Sir,

We read with great interest the paper by Rosa Tang *et al*. titled 'Retinal changes associated with tamoxifen treatment for breast cancer'.[1] While we agree that 'the clinical significance of retinal findings in the absence of visual changes remains unknown', we must emphasise that once visual loss has occurred it is not always reversible, even if recognised early. We wish to present a case of persistent and progressive visual loss induced by tamoxifen.

Case report

A 57-year-old woman was referred to the Eye Clinic with a 6 month history of difficulty reading. There was no history of amblyopia. She was an ex-smoker. Her past medical history included type II diabetes controlled on diet, and heart failure treated with Dyazide (SmithKline Beecham). Thirty-three years previously carcinoma of the left breast had been diagnosed. This was treated by left mastectomy and radiotherapy. Local recurrence had been treated with further lumpectomies and radiotherapy. She had been started on low-dose tamoxifen (Nolvadex, Zeneca; 40 mg daily) 9 years before the onset of visual symptoms (total dose 138 g).

Approximately 2 years after the onset of her visual symptoms she was commenced on metformin, atenolol, frusemide, isosorbide mononitrate, glyceryl trinitrate spray and aspirin. Tamoxifen is therefore the only drug with cationic, amphiphilic properties to which she had been exposed.

Visual acuities at presentation were 6/9−3 in the right eye and 6/24+1 in the left eye. Funduscopy showed characteristic refractile lesions at both posterior poles (Fig. 1). Fundus fluorescein angiography showed bilateral cystoid macular oedema.

Despite discontinuation of the tamoxifen, visual acuity continued to deteriorate in both eyes. Five years after stopping the tamoxifen the refractile lesions, although reduced, were still present (Fig. 2), and visual acuities were 6/36 in the right eye and 6/60 in the left eye, with no other significant ocular pathology.

Resolution of retinopathy and improvement in vision may occur after discontinuation of low-dose tamoxifen. Ocular toxicity is considered to be reversible if recognised early and there have been many case reports documenting stabilisation of or improvement in visual acuity.[2–5] To our knowledge, this is the first case of progressive loss of vision with persistent retinopathy 5 years after discontinuation of the drug.

Discussion

Tamoxifen is the commonest anti-cancer drug in use. Worldwide, more than 1 million women are using the drug as an adjuvant in the treatment of breast cancer. Tamoxifen was approved in 1977 by the Food and Drug Administration (FDA) in the United States for treatment of advanced breast cancer in postmenopausal women. During the past 20 years additional approvals have been obtained from the FDA for other wider applications of tamoxifen. These include adjuvant therapy with chemotherapy in postmenopausal women with node-positive disease, adjuvant therapy alone in the same group, treatment for premenopausal women with oestrogen-receptor-positive advanced breast cancer, treatment for pre- and postmenopausal women with node-negative, oestrogen-receptor-positive breast cancer, and treatment for advanced breast cancer in men.[6]

Questions remain, however, concerning the optimal duration of therapy. Comparison between trials of different tamoxifen durations suggests that more prolonged treatment confers a greater survival benefit. The most recent results from randomised studies comparing different durations of tamoxifen treatment suggest that 5 years of treatment is better than 2 years, but substantial uncertainty remains about whether longer than 5 years will provide any benefit.[7–9]

In addition to long-term adjuvant therapy, the indications for tamoxifen use have broadened. National multicentre trials are currently under way in the United States, United Kingdom and Italy aimed at evaluating tamoxifen as a breast cancer chemo-preventative agent in selected high-risk women with a strong family history of breast cancer. Healthy young women with no history of cancer will therefore be exposed to the long-term effects of tamoxifen. In addition, its oestrogenic effects appear to account for a reduction in coronary heart disease and osteoporosis, and maintenance of bone density. Its use has therefore recently been advocated in the prevention and treatment of osteoporosis, and its administration is likely to become even more widespread.

