cases were managed by frozen section controlled excision (FSCE) or not (as one tends to remove all the histopathologically proved lesions if the frozen section facility is available during surgery).

The authors have very rightly documented the risk factors for recurrence. However, by employing FSCE we did not come across a recurrence in any of our patients and we feel that FSCE combined with double freeze-thaw cryotherapy to the surgical margins and should become mandatory in all cases. We had a clinical impression of recurrence in three eyes which after removal revealed granulomatous lesions on histopathology. However, as we have operated on a large number of recurrent lesions, our impression is that recurrent tumours have an aggressive look and grow at a rapid pace.

Though we do not have any experience on impression cytology or the proliferation index for these lesions, we appreciate that these two are very sensitive parameters to guide the clinicians regarding recurrences and feel that all ophthalmologists should have access to these facilities.

We do not agree with the authors’ comment that orbital exenteration may be required for control of disease. Rather we feel, if there is clinical suspicion of intraocular spread the lesions should be subjected to a 20 MHz high frequency ultrasound assessment to check for intraocular involvement and computed tomography to rule out orbital extension before the decision of exenteration.

In our series we could save three eyes with optimal visual preservation by performing local excision in cases where previous excision had been advised. Further, so far we have not come across the problem of death due to metastasis (and we have followed up some patients over 20 years). However, this is a very rare issue and all ophthalmologists should remain alert while managing the SCC, more so for extensive lesions.

Finally, we congratulate the authors for their well-documented series which, no doubt, will guide the ophthalmic clinicians dealing with these lesions.

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References


NOTICES

Role of optometry in Vision 2000

The latest issue of Community Eye Health (No 43) discusses the mobilisation of optometry to deal with uncorrected refractive error, which is now a major cause of preventable blindness. For further information please contact: Journal of Community Eye Health, International Centre for Eye Health, Institute of Ophthalmology, 11–43 Bath Street, London EC1V 9EL, UK (tel: +44 (0)20 7608 6910; fax: +44 (0)20 7250 3207; email: eyeresource@ucl.ac.uk; web site: www.jceh.co.uk). Annual subscription (4 issues) UK£25/US$40. Free to workers in developing countries.

International Centre for Eye Health

The International Centre for Eye Health has published a new edition of the Standard List of Medicines, Equipment, Instruments and Optical Supplies (2001) for eye care services in developing countries. It is compiled by the Task Force of the International Agency for the Prevention of Blindness. Further details: Sue Stevens, International Centre for Eye Health, 11–43 Bath Street, London EC1V 9EL, UK (tel: +44 (0)20 7608 6910; email: eyeresource@ucl.ac.uk).

Second Sight

Second Sight, a UK based charity whose aims are to eliminate the backlog of cataract blind in India by the year 2020 and to establish strong links between Indian and British ophthalmologists, is regularly sending volunteer surgeons to India. Details of this charity web site (www.secondsight.org.uk) or by contacting Dr Lucy Mathen (lucymathen@yahoo.com).

Specific Eye ConditionsS (SPECS)

Specific Eye ConditionsS (SPECS) is a not for profit organisation which acts as an umbrella organisation for support groups of any conditions or syndrome with an integral eye disorder. SPECS represents over fifty different organisations related to eye disorders ranging from conditions that are relatively common to very rare syndromes. We also include groups who offer support of a more general nature to visually impaired and blind people. Support groups meet regularly in the Boardroom at Moorfields Eye Hospital to offer support to each other, share experiences and explore new ways of working together. The web site www.eyeconditions.org.uk acts as a portal giving direct access to support organisations, web sites. The SPECS web page is a valuable resource for professionals and may also be of interest to people with a visual impairment or who are blind. For further details about SPECS contact: Kay Parkinson, SPECS Development Officer (tel: +44 (0)1803 524238; email: k@eyeconditions.org.uk; web site: www.eyeconditions.org.uk).

The British Retinitis Pigmentosa Society

The British Retinitis Pigmentosa Society (BRPS) was formed in 1975 to bring together people with retinitis pigmentosa and their families. The principle aims of BRPS are to raise funds to support the programme of medical research into an eventual cure for this hereditary disease, and through the BRPS welfare service, help members and their families with all aspects connected with the everyday problems of retinitis pigmentosa. Part of the welfare service is the telephone helpline (+44 (0)1280 860 363), which is a useful resource for any queries or worries relating to the problems retinitis pigmentosa can bring. This service is especially valuable for those recently diagnosed with retinitis pigmentosa, and all calls are taken in the strictest confidence. Many people with retinitis pigmentosa have found the Society helpful, providing encouragement and support through the Helpline, the welfare network and the BRPS branches.
The International Strabismological Association Fellowship

The International Strabismological Association (ISA) has established one fellowship for either basic or advanced training in strabismus/pediatric ophthalmology supported in the amount of $10,000 (US). Applications may be obtained from the Secretary/Treasurer of the ISA, Derek T Springer, MD, at Indiana University School of Medicine, 702 Rotary Circle, Indianapolis, Indiana 46202 (email: isa.lms@juno.com). The last day for this application is 15 January 2003.

Retinal Detachment Course with international faculty and case presentations preceding Vitrektomie-Kurs—Wetlab

The Retinal Detachment Course with international faculty and case presentations and Vitrektomie-Kurs—Wetlab will be held 13 February 2003 (in English) and 14–15 February 2003 (in German) respectively, at Verwaltungsgebäude der KA Rudolfstiftung, 1030 Vienna, Boerhaavegasse 8a, Austria. Further details and registration: Firma Askin & Co, Albert-Schweitzer-Gasse 6, A-1140 Vienna, Austria (tel: +43 (1) 979 88 44; fax: +43 (1) 979 88 46).

Detachment Course with international faculty on: Retinal and Vitreous Surgery with Case Presentations preceding Retina Meeting

The detachment course with international faculty on: Retinal and Vitreous Surgery with Case Presentations and the Retina Meeting will be held 14–15 March 2003 and 16 March 2003 respectively, in Mexico City, Mexico. Further details: Scientific programme: Prof Ingrid Kreissig, University of Tuebingen, Schleichstr. 12, 72076 Tuebingen, Germany (tel: +49 7071 295209; email: ingrid.kreissig@med.uni-tuebingen.de).

Local organisation: Prof. Quiroz-Mercado, Prof. Munoz, and Prof. Gonzalez “Hospital Luis Sanchez Bulnes”, Asociacion para Evitar la Ceguera en Mexico Vicente Garcia Torres #46, Coyoacan, Mexico DF 04330 (fax: +52 55 5659 5928; email: retinamex@yahoo.com).

16th Annual Meeting of German Ophthalmic Surgeons

The 16th Annual Meeting of German Ophthalmic Surgeons will be held 8–11 May 2003 in Nürnberg, Germany, Messezentrum. Organised by the Professional Association of German Ophthalmologists Ophthalmic Surgery Group the conference will cover cataract surgery, refractive surgery, glaucoma surgery, vitreoretinal surgery, corneal surgery, eye surgery in developing countries, and orbita, lacrimal and lid surgery. Further details: MCN Medizinische Congress organisation Nürnberg AG, Zerzabelshofstr 29, 90478 Nürnberg, Germany (tel: +49 911 3931621; fax: +49 911 3931620; email: doc@mcnag.info; web site: www.doc-nuernberg.de).

13th Meeting of the EASD Eye Complication Study Group

The 13th Meeting of the EASD Eye Complication Study Group will be held on the 23–25 May 2003, in Prague, Czech Republic. The scientific programme includes keynote lectures from Professor John H Fuller (UK) on The epidemiology of diabetic retinopathy; Dr P Martin van Hagen (The Netherlands) on Growth factors and diabetic retinopathy; Professor Terezie Pelikanova (Czech Republic) on Pathophysiology of diabetic microvascular complications; Dr Tomas Sosna (Czech Republic) on Risk and protective factors of diabetic retinopathy.

Three travel grants of €1000 each, sponsored by GlaxoSmithKline for young scientists (under 35 years at the time of the meeting). Applications should be made with the submission of abstracts. The deadline for abstracts is 14 February 2003.

Further details: Ortopedické Centrum, s.r.o., Strekůské nábřeží 51, 400 03 Usti nad Labem, Czech Republic (tel: +420 47 521 6588; fax: +420 47 533 40 77; email: ortcentrum-ul@volnv.cz; web site: www.ortopedické-centrum.cz).

Detachment Course with international faculty on: Retinal and Vitreous Surgery with Case Presentations preceding the Annual Meeting of Iranian Society of Ophthalmology

The detachment course with international faculty on: Retinal and Vitreous Surgery with Case Presentations preceding Annual Meeting of Iranian Society of Ophthalmology will be held on 29–30 November 2003 and 1–4 December 2003 respectively, at the Razi Conference Center, Hemmat Hyw, Tehran, Iran. Further details: Scientific programme: Prof Ingrid Kreissig, University of Tuebingen, Schleichstr. 12, 72076 Tuebingen, Germany (tel: +49 7071 295209; email: ingrid.kreissig@med.uni-tuebingen.de). Local organisation: Dr Arman Masheyekhi, Dr Siamak Moradian, Dept of Ophthalmology, Labbanfinejad Medical Center, Pasdaran Ave, Boostan 9, Tehran, 16666, Iran (fax: +98 21 254 9039; email: labbafi@hotmail.com).