

# PostScript

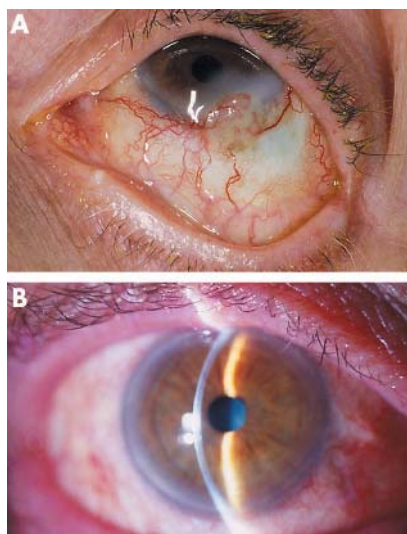
## LETTERS

### Treatment of biopsy proved conjunctival intraepithelial neoplasia with topical interferon alfa-2b

Conjunctival intraepithelial neoplasia (CIN) is the most common conjunctival malignancy in the United States. It occurs in exposed areas of the bulbar conjunctiva with frequent involvement of the adjacent corneal epithelium. Recent studies<sup>1</sup> have noted a recurrence rate of about 50% when there is pathological evidence of residual tumour in the surgical margin and a 5–33% recurrence rate with clear margins.<sup>2</sup> We describe two cases of primary CIN successfully treated with topical INF $\alpha$ -2b. This chart review was conducted with a waiver from the Ochsner Clinic Foundation's institutional review board, and conforms to HIPPA regulations.

#### Patient 1

A 65 year old retired welder was referred for further treatment of a partially resected CIN 1 month earlier. The patient had a long history of ultraviolet light exposure, multiple skin cancers of the face and hands, and tobacco use. He complained of redness and foreign body sensation in the right eye. Examination revealed a best corrected visual acuity of 20/25 in both eyes. The left eye examination was unremarkable. Slit lamp examination of the right eye showed an elevated white corneal and conjunctival plaque extending 90 degrees along the limbus (fig 1A). The referring physician had performed a biopsy of the central portion of the lesion which, upon pathological examination, was consistent with severely dysplastic conjunctival intraepithelial



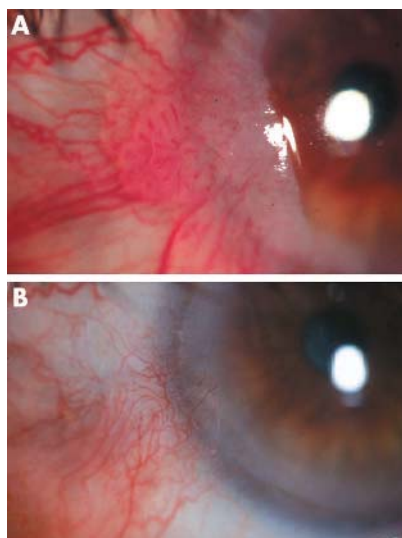
**Figure 1** Patient 1. (A) Clinical appearance of conjunctival squamous cell carcinoma before treatment with INF $\alpha$ -2b. (B) Regression of conjunctival squamous cell carcinoma 70 days after starting treatment with INF $\alpha$ -2b.

neoplasia with chronic subconjunctival inflammation, suggestive but not diagnostic of squamous cell carcinoma. After punctal plugs were placed, treatment with INF $\alpha$ -2b (1 million units/ml) four times a day was initiated. The lesion regressed completely after 44 days of treatment (fig 1B). The interferon drops were discontinued after 70 days. No recurrences have been seen after 6 months of follow up.

#### Patient 2

A 73 year old white male was referred for an asymptomatic left corneal/conjunctival mass. There was no history of skin cancer, but there was a long history of sun exposure. The best corrected visual acuity was 20/50 in both eyes. Slit lamp examination showed an elevated, gelatinous conjunctival/corneal lesion with feeder vessels extending 150 degrees along the limbus (fig 2A). A biopsy revealed moderate to severe dysplasia. The patient was treated with INF $\alpha$ -2b (1 million units/ml) four times a day after placement of upper and lower lid punctal plugs. The lesion resolved after 84 days (fig 2B). No recurrence was observed after 3 months of treatment.

Traditional therapy for CIN has involved wide surgical excisions with adjunctive cryotherapy,  $\beta$  radiation, mitomycin C, and 5-fluorouracil. All of these treatments may cause ocular surface inflammation, limbal stem cell deficiency, and epitheliopathy. Combination therapy of intraslesional/subconjunctival injections and topical application of interferon effectively treats CIN.<sup>3</sup> However, perilesional interferon has systemic side effects that include transient fevers and myalgias; therefore, topical therapy is preferred.<sup>4,5</sup> While presumptive treatment of CIN with topical INF $\alpha$ -2b has demonstrated good results, to our knowledge there is only one case series of regression of biopsy proved



**Figure 2** Patient 2. (A) Clinical appearance of CIN before treatment. (B) Complete regression of CIN with topical INF $\alpha$ -2b 84 days after treatment.

primary and recurrent CIN with treatment with INF $\alpha$ -2b.<sup>4,5</sup>

Here we report treatment of CIN using INF $\alpha$ -2b that was extremely well tolerated and had minimal side effects. At approximately \$US300 per treatment, INF $\alpha$ -2b costs three and two times more than 5-fluorouracil and mitomycin C, respectively. However, the enhanced safety and reduced side effects should offset the additional expense. In conclusion, topical INF $\alpha$ -2b offers an effective alternative for the treatment of primary CIN. Larger population studies with longer follow up would better assess the risk of side effects or recurrence.

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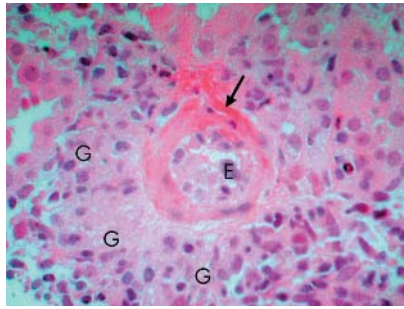
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## Henoch-Schonlein purpura with keratitis and granulomatous anterior uveitis

Henoch-Schonlein purpura (HSP) is a vasculitis with IgA dominant immune complexes.<sup>1</sup> The small vessel vasculitis is characterised by inflammation and necrosis. We report a case of granulomatous HSP nephritis (HSPN) in association with keratitis and bilateral anterior granulomatous uveitis.

## Case report

A 42 year old man presented to the casualty department with acute polyarthropathy, purpura, and nephritic syndrome. The urinalysis demonstrated 3+ blood and protein, blood pressure was 152/96, serum creatinine was 130  $\mu$ mol/l, complement C3 titre was 0.78 g/l (normal 0.88–1.82), and immunoglobulin IgA titre was 4.6 g/litre (normal 0.80–2.80).



**Figure 1** Glomerular arteriole showing a vasculitis with fibrinoid necrosis of the vessel wall (arrow) and swelling of the endothelial cells (E). Surrounding the vessel there is granulomatous inflammation (G) (haematoxylin and eosin,  $\times 400$ ).

He underwent a left native kidney needle biopsy. Light microscopy demonstrated mesangial proliferative glomerulonephritis with no signs of interstitial nephritis. There was prominent vasculitis with a granulomatous response and fibrinoid necrosis (fig 1), mainly affecting the glomerular arterioles. Immunofluorescence studies demonstrated a predominantly granular staining for IgA and C3. Electron microscopy of the glomerulus demonstrated prominent endocapillary cellularity and neutrophil populations, with a number of subepithelial immune complexes.

The clinical and immunopathological findings were consistent with HSPN. His condition responded to oral prednisolone (1 mg/kg), and the laboratory parameters normalised within a 5 month period. The steroid therapy was discontinued and the patient remained systemically well with normal renal function.

One month after remission of the HSPN, he attended the ophthalmic casualty department with a painful right eye. He was treated for a punctate keratitis and corneal epithelial erosion with topical antibiotics and ocular lubricants. This developed into an epithelial defect, but soon resolved. Corneal sensation was intact. One month later, he represented with blurred vision in the right eye. Examination of the left eye was normal. Vision was 6/24, with severe scleral hyperaemia, corneal oedema, mutton-fat keratic precipitates, fibrinous anterior chamber reaction, posterior synechiae, and 2+ anterior vitreal cells. Intraocular pressure was 32 mm Hg and fundal examination was unremarkable.

Routine blood tests and a vasculitis screen, including antinuclear antibodies, antineutrophil cytoplasmic antibody (ANCA), rheumatoid factor, viral serology, autoantibody titres, antistreptolysin O titre, VDRL, and serum angiotensin converting enzyme levels were all normal. The erythrocyte sedimentation rate, C reactive protein, chest x ray, complement titre, urinalysis, and renal function were normal.

The granulomatous anterior uveitis and trabeculitis were treated with dexamethasone 1% eye drops, cyclopentolate 1% eye drops, and oral acetazolamide. After 1 week, he developed bilateral granulomatous anterior uveitis and was treated with topical steroids. After 2 months, the uveitis resolved completely and the intraocular pressure normalised. He reported no recurrence of HSP symptoms during this period.

## Comment

The relation between idiopathic acute interstitial nephritis and uveitis is well established in the literature.<sup>2</sup> There is only a single report of ocular inflammatory disease associated with classic HSP.<sup>3</sup> Our patient fulfilled the American College of Rheumatology diagnostic criteria for HSP<sup>4</sup>; however, the histopathological features demonstrated an unusual type of HSPN.

The differential diagnosis in this case included sarcoidosis, tubulointerstitial nephritis syndrome, ANCA associated granulomatous nephritis, post-streptococcal nephritis, herpetic infections, syphilis, tuberculosis, and Wegener's granulomatosis. The clinical and immunopathological findings in our patient were consistent with HSPN. The laboratory investigations excluded the other potential aetiologies.

There are anatomic and haemodynamic relations between uveal and renal vasculature, which are important determinants for the site of immune complex deposition. Plasma passes through at high hydrostatic pressure and in large volumes through both the capillaries in the renal glomerulus and uveal tissue, and both vessels contain endothelial fenestrations.<sup>5</sup>

In classic HSP, there is alternative complement pathway activation with elevated levels of abnormally glycosylated serum IgA1. This is not sufficiently cleared by the liver and leads to increased levels of IgA1 containing circulating immune complexes.<sup>6</sup> The immune complexes may reach the eye in the circulation and then deposit in the uveal tissue. The sites of immune complex deposition are ocular resident cells—namely, vascular endothelial cells, pigmented epithelial cells, and corneal endothelial cells.<sup>7</sup> There is expression of adhesion molecules on the ocular resident cells, which allows leucocytes to migrate to the uveal tissue and cornea and cause tissue injury—namely, uveitis and keratitis.

In our patient, the finding of a granulomatous vasculitis is highly unusual. Activation of MHC restricted autoreactive CD4+ T cells in renal and uveal tissue may lead to strong macrophage responses, with the formation of granulomas. However, overlap syndromes with other forms of granulomatous vasculitis may occur.<sup>8</sup> This expression of MHC class II markers on ocular resident cells has been observed in various experimental uveitides,<sup>9,10</sup> and may explain the later presentation of uveitis in this case following remission of the HSPN.

We report an unusual case of a granulomatous HSPN in association with bilateral granulomatous anterior uveitis and keratitis. The inflammatory eye disease may be insidious in onset with an aggressive clinical course.

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## Lymphoepithelioma-like carcinoma of the eyelid: a report of two cases

Lymphoepithelioma-like carcinoma (LELC) of the skin is a rare malignant epithelial neoplasm, which resembles histologically the nasopharyngeal neoplasm of the same name.<sup>1,2</sup> Similar tumours have been reported at a variety of sites including salivary gland, tonsil, thymus, stomach, and uterus. Those involving the skin usually present as a papulonodular lesion on the head or neck of patients above 50 years of age. Only one case originating in the eyelid has been previously described.<sup>3</sup> We describe a further two cases and discuss the differential diagnosis.

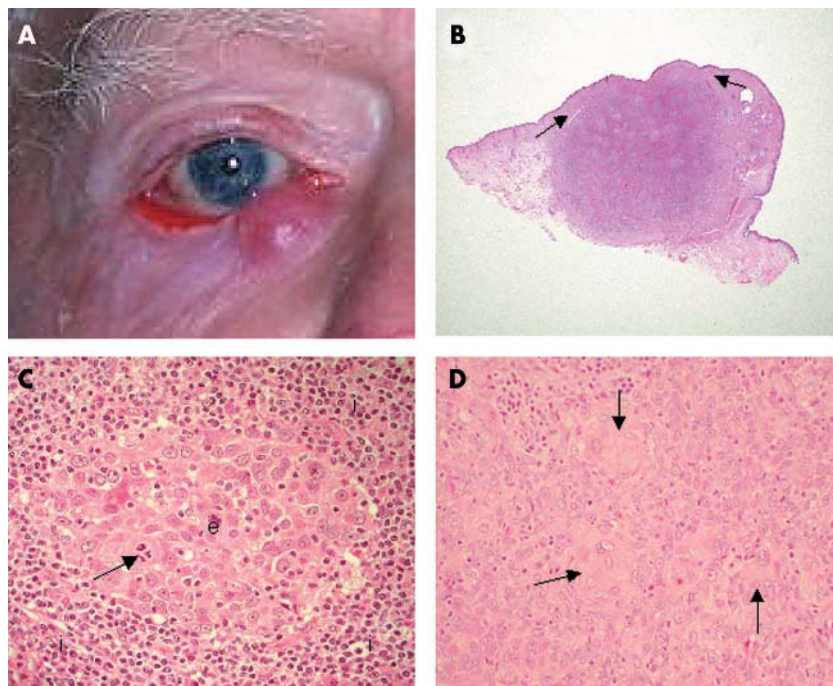
## Case 1

A 79 year old man presented with a fusiform swelling occupying the medial half of his right lower lid (fig 1A). This had developed 8 months previously and was gradually increasing in size. An ectropion repair had been performed on this lid 7 years before presentation. The patient underwent excision of the lesion with reconstruction of the lid using a pedicle flap. The excised lesion was submitted for histopathological examination.

The patient had a medical history of carcinoma in situ of the right vocal cord, which was treated with laser excision in 2000 with no recurrence on follow up.

## Case 2

A 67 year old man presented with a subcutaneous cystic lesion at the margin of the lower eyelid. This had been present for 8 months and was gradually increasing in size. A clinical diagnosis of sebaceous cyst



**Figure 1** (A) Clinical photograph of case 1 showing a smooth surfaced swelling at the medial aspect of the right lower eyelid. (B) Histological section from case 1 showing a relatively well circumscribed nodule of tumour situated within the superficial and deep dermis. There is clear demarcation from the overlying epidermis (arrows) (haematoxylin and eosin,  $\times 10$ ). (C) Histological section from case 1 showing a cluster of large epithelial cells (e), with an abnormal mitotic figure (arrow), surrounded by inflammatory cells (i) (haematoxylin and eosin,  $\times 200$ ). (D) Histological section from case 2 showing focal squamous eddies (arrows), reminiscent of an inverted follicular keratosis, a tumour of the follicular infundibulum (haematoxylin and eosin,  $\times 100$ ).

was considered. The lesion was excised and submitted for histopathological examination.

### Histopathological examination

Histopathological examination of both lesions showed a relatively well circumscribed lesion situated within the dermis with no connection with the overlying epidermis (fig 1B). The lesions consisted of clusters of malignant epithelial cells with vesicular nuclei and large nucleoli (fig 1C). Foci suggestive of hair follicle differentiation were identified in case 2 (fig 1D). These clusters of malignant epithelial cells were surrounded by a mixed reactive inflammatory cell infiltrate composed predominantly of lymphocytes and plasma cells. Eosinophils and polymorphs were also identified in the inflammatory infiltrate from case 2.

In both cases immunohistochemical staining showed strong positivity for cytokeratins and epithelial membrane antigen in the islands of malignant epithelial cells. Immunohistochemical staining for Epstein-Barr virus was negative.

### Comment

LELC, first described in 1988 by Swanson *et al.*,<sup>1</sup> is a rare cutaneous neoplasm that usually presents as a cutaneous nodule of short duration covered by an intact epidermis. The clinical diagnosis is often non-specific such as "lump" or "cyst." In contrast, the microscopic appearances, as described above, are distinctive.

The histogenesis of LELC is uncertain. Most authors support an adnexal origin.<sup>1,4</sup> This is suggested by the tumour location within the dermis and the absence of a

connection with the overlying epidermis. This is further supported by the identification of areas of adnexal differentiation in some tumours, as in case 2.<sup>4</sup> Conversely, cases displaying dysplasia in the overlying epidermis have been reported and this is suggestive of epidermal origin for LELC.<sup>5</sup>

Metastatic disease within the eyelid from underlying primary nasopharyngeal carcinoma (NPC) must be excluded before diagnosing LELC of the skin. The first patient had a history of carcinoma in situ of the larynx. The histology of this was reviewed and confirmed as squamous cell carcinoma in situ without evidence of invasion and there has been no evidence of recurrence on regular follow up. Furthermore, the surface epithelial cells of the laryngeal lesion were morphologically unlike the clusters of malignant epithelial cells seen in the LELC of the eyelid. Both patients also underwent endoscopy of the nasopharynx and no tumour or other abnormalities were identified.

NPC has a strong association with Epstein-Barr virus (EBV) infection. LELC at other sites has rarely been shown to have this association. Similar to those previously reported in the skin, EBV was not identified in either of our cases.<sup>6</sup> Other differential diagnoses include anaplastic lymphoma, poorly differentiated squamous cell carcinoma, sebaceous carcinoma, melanoma, Merkel cell tumour, and cutaneous lymphadenoma.<sup>7</sup> These can usually be discriminated from LELC with immunohistochemistry.

In the small number of cases reported so far, LELC appears to be of low malignant potential with a tendency towards local recurrence but a very low metastatic potential.<sup>1,2,4,5</sup> Both cases presented have shown no

sign of recurrence to date. LELC is a rare but distinctive malignant neoplasm that should be considered in the differential diagnosis of cyst like or nodular lesions of the eyelid.

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### Nylon paper: an alternative to cellulose acetate paper for use in conjunctival impression cytology

Conjunctival imprint cytology (CIC) offers valuable clues to the diagnosis and study of the pathogenesis of conjunctival disorders.<sup>1-3</sup> The technique involves the use of a membrane filter paper to pick up a layer of cells from the conjunctival surface.

This study was conducted to evaluate the results of CIC using a nylon filter paper compared to routinely used cellulose acetate paper. It involved 20 normal asymptomatic eyes of 10 participants. The participants had no ocular complaints and they were evaluated to rule out any conjunctival disease.

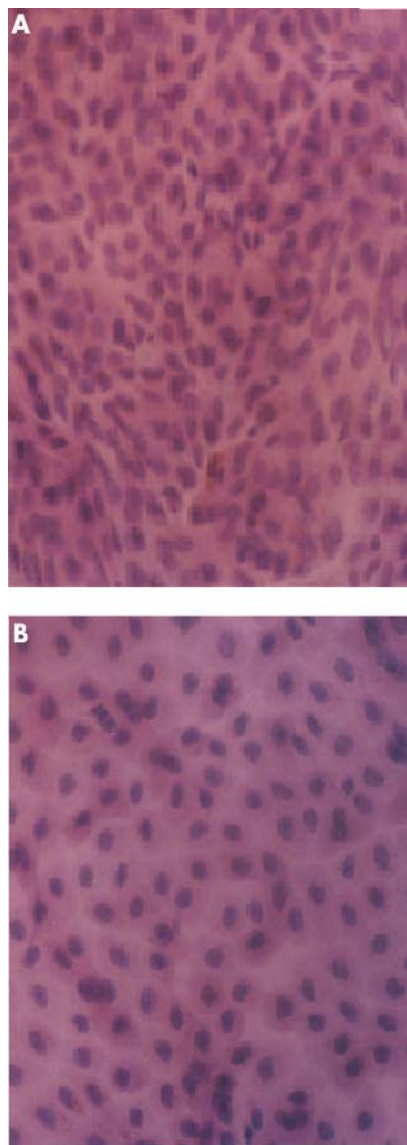
The procedure was explained to the participants and their consent was given.

CIC was done to assess the normal conjunctival cytology using Ultipor (nylon6, 6) and sartorius-type 111 (cellulose acetate paper).

The physical properties such as pore size and thickness of the two papers were matched.

### Technique

Cellulose acetate and nylon membrane filters were cut into small triangles and squares respectively to make their identification easy after staining. The conjunctiva was anaesthetised by topical 4% xylocaine. The filter



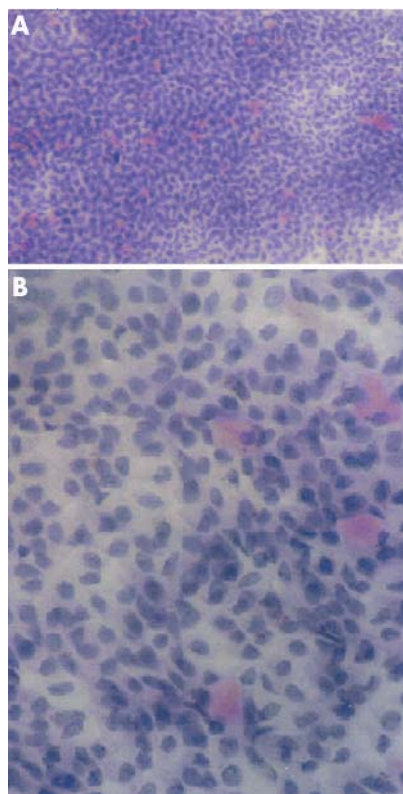
**Figure 1** (A) Haematoxylin and eosin stained nylon paper at 40 $\times$  magnification showing sheets of epithelial cells. (B) Haematoxylin and eosin stained cellulose acetate paper at 40 $\times$  magnification revealing sheets of small round epithelial cells.

paper was applied to the bulbar conjunctiva with blunt forceps. Gentle pressure was applied for 3–5 seconds and the paper was removed in a peeling motion. It was fixed thereafter in 95% ethanol and stained with either haematoxylin and eosin (H&E) or periodic acid Schiff (PAS) and haematoxylin stains.

The filter papers after staining were cleared in acetone and xylene, mounted in DPX and viewed under the light microscope. The morphology of epithelial cells in H&E stain and number of goblet cells in PAS stain were noted.

## Results

The participants involved in this study were in age group 22–37 years. A few initial slides were discarded because of overstaining. The time required to stain the filter papers compared to any other fixed tissue is



**Figure 2** Periodic acid Schiff (PAS) stained nylon paper at 10 $\times$  and 40 $\times$  magnification showing plump, oval, deeply pink PAS positive goblet cells amidst PAS negative cohesive sheet of epithelial cells.

lessened, and staining time is reduced to half with nylon paper compared with cellulose acetate paper.

Average time required for staining nylon and cellulose acetate paper was 20 minutes and 35 minutes, respectively, for PAS staining and with H&E stain it was 5 minutes and 10 minutes, respectively.

The specimens revealed sheets of small round epithelial cells in H&E stained nylon paper (fig 1A) and cellulose acetate paper (fig 1B).

Additional plump, oval, deeply pink PAS positive goblet cells amidst PAS negative cohesive sheet of epithelial cells were seen in schiff stained specimens on nylon paper. (fig 2).

The cell layer varies from one to several cells thick with occasional gaps where no cells adhere to the membrane filter. Cellulose acetate paper revealed a single layered sheet but the Ultipor showed that there were multiple layers in most places.

Occasionally the cells were not picked up or they were clumped so as to be visible as layers. This was seen equally with both the filter papers.

Cells were collected on nylon paper even in presence of lacrimation during the procedure. The cell morphology of specimens collected on either of the filter papers was comparable.

## Comment

CIC has been in use, as diagnostic tool since 1978, when Egbert first demonstrated its successful use with absorbent filter paper.<sup>3</sup> Before this Thatcher used a plastic device to

collect the epithelia.<sup>5</sup> Since then membrane filters like cellulose acetate have been widely used for this technique.<sup>6,7</sup>

The filtration membrane is a thin, polymeric film made up of microscopic pores. They can be composed of variety of natural and synthetic materials like cellulose acetate and cellulose nitrate in the former category, and PTFE, PVDF, glass fibres, and nylon in latter.

In this study nylon and cellulose acetate were used for comparison of the results.

The nylon paper is more compatible with the organic solvents used in staining procedures. The adsorption is better with nylon than the cellulose acetate paper. Also there is a cost difference between the two, with cellulose acetate paper costing three times that of nylon.

The cytological features of epithelial as well as goblet cells were studied. The goblet cells are identified conclusively by the PAS positive cytoplasm or by their eccentrically placed nuclei and plump shape and large size. The epithelial cells are small and round with eosinophilic cytoplasm. The nuclei are large and basophilic.

Added benefit of nylon over cellulose acetate are:

- (1) Cost effective
- (2) Less staining time
- (3) Ability to collect cell even if lacrimation wets the paper
- (4) Comparable morphological results to cellulose acetate
- (5) Compatible with variety of solvents hence more stable
- (6) Deeper layers also picked, hence detailed evaluation of biopsy.

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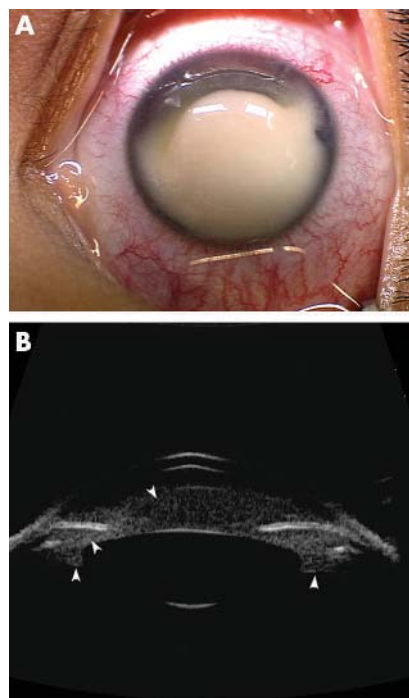
## “C-scan” ultrasound imaging of optic nerve extension of retinoblastoma

Three dimensional ultrasound based coronal “C-scan” imaging technique was used to demonstrate optic nerve extension of retinoblastoma. With a clinical diagnosis of retinoblastoma based on clinical evaluation, ultrasound, and computed radiographic tomography, this patient was treated by primary enucleation. Subsequent histopathological evaluation of the enucleated globe revealed three risk factors for metastatic retinoblastoma (including optic nerve extension).<sup>1,2</sup> Both systemic chemotherapy and orbital radiation therapy were employed.<sup>3</sup>

### Case report

A 2 year old black female presented with a 1 month history of conjunctival vascular dilation, leucocoria, strabismus, and ptosis involving the right eye. Slit lamp examination revealed a yellow-white tumour filling 70% of the anterior chamber and obscuring view of the posterior segment (fig 1A).

High frequency ultrasonography (35 MHz) demonstrated the presence of tumour cells in both the anterior and posterior chambers, as well as the vitreous (fig 1B).<sup>4</sup> Three dimensional B-scan ultrasonography (3DUS) (12 MHz) revealed a mushroom-shaped retinal detachment and a large endophytic retinoblastoma with orbital shadowing. A V-shaped widening of the optic nerve shadow as it exited the globe was noted (fig 2A). This patient was examined by magnetic resonance imaging (MRI) before enucleation surgery and no optic nerve invasion was noted.



**Figure 1** (A) External photograph of the anterior segment filled with retinoblastoma. (B) 35 MHz high frequency ultrasound demonstrates tumour cells in both anterior and posterior chambers, and anterior vitreous (arrowhead).

Enucleation was subsequently carried out with care to obtain as long an optic nerve stump as possible. There was no difficulty in transecting the optic nerve. Histopathological sections revealed anterior segment infiltration, massive choroidal involvement, and a corresponding similar V-shaped enlargement of the nerve posterior to the lamina cribrosa (fig 2B). Preoperative coronal C-scan ultrasound views of the optic nerve also demonstrated an enlarged optic nerve sheath diameter (ONSD) (fig 2C). This finding was consistent with full thickness retinoblastoma infiltration of the optic nerve fibre bundles as seen on histopathology (coronal sectioning of the distal end of the transected optic nerve) (fig 2D).

Subsequent MRI of the brain and lumbar cerebrospinal fluid cytology were interpreted to be normal.

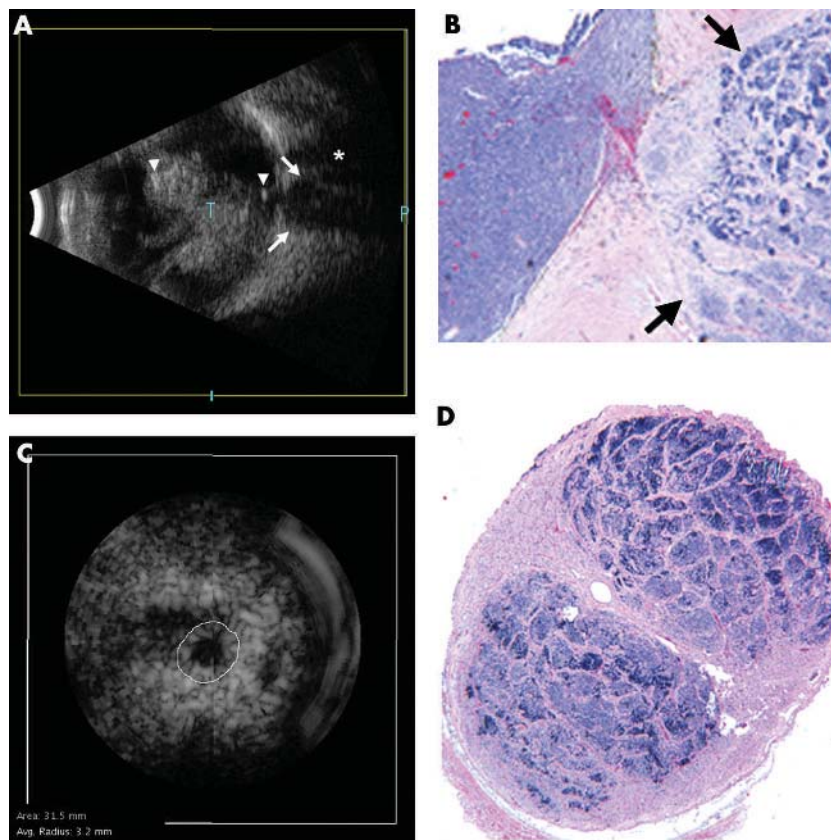
### Comment

Retinoblastoma can invade the optic nerve.<sup>1,2</sup> Though the entire optic nerve is best evaluated by CT or MRI,<sup>5,6</sup> 3DUS C-scan imaging has recently been found to be capable of measuring the ONSD. These measurements have been reported from normal healthy subjects and approximate normative values

by CT or MRI reports. This technique has also been used in clinical assessment of optic nerve sheath meningiomas.<sup>7-9</sup> The relative cost of a three dimensional ophthalmic ultrasound machine is far less than a CT and even less than MRI. Consider that CT and MRI require shielded rooms. Ultrasound examinations are typically shorter than CT or MRI, the ultrasound machine is more mobile, less personnel intensive, and does not require contrast agents.

Optic nerve measurements are based on 3DUS generated coronal C-scan images derived from 97 successive B-scans recorded at 2 degree intervals around the axis of the nerve.<sup>9,10</sup> Utilising a representative C-scan image of the nerve, one can trace its outline and obtain an average measurement of the enclosed area. This image is carefully selected from a series of consecutive coronal images of the nerve at a predetermined distance behind the globe. A good correlation between ONSD measurements by C-scan imaging and MRI has been reported.<sup>8</sup> The normal ONSD found in healthy adults ranges from 3.9–6 mm by 3DUS, whereas the normative measurement in cadaver eyes is 4 mm.<sup>6,7</sup>

In this case of retinoblastoma, the measurement obtained 1.5 mm behind the globe



**Figure 2** (A) Three dimensional ultrasound (12 MHz) reconstruction demonstrates a longitudinal view of the V-shaped and widened optic nerve shadow (retinoblastoma infiltrated) as it exits the eye (arrow). Intratumoral calcification (arrowhead) with orbital shadowing (asterisk) consistent with retinoblastoma was noted. (T, temporal, P, posterior, I, inferior). (B) Histopathological evaluation reveals a similar V-shaped, retinoblastoma induced bulging of the optic nerve (arrow) posterior to the globe secondary to diffuse tumour infiltration (haematoxylin and eosin, original magnification,  $\times 40$ ). (C) A posterior coronal “C-scan” image shows an enlarged optic nerve sheath diameter (ONSD) of 6.4 mm (circle). The dark area just superotemporal to the nerve is orbital shadowing caused by retinoblastoma. (D) Higher power view shows a cross section of the distal end of the optic nerve (average ONSD 4.5 mm) with full thickness infiltration by retinoblastoma (haematoxylin and eosin, original magnification,  $\times 100$ ).

was 6.4 mm by 3DUS, and 4.5 mm by histopathology (similar discrepancies have been related to fixation). In this 2 year old patient, both measurements were larger than normal as a result of the mass effect of infiltrated retinoblastoma cells.

Coronal C-scan ultrasound imaging is a new, effective, and relatively inexpensive method to screen for the increased ONSD associated with optic nerve extension of retinoblastoma.

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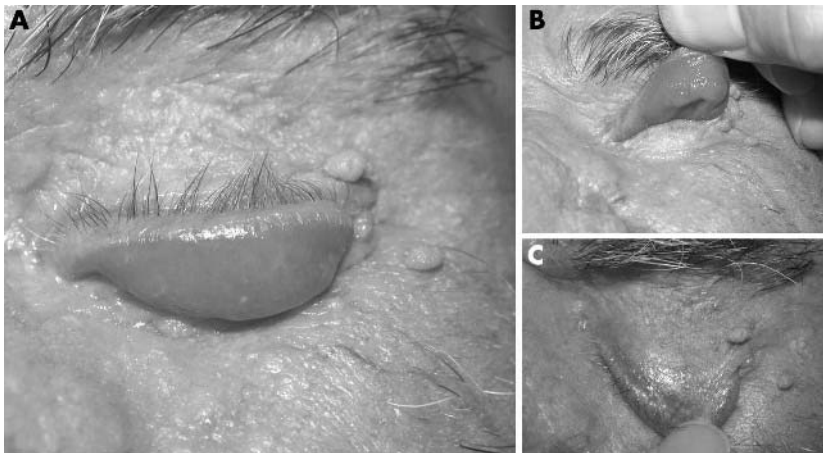
Competing interests: none declared

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## Non-cicatricial upper eyelid ectropion

We present three rare cases of non-cicatrising upper lid ectropion, seen in two oculoplastic units.



**Figure 1** Patient 1. (A) Preoperative picture showing marked left upper lid eversion. (B, C) The marked lid laxity is shown, with no signs of anterior lamella cicatrization.

### Case 1

A 92 year old man with progressive dementia presented with a left upper lid ectropion, which could not be repositioned manually. The patient was of normal weight and had no history of obstructive sleep apnoea (OSA), joint laxity, or skin laxity. An injected, oedematous and hypertrophied upper lid tarsus was noted (fig 1A), but no obvious chronic staphylococcal changes. There was no evidence of anterior lamella cicatrization (fig 1B and 1C). Moderate to severe horizontal laxity of the left upper eyelid and significant laxity of the left lateral canthal tendon (10 mm medial distraction) were noted. On the right side there was an aponeurotic ptosis, with a milder degree of horizontal laxity and lateral canthal tendon laxity (6 mm medial distraction). There was no evidence of enophthalmos. Conservative treatment with an eye shield, lubricants and topical steroids resulted in no improvement and the everted tarsus failed to remain in the correct position when manual repositioning was attempted. The patient underwent a left upper lid lateral full thickness pentagonal wedge resection of 15 mm, and levator aponeurosis reattachment, with no recurrence of ectropion after a 5 month follow up period.

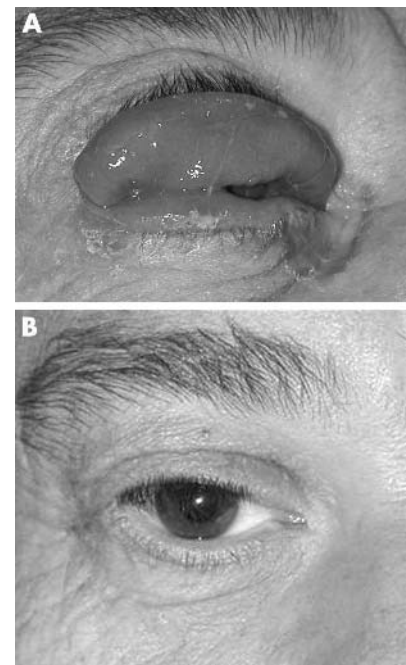
### Case 2

A 49 year old man with obesity and OSA, presented with a constant right upper and lower lid ectropion with a severely injected and hypertrophied conjunctiva (fig 2A). He reported usually sleeping on his right side. On examination there was significant horizontal lid laxity of upper and lower lids, as well as of the lateral canthal tendons bilaterally, but no cicatrization of the anterior lamella. There was marked ptosis on the right and normal levator function. The everted right upper eyelid could not be manually repositioned and there was marked oedema and inflammation of the upper tarsal conjunctiva. He was diagnosed with a floppy eyelid syndrome and right upper and lower lid ectropion, and underwent a right lower lid lateral tarsal sling and a bilateral upper lid lateral full thickness pentagonal wedge resection (10 mm) and blepharoplasty. Several months later, he underwent a right aponeurotic ptosis repair and a second upper lid lateral wedge resection (5 mm) with horizontal tightening

for residual upper lid ectropion. No recurrence was noted over a 48 month follow up period (fig 2B).

### Case 3

A 90 year old woman with early senile dementia presented with a right upper eyelid tarsal ectropion which could not be repositioned manually. She denied any history of OSA or eye rubbing and had no significant joint or skin laxity. She was not underweight or overweight for her height and there was no enophthalmos. The everted tarsus was markedly injected and hypertrophied, but no obvious chronic staphylococcal changes were seen and no cicatrization of the anterior lamella was noted. In addition, she had



**Figure 2** Patient 2. (A) Right upper and lower lid ectropion with marked conjunctival injection and hypertrophy. (B) Postoperative result shows correction of the upper and lower lid ectropions.

bilateral medial lower lid ectropions with moderate to severe horizontal lid laxity of upper and lower lids, as well as the lateral canthal tendons (10 mm medial distraction). The patient did not respond to conservative treatment with lubricants and topical steroids, and she underwent right upper lid ectropion repair with a lateral full thickness pentagonal wedge excision (15 mm) and levator aponeurosis reattachment. No recurrence was noted after a 6 month follow up period.

### Comment

We have described three patients with an unusual presentation of a non-cicatrising constant upper lid ectropion. Correcting the upper lid laxity with a full thickness pentagonal wedge resection and horizontal tightening<sup>1</sup> resulted in a good outcome in all patients.

Upper lid ectropion is not common. In newborns, it is usually temporary and responds to conservative measures. Less commonly, it may result from shortage of anterior lamella, as in blepharophimosis syndrome and congenital ichthyosis.<sup>2</sup> A recent report found mild degrees of upper lid eversion in a series of patients with multiple endocrine neoplasia type 2B.<sup>3</sup> Upper lid ectropion in adults usually results from pathologies affecting the anterior lamella such as chronic sun damage, irradiation, chronic dermatitis, skin infections, ichthyosis, chemical burns, and previous surgery.<sup>2</sup> In patients with the floppy eyelid syndrome the spontaneous upper lid eversion usually occurs during night sleep and is easily repositioned manually.<sup>4,5</sup> In a recent report, Burkat and Lemke<sup>6</sup> described 80 patients with acquired lax eyelid syndrome who were treated with the four eyelid tarsal strip periosteal flap technique. Although all patients had significant horizontal laxity, none of them had spontaneous upper lid eversion. While spontaneous upper eyelid eversion may occur in conditions such as floppy eyelid syndrome or lax eyelid syndrome which induce sufficient lid laxity, manual repositioning is generally possible. In all our patients the ectropion remained constant and could only be corrected surgically. Only patient 2, who was the youngest, was diagnosed with the floppy eyelid syndrome. The other two were older, had no systemic signs of the floppy eyelid syndrome, and the eyelid changes appeared to be age related.

