a spontaneous first trimester miscarriage. Chromosomal analysis of his son with Down's syndrome showed a 47XY+21 karyotype, but no evidence of a deletion of 13q14. Chromosome analysis of the patient himself was not performed as the absence of the deletion in his son indicated that he would not be a carrier of the abnormality.

Discussion

The inheritance of retinoblastoma is autosomal dominant with a 90–95% penetrance. The offspring of all gene carriers therefore have a 50% risk of inheriting the mutant gene.⁴ Knudson⁵ showed that in those individuals carrying a predisposing mutation, a single additional event is sufficient for tumorigenesis. As the chance of this event occurring in the precursor retinal cell population is relatively high, gene carriers usually develop multiple bilateral tumours at an early age. In sporadic cases both mutations are somatic and must occur in homologous genes in the same retinal precursor cell. They are usually unilateral, unifocal and have a later age of onset.

This 'two-hit' hypothesis represents one explanation for the incomplete penetrance observed in familial retinoblastoma. However, incomplete or 'low penetrance', i.e. individuals with unilateral or regressed retinoblastoma, appears to occur more commonly in some families.⁶ It has therefore been suggested that the nature of the mutation may also play a role, and a recent series demonstrated that most mutations had altered rather than absent gene function in these families (J. K. Cowell, personal communication).

Spontaneous regression is an uncommon but well-described feature of retinoblastoma. In one study of 1500 cases of retinoblastoma at the Harkness Institute in New York, 1.8% of cases were classified as spontaneously regressed tumours; over half of these were associated with the familial variant.⁷ Seventy-eight per cent of patients had visual acuities of 20/40 or better.

This case demonstrates again the importance of ocular fundus examination in first degree relatives of a patient with a unilateral, apparently sporadic case of retinoblastoma, as the finding of spontaneously regressed tumours in a parent substantially alters the risk ratio of tumour development in subsequent family members.⁸ This therefore affects the advice given in genetic counselling. Current figures suggest a 1% recurrence risk to siblings of a unilaterally affected child, whereas the offspring of an affected parent have a 45% chance of developing retinoblastoma (1 in 2 chance of inheriting the mutation and 90% penetrance).

Since the retinoblastoma gene (RB1) was cloned, several RFLPs (restriction fragment length poly-

morphisms) and VNTRs (variable number tandem repeats) have been identified for linkage analysis in familial cases and are informative in about 85–95% of cases.⁹ This enables identification and targeted screening of gene carriers, and will reduce the screening load for ophthalmology departments. It also facilitates prenatal diagnosis. Our family was offered linkage analysis to assess the gene carrier status in their unaffected son, but they declined.

In summary, we suggest that all family members of a patient with retinoblastoma should have an ophthalmological examination and the family be offered linkage analysis.

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Sir,

Temperature-Dependent Resistance to Gentamicin in Graft Keratitis by *Stenotrophomonas (Xanthomonas) maltophilia*

A 58-year-old woman with congenital epithelial dyskeratosis was admitted with bacterial keratitis of her right eye. She underwent a penetrating kerato-

plasty (PK) combined with a cataract extraction and lens implant, following which she developed an episode of *Pseudomonas fluorescens* keratitis. A therapeutic corneo-scleral graft was performed, in which a second keratitis then developed (Fig. 1).

A corneal scrape was performed and cultured on Columbia blood agar (incubated at 37°C), heated Columbia blood agar (incubated aerobically with 5% added CO₂ at 37°C) and Sabouraud agar (incubated aerobically without CO₂ at 30°C). *Acanthamoeba* cultures were also performed¹ but remained negative. Gram stain of the scrape material showed leucocytes and Gram-negative bacilli, and topical cefuroxime (50 mg/ml) and gentamicin (14 mg/ml) at hourly intervals were started whilst culture sensitivity results were awaited.

Initial cultures yielded a moderate growth of three colonial types of Gram-negative bacilli, two of which were oxidase-negative and one which was oxidase-positive. These organisms were identified, using commercial identification kits (API 20E, and 20NE Biomerieux, Basingstoke, UK), as *Klebsiella oxytoca* (identification value 97.5%), *Pseudomonas fluorescens* (identification value 96.9%) and *Stenotrophomonas maltophilia* (identification value 99.9%). *K. oxytoca* and *S. maltophilia* were oxidase-negative whilst *P. fluorescens* was oxidase-positive. Susceptibility tests were performed on all these organisms at 37°C using a break-point method and all were shown to be susceptible to gentamicin at a break point of 2 mg/l, ceftazidime at 8 mg/l and colistin at 10 mg/l.

After 3 days gentamicin was continued as the only topical antibiotic. On the fourth day the clinical appearance deteriorated, and the abscess continued to increase in size despite the reintroduction of cefuroxime. After stopping all antibiotics for 12 hours a corneal scrape was performed and gentamicin and cefuroxime recommenced. These cultures also yielded *K. oxytoca*, *P. fluorescens* and *S. maltophilia*, which were all sensitive to gentamicin when tested at 37°C. Further *in vitro* tests on all three organisms

revealed that only *S. maltophilia* was resistant to gentamicin when incubated at 30°C, but was sensitive to ciprofloxacin at both temperatures. Therefore the treatment was changed to ciprofloxacin 0.3% at hourly intervals and the abscess resolved.

Comment

A recognised standard therapy following a corneal scrape for suspected bacterial keratitis is topical gentamicin and a cephalosporin² or ciprofloxacin³ at frequent intervals. Further management is based on the results of the Gram stain, culture and sensitivities. If the cultures are negative or the infection does not appear to respond to therapy, then a rescrape and corneal biopsy are recommended² using standard and other specified conditions.

S. maltophilia is primarily a plant pathogen and in humans it can cause opportunist infections; however, there was no history of plant material being involved in this case. *S. maltophilia* can cause serious ocular infections including endophthalmitis⁴ and bacterial keratitis.⁵ In conditions where the site of infection is at a reduced temperature, such as continuous ambulatory peritoneal dialysis, different *in vitro* sensitivities to gentamicin when tested at 30°C and 37°C have been shown to have a direct effect on clinical outcome.⁶

Emergence of resistance to gentamicin at 30°C rather than 37°C after treatment with topical gentamicin has been reported in *Pseudomonas aeruginosa*⁷ and was linked to poor growth of this organism.⁸ In this case the growth rate of *S. maltophilia* was the same at both 30°C and 37°C. Resistance of *S. maltophilia* to gentamicin when tested at 30°C has been reported previously⁹ and is a recognised characteristic of this organism. *S. maltophilia* has been shown to express additional outer membrane proteins when grown at 30°C that reduce the permeability of the cell membrane to gentamicin.⁹ For these reasons we believe that resistance to gentamicin did not emerge during treatment but was present before treatment was commenced.

The temperature of the anterior segment is less than core body temperature and may have been a factor in the persistence of *S. maltophilia* despite topical gentamicin. Performing susceptibility tests at 30°C rather than 37°C may provide a better indication of clinical success when *S. maltophilia* is the infecting organism.

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Fig. 1. Corneo-scleral graft keratitis with infiltrate inferiorly and purulent exudate.

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Sir,

Long-Term Oral Corticosteroids and Osteoporosis Prevention in an Ophthalmology Clinic

Osteoporosis is a disease characterised by low bone mass with microstructural changes which enhance bone fragility and thereby increase the fracture risk.¹ It is recognised in postmenopausal women as an important cause of morbidity: fractured neck of femur, vertebral crush fractures and chronic back pain. Osteoporosis is now also recognised as an important problem in patients on high-dose corticosteroid therapy.^{2,3} The steroid effect on bone mass

may occur early during treatment and once established the osteoporosis may be hard to reverse.⁴ The Department of Health Advisory Group Report on Osteoporosis³ states that patients on more than 5 mg of prednisolone daily for more than 3 months are candidates for screening.

Several agents including calcitonin,⁵ bisphosphonates,⁶ calcium supplements,⁷ vitamin D analogues⁴ and hormone replacement therapy (HRT)⁸ are being used to treat osteoporosis. There is no consensus as to how and when these agents should be used to prevent steroid osteoporosis. An exception to this is calcium supplementation, which should be given routinely to steroid patients.^{5,7,9} There is also evidence to suggest that HRT should be given to women put on corticosteroids who are postmenopausal or have had a hysterectomy.^{3,7}

In this study we reviewed patients on oral steroids for longer than 4 months who were managed by an ophthalmologist to find the numbers on osteoporosis prophylaxis or who had been given written information regarding increased calcium in their diet.

Methods and Results

Using the pharmacy computer, patients numbers and names given prescriptions of oral steroids from the ophthalmology department in the previous 3 years were identified. Case notes were reviewed for: age; sex; clinical problem; length of time on oral steroids; who was managing the patient; and advice on osteoporosis given, either written in the notes or in a letter to the patient's general practitioner (GP).

Corticosteroids were prescribed for at least 4 months to 112 patients. All patients started with greater than 30 mg prednisolone. These were co-managed in 29 cases. In 83 cases management was purely by the ophthalmology department with the GP. The indications consisted of 52 giant cell arteritis (not all biopsy proven), 7 dysthyroid eye disease, 6 retinal vasculitis, 8 scleritis and 10 others. Fifty-eight patients were female (17 younger than 45 years), mean age 68.2 years range (15-84 years), and 25 were male, mean age 66.4 years (range 18-82 years).

A review of the 83 case notes revealed no evidence of any advice on osteoporosis prevention being given to any of the patients studied and no mention of this requirement to the GP. A review of the eye department pharmacy area (separate from the main pharmacy) failed to reveal any osteoporosis prevention leaflets. The pharmacists when questioned also said that they did not inform patients of this problem.

Discussion

Oral steroids have a large effect on bone metabolism. Corticosteroids inhibit calcium absorption,¹⁰ suppress circulating oestrogen¹¹ levels in women and