Tamoxifen use is undoubtedly on the increase. The average duration of treatment is also likely to increase if the large-scale randomised trials currently under way show further survival benefits from prolonging treatment for more than 5 years. Although visual loss is uncommon and may be reversible on

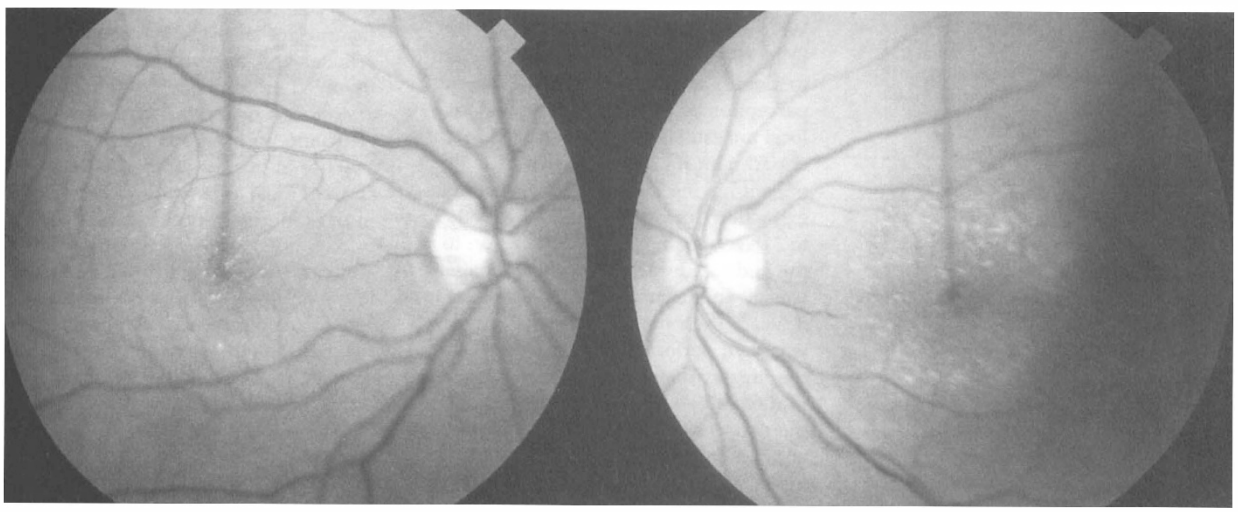

Fig. 1. *May 1992: red-free fundus photographs of right and left eyes showing crystals in the retina.*

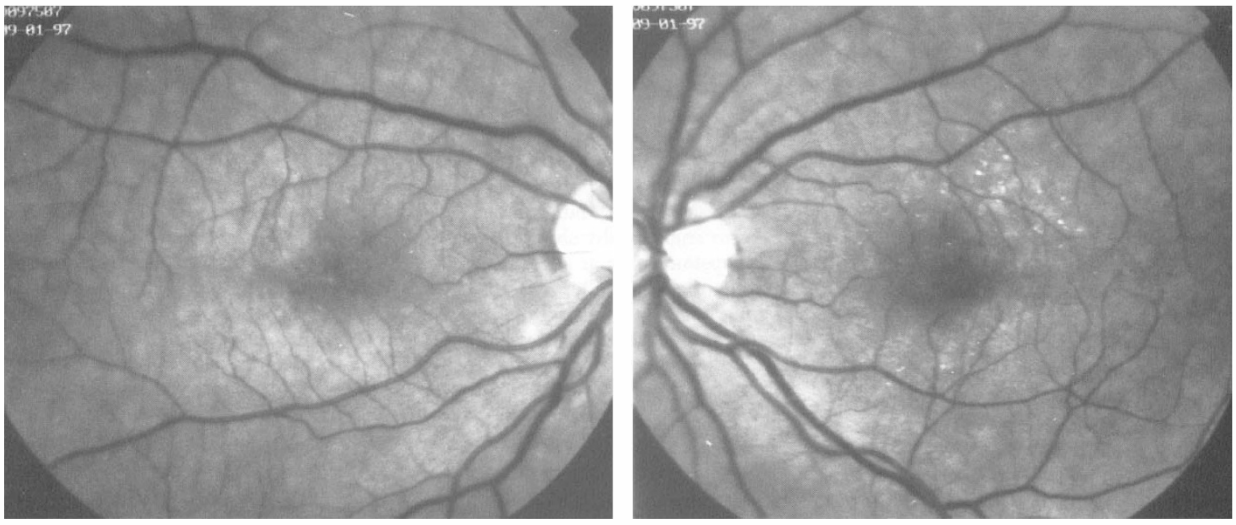

Fig. 2. *January 1997: red-free fundus photographs of right and left eyes showing persistent refractile crystals in the superficial retina.*

discontinuation of the drug, this is not universally the case. The case that we report shows that severe loss of vision can occur despite prompt cessation of the drug on development of visual symptoms.

At present the *British National Formulary*[10] mentions only 'visual disturbances . . . usually with very high doses' as a possible side effect of tamoxifen therapy. We feel, however, that patients on even low-dose therapy should be warned of potential ocular effects. Recommendations for women taking tamoxifen should be expanded to include advice to report any visual symptoms to the prescribing doctor immediately.

References

1. Tang R, Shields J, Schiffman J, Li H, Locher D, Hampton J, *et al*. Retinal changes associated with tamoxifen treatment for breast cancer. Eye 1997;11:295–7.
2. Ashford AR, Donev I, Tiwari RP, Garrett TJ. Reversible ocular toxicity related to tamoxifen therapy. Cancer 1988;61:33–5.
3. Vinding T, Nielsen NV. Retinopathy caused by treatment with tamoxifen in low dosage. Acta Ophthalmol (Copenh) 1983;61:45–50.
4. Griffiths MFP. Tamoxifen retinopathy at low dosage [letter]. Am J Ophthalmol 1987;104:185–6.
5. Gerner EW. Ocular toxicity of tamoxifen. Ann Ophthalmol 1989;21:420–3.
6. Jordan VC. Tamoxifen: a guide for clinicians and patients. New York: PRR, 1996.
7. Swedish Breast Cancer Cooperative Group. Randomized trial of two versus five years of adjuvant tamoxifen for postmenopausal early stage breast cancer. J Natl Cancer Inst 1996;88:1543–9.
8. Fisher B, Dignam J, Bryant J, DeCillis A, Wickerham DL, Wolmark N, *et al*. Five versus more than five years of tamoxifen therapy for breast cancer patients with negative lymph nodes and estrogen receptor-positive tumors. J Natl Cancer Inst 1996;88:1529–42.
9. Tormey DC, Gray R, Falkson HC, for the Eastern Cooperative Oncology Group. Postchemotherapy adjuvant tamoxifen therapy beyond five years in patients with lymph node-positive breast cancer. J Natl Cancer Inst 1996;88:1828–33.
10. British national formulary. London: BMA/Royal Pharmaceutical Society of Great Britain, 1998;35:385–6.

Desirée C. Murray ✉
Jonathan M. Gibson
Birmingham and Midland Eye Centre
City Hospital NHS Trust
Dudley Road
Birmingham B18 7QU, UK

Sir,

We read with interest the paper by Briggs *et al*.[1] We too undertook an audit to identify any difference in the patients' perception of pain during the various local anaesthetic techniques used in our department for cataract surgery. Every patient having local anaesthetic cataract extraction during the period 1 May 1995 to 31 October 1995 was enrolled on to the audit. After the injection the patient was given the choice of five responses to describe their pain experience. Surgery was then performed. Immediately after the surgery the same options were given to the patients to describe the pain of their surgery. The answers were then entered on a proforma. The surgeon indicated the type of anaesthetic and whether the surgery had been complicated or not.

A Kruskal–Wallis one-way analysis of variance (ANOVA) was used to test for differences between the four groups. Where differences were detected the Mann–Whitney *U*-test was used for individual comparisons. To allow for multiple comparisons $p < 0.01$ was considered to be statistically significant.

Some 339 cataract extractions were performed using four anaesthetic techniques: Sub-Tenon's, peribulbar, retrobulbar and subconjunctival. Administration of peripulbar and retrobulbar anaesthesia produced significantly higher pain scores than the sub-Tenon's and subconjunctival anaesthetic techniques. Patients who received subconjunctival anaesthesia experienced significantly higher pain scores during surgery in comparison with patients in the other groups. The results are shown in Table 1 and the average pain scores in Fig. 1.

An anaesthetist gave nine of the blocks; the rest were given by ophthalmic staff. An anaesthetist was recorded as being present in only 49 (15%) of the procedures and many lists had no anaesthetic staff in theatre. This may well reflect factors such as insufficient anaesthetic resources, the reluctance of anaesthetists to become involved in ophthalmic regional anaesthesia or ophthalmologists' reluctance to train and involve them. Practice in our institution currently falls short of ideal or best practice as outlined in the joint report of the Royal Colleges.[2]

A 5-point scale was used for the study as previous studies have shown low pain levels for these procedures.[3] Visual analogue scales can be difficult for patients who have just had cataract surgery as they may have impaired acuity in their unoperated eye.

The rates of surgical complications were similar in all groups and the results of this study do not suggest that choice of anaesthesia influences the outcome. However, a large controlled trial would