We believe that the marked horizontal laxity was the main causative factor causing upper lid ectropion in our cases, but poor levator muscle function, dehiscence of the aponeurosis, and involutional tarsal changes<sup>7,8</sup> may further contribute to tarsal instability and upper lid ectropion. Two of the patients in our series had significant dementia, and frequent eye rubbing resulting in conjunctival fornical oedema with tarsal conjunctival oedema and inflammation, may have been a factor in preventing repositioning of the everted tarsus. In the case of the patient with floppy eyelid syndrome, traumatic irritation during sleep may have led to sufficient tarsal conjunctival oedema and inflammation to prevent repositioning of the eyelid.

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## MAILBOX

### Sub-Tenon's block versus topical anaesthesia for cataract surgery

We read with great interest the article by Ruschen *et al* comparing patient satisfaction during cataract surgery with sub-Tenon's block (STB) versus topical anaesthesia (TOP).<sup>1</sup> The authors concluded that in the setting of day case cataract surgery, patients reported significantly higher satisfaction scores with STB than TOP.

We would like to raise two issues for discussion. Firstly, the lower satisfaction score in the TOP group may only reflect a suboptimal TOP that was given in the current study and may not be generalisable to other forms of TOP. In our experience, lignocaine gel (lidocaine hydrochloride 2%, AstraZeneca, Sweden) produces significantly better anaesthetic effects than local anaesthetic eye drops. Lignocaine gel has been previously shown to be an effective<sup>2,3</sup> and possibly a more superior<sup>4,5</sup> anaesthetic agent in cataract surgery, as well as giving better patient cooperation with less intraoperative supplement.<sup>5</sup> To further evaluate the apparent lower satisfaction scores with TOP than STB, we would be grateful if the authors could provide the details of their TOP anaesthetic procedure—for example, how long before the actual surgery were proxymetacaine and amethocaine given and whether supplementary anaesthetic eye drops were allowed during the surgery?

Secondly, even though the median satisfaction score in the TOP group was

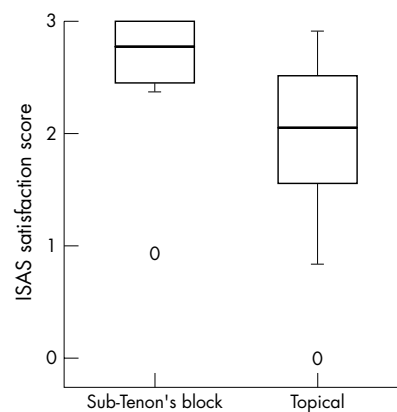


Figure 1 Box and whisker plot of satisfaction score with sub-Tenon's block or topical anaesthesia. (From Ruschen *et al*)

significantly lower than that of the STB group, there was a much larger variation in the TOP group (fig 1). This would imply some patients were satisfied while some were dissatisfied. We certainly believe not all patients can tolerate TOP and it would be highly desirable for cataract surgeons to identify the latter group preoperatively. Were there any specific characteristics in this group showing such dissatisfaction? Moreover, we noted that there were more females (12 out of 14 patients) in the TOP group, compared to the STB group (five out of 14 patients). This difference was statistically significant ( $p = 0.018$ , Fisher's exact test). We recognise that randomisation had been implemented in the present study and any significant differences in patients' demographics were beyond the control of the authors. However, such difference might have impacted the satisfaction scores, as it is known that women have high rates of physical symptom reporting.<sup>6</sup>

None the less, we do commend the authors' work on this important topic. We agree with the authors that sub-Tenon's anaesthesia may be a better choice in some patients undergoing cataract surgery. However, other forms of topical anaesthesia may produce equally good, if not better, patient satisfaction especially in selected patients.

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## Patient satisfaction with anaesthesia comparing sub-Tenon's block and topical anaesthesia

We read with great interest the results of the pilot study comparing patient satisfaction between topical and sub-Tenon's anaesthesia.<sup>1</sup> In conclusion, the authors state that sub-Tenon's block produces higher satisfaction scores than topical anaesthesia.<sup>1</sup>

The scores used were obtained using the Iowa Satisfaction with Anesthesia Scale (ISAS), which has been used many times during other forms of surgery.<sup>2</sup>

However, the ISAS has not been used in the setting of unmonitored anaesthetic care and has not as yet been fully validated in a purely local anaesthetic environment. Dexter, who was part of the team that developed the ISAS, has said that the ISAS is still to be validated in this setting. Therefore, we would suggest that the conclusions that sub-Tenon's anaesthesia gives better satisfaction than topical anaesthesia, purely based on this scale, is slightly premature.

The ISAS is due to be validated soon using local anaesthesia and sedation<sup>3</sup>; however, it is still used specifically during monitored anaesthetic care and is as yet not tested on unmonitored anaesthetic care, which is often found during topical cataract lists.

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## Cataract surgery and IOP

We would like to congratulate Issa *et al*<sup>1</sup> on their excellent and, we believe, important paper regarding cataract surgery and intraocular pressure drop.

It has become increasingly obvious to us, in our practice, that many patients do indeed get a significant drop in intraocular pressure (IOP) after phacoemulsification. We now have a substantial number of patients with both acute and chronic angle closure who, following cataract surgery, have been able to come off all antihypertensive medications. We would now go as far as to say that in these patients it is now the operation of choice (when medical therapy has deemed to have failed) and this is supported by a number of studies.<sup>2–5</sup> There is also the added benefit of a reduction in the incidence of aqueous misdirection.

It is interesting that Issa *et al* used “normal” patients in their study and still found a significant reduction in IOP. We have thought for sometime that a number of glaucoma patients who, on gonioscopy, are seen to have “open angles” but on closer inspection have some (usually central) anterior chamber shallowing, often seem to have profound drops in their IOP following cataract surgery. Although many of these patients have degrees of hypermetropia, this is not always the case. Indeed with increasing nuclear sclerosis some may be myopic at presentation.

The authors rightly state that their study needs to be repeated by others to confirm their results. We think that lens thickness has more of a role than this study suggests. There is an important flaw—acknowledged by the authors—regarding the lack of data on corneal thickness. Any future studies need to correct for this, not only to allow a more accurate assessment of the IOP, but because the cornea itself is part of the anterior structure of the eye and may not necessarily be an independent variable.

Finally we speculate that there is likely to be a measurable relation between IOP, volume of the anterior segment, lens size, and possibly corneal thickness. Once we have quantified this it may then allow us not only to be able to assess the likely magnitude of IOP drop after phacoemulsification, but will give an essential insight into some of the underlying mechanisms of raised IOP.

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after acute angle-closure glaucoma. *Ophthalmology* 1999;**106**:669–74.

## Normal tension glaucoma

I enjoyed the recent study by Ogata *et al*, in which they attempted to assess the interrelation between intracranial vascular compression of the optic nerves and normal tension glaucoma.<sup>1</sup> Coronal magnetic resonance images of the optic nerves were used to assess the degree of compression of the intracranial optic nerves and the supraclinoid internal carotid arteries. Compression of an optic nerve by a normal internal carotid artery was found in 51 of 103 eyes (49.5%) of patients with normal tension glaucoma and in 36 of 104 (34.6%) eyes of control patients. The degree of compression was noted to be greater in patients with normal tension glaucoma. These findings led the authors to conclude that one cause of normal tension glaucoma may be compression of the optic nerve by the internal carotid artery.

As noted in the discussion, Jacobson *et al* found compression of the intracranial optic nerve by the internal carotid artery to be common in asymptomatic patients (bilateral contact in 70%, bilateral compression in 12%, unilateral contact or compression in 5%).<sup>2</sup> In symptomatic patients, Jacobson noted glaucomatous visual field defects and “saucer-like temporal excavation” of the optic disc on the side of the compression.<sup>3</sup> Symptomatic patients also had temporal neuroretinal rim pallor and other signs of compressive optic neuropathy such as decreased visual acuity and decreased colour vision, thereby distinguishing them from patients with normal tension glaucoma.<sup>4</sup>

In the Ogata study, inclusion of three additional outcome measures would be useful in defining any association that may exist between intracranial optic nerve compression and pseudoglaucomatous cupping. Firstly, did patients with normal tension glaucoma and intracranial optic nerve compression have decreased visual acuity, decreased colour vision, or associated pallor of the temporal neuroretinal rim on the side of the compressed optic nerve? Secondly, was the observed cupping in eyes with normal tension glaucoma and optic nerve compression vertical in orientation (that is, pseudoglaucomatous) or horizontal or round (that is, non-glaucomatous), and did this configuration differ in eyes without optic nerve compression? Finally, was the diagnosis of normal tension glaucoma confined to the involved side in the nine patients with unilateral optic nerve compression, as the study hypothesis would predict?

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## Vision restoration therapy

A recent paper<sup>1</sup> and accompanying editorials<sup>2,3</sup> in the *BJO* have raised the question of whether vision restoration therapy is effective in the rehabilitation of visual field defects. As members of the scientific medical advisory board of NovaVision, we believe these editorials require comment and refer the interested reader to an opposing editorial in a recent issue of the *BJO* by Sabel and colleagues<sup>4</sup> and to an article in press in *Restorative Neurology and Neuroscience*.<sup>5</sup> Although we acknowledge that statements by members of an advisory board are always complicated by potential conflicts of interest, we hope that our colleagues will recognise our commitment to scientific debate.

We believe the current evidence does not support Horton's contention that "no therapeutic intervention...can correct effectively the underlying visual field deficit" after post-chiasmatic injury. On the contrary, a comprehensive and critical review of the literature reveals that there is a sound scientific basis for recommending vision restoration therapy for some patients with hemianopia. Studies of the practical effectiveness and scientific basis of vision restoration therapy are now ongoing, and patients are being treated at nine US centres. We urge physicians and scientists to review the current literature and the results of future studies as they become available. Although there are clearly important questions regarding this intervention that need to be elucidated, it is evident that the main goal, that of visual rehabilitation, is attained for some of those treated with vision restoration therapy. In our opinion, the preponderance of the data supports the notion that this intervention is valuable and results in visual improvement for certain patients with visual field defects.

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Disclosure: The authors are members of the Scientific and Medical Advisory Board of NovaVision, the company that has developed vision restoration therapy.

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## NOTICES

### EVER 2005 meeting

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

### World Ophthalmology Congress 2006 – Brazil

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

For further information on the congress and committees, scientific program and coordinators of different areas are available at the congress website [www.ophthalmology2006.com.br](http://www.ophthalmology2006.com.br)

### Red eye

The latest issue of *Community Eye Health* (No 53) discusses the role of primary care in the treatment of red eye. For further information

please contact: Journal of Community Eye Health, International Resource Centre, International Centre for Eye Health, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK (tel: +44 (0)20 7612 7964; email: [Anita.Shah@lshtm.ac.uk](mailto:Anita.Shah@lshtm.ac.uk); online edition: [www.jceh.co.uk](http://www.jceh.co.uk)). Annual subscription (4 issues) UK £28/US\$45. Free to developing country applicants.

### ORBIS introduces surgical simulator to train ophthalmologists across developing world

International development agency, ORBIS, is using a high-tech ophthalmic surgical simulator for the first time this month, as part of its Flying Eye Hospital training programme in Varna, Bulgaria (8-24 June). The 'Eyes-1' training system will be used by ORBIS to help train eye specialists in developing countries in the latest surgical techniques to prevent and treat avoidable blindness.

Through its work as an international development agency ORBIS has completed over 500 training programmes in 76 countries and has established permanent country programme offices in five nations – Bangladesh, China, Ethiopia, India, and Vietnam. Since 1982 ORBIS volunteers have treated more than 25000 patients and trained over 70000 medical professionals.

The Eyes-1 surgical simulator was created by VRmagic Technology Group in 2002, a German company specialising in image processing and display technology.

For further information or contributions of any kind please call +44 (0)20 7608 7260 or visit [www.ukorbis.org](http://www.ukorbis.org)

### 4th International Conference on Ocular Infections

This will take place on 1-4 October 2005 in Hokkaido, Japan. For further information please contact the Management Secretariat, [icoi2005@convention.co.jp](mailto:icoi2005@convention.co.jp).

### Thoughts on Ophthalmology and Development

The Matus Eye Foundation is a small, privately-financed organisation, established 17 years ago by a former international banker who began his medical studies at age 40 with the specific intention of working in third world surgical ophthalmology. The Foundation's experiences and lessons learned are presented in a 26 page bound summary entitled *Thoughts on Poor World Ophthalmology Development*, an often critical look at eye surgery programs in Latin America, Africa, and Haiti. To obtain this report without cost, please contact. [jheatherly@taylormathis.com](mailto:jheatherly@taylormathis.com).



## Treatment of biopsy proved conjunctival intraepithelial neoplasia with topical interferon alfa-2b

S Esquenazi, C L Fry and E Holley

*Br J Ophthalmol* 2005 89: 1221  
doi: 10.1136/bjo.2004.063339

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