Figure 2 Fundal appearances during an acute relapse (December 1990), demonstrating moderate vitreal haze, optic disc pallor (secondary to recurrent episodes of optic nerve vasculitis), and active posterior pole choroidal infiltrate with accompanying retinal vasculitis (arrow).

6/12 in the right eye with the patient on 10 mg prednisolone per day. Unfortunately, our patient died shortly thereafter following three myocardial infarctions. Postmortem examination was not performed. Therapy with Campath-1H was uncomplicated apart from a 'first dose reaction'⁸ although at 12 months there was a persisting peripheral blood lymphopenia (Fig 1).

COMMENT

Available evidence suggests that intraocular inflammation is often the result of an autoimmune attack.¹ Animal models such as experimental autoimmune uveitis (EAU) support this concept, while the phenomenon of anterior chamber associated immune deviation (ACAID) has increased our understanding of the immunomodulatory mechanisms that prevent intraocular inflammation. This appears to operate via the elaboration of anti-inflammatory cytokines by a subset of T cells and it may be an imbalance between these and pro-inflammatory autoaggressive T cells that triggers ocular autoimmunity.² Although EAU can be precipitated by immunisation with autoantigen or by adoptive transfer of antigen specific effector cells, the trigger for human disease is not usually known. The ideal therapy would redress the balance between T cell subsets with a return of tolerance and immune homeostasis.

One possibility for controlling an autoimmune reaction to an unknown antigen is to deplete lymphocytes and rely upon immune reconstitution to re-establish tolerance. Indeed, T cell mabs (depleting and non-depleting) are effective treatments for autoaggressive pathologies in animals⁴ and have been used in EAU.⁵ Furthermore, one result is the 'unmasking' of regulatory T cells which protect against future autoimmune attack, giving long term protection from a short term

treatment.⁶ The Campath-1 antigen (CD52) is a small glycoprotein present at high density on all lymphocytes and at lower density on monocytes and natural killer cells.⁷ It is a good target for antibody mediated lysis via complement and Fc receptors and antibodies against the antigen are potentially lytic. Campath-1H is a humanised CD52 mab which has now been used to treat a number of autoimmune conditions in humans including rheumatoid arthritis,⁸ vasculitis,³ and multiple sclerosis.⁹ Therapy is followed by profound depletion of peripheral blood lymphocytes and, in some patients, short term treatment has provided long term remission of symptoms although this may require additional treatment with a CD4 mab. While the mechanisms underlying such responses have not yet been established, this experience encouraged us to offer Campath-1H to the subject of this report. Therapy was associated with a rapid and dramatic decrease in intraocular inflammation although two relapses occurred during 4 months of follow up. The first, however, responded to a modest increase in steroid dose, and the second spontaneously regressed without a change in therapy.

As can be seen from Figure 1, the rapid deterioration in right visual acuity evident between 1991 and 1994 plateaued after therapy with Campath-1H, which was therefore associated with very effective control of the intraocular inflammation. Until regulatory T cells are identifiable it will not be possible to monitor their kinetics following lymphocyte depletion. The persistent lymphopenia that follows Campath-1H therapy, however, may create a favourable environment for the re-establishment of regulatory circuits and immune homeostasis. It should be noted that peripheral blood lymphopenia, particularly affecting the CD4+ subset, is long lasting in patients treated with Campath-1H.¹⁰ There is a small risk of opportunistic infection during the first 6–8 weeks after therapy, although such infections are self-limiting or respond to appropriate therapy. Beyond that period there does not appear to be an increased risk of infection in the absence of additional immunosuppression. The pre-terminal cardiac events in our patient were felt not to be primarily related to his vasculitic illness, which was never manifest beyond the small vessels of the eye although earlier therapies, particularly corticosteroids and cyclosporin A, would have increased his coronary risk.

Campath-1H had a profound effect on the course of intraocular inflammation in this patient. While the mechanisms underlying the actions of Campath-1H remain unclear, we would advocate the treatment of other similar patients, ideally as part of a controlled clinical trial.

JDI is a Medical Research Council clinician scientist. Campath-1H was produced at the Wellcome/MRC therapeutic antibody centre. Campath is a trade mark of Wellcome group companies. Registered in US Patent and Trademark Office.

J D ISAACS
G HALE

H WALDMANN
Department of Pathology (Immunology Division),
University of Cambridge

A D DICK
R HAYNES
J V FORRESTER

Department of Ophthalmology,
University of Aberdeen Medical School

P WATSON
P R MEYER
Department of Ophthalmology,
Addenbrooke's Hospital,
Cambridge

Correspondence to: Dr J D Isaacs, Division of Immunology, Department of Pathology, Tennis Court Road, Cambridge CB2 1QP.

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- Forrester JV. Duke-Elder lecture: new concepts on the role of autoimmunity in the pathogenesis of uveitis. *Eye* 1992; 6: 433–46.
- Streilein JW, Wilbanks GA, Taylor A, Cousins S. Eye derived cytokines and the immunosuppressive intraocular environment: a review. *Curr Eye Res* 1992; 11: 41–7.
- Lockwood CM, Thiru S, Isaacs JD, Hale G, Waldmann H. Long-term remission of intractable systemic vasculitis with monoclonal antibody therapy. *Lancet* 1993; 341: 1620–2.
- Cobbold SP, Qin S, Leong LYW, Martin G, Waldmann H. Reprogramming the immune system for peripheral tolerance with CD4 and CD8 monoclonal antibodies. *Immun Rev* 1992; 129: 165–201.
- Atalla L, Linker-Israeli M, Steinman L, Rao NA. Inhibition of autoimmune uveitis by anti-CD4 antibody. *Invest Ophthalmol Vis Sci* 1990; 31: 7–11.
- Qin S, Cobbold SP, Pope H, Elliott J, Kioussis D, Davies J, et al. 'Infectious' transplantation tolerance. *Science* 1993; 259: 974–7.
- Hale G, Xia M-Q, Tighe HP, Dyer MJS, Waldmann H. The Campath-1 antigen (CDw52). *Tissue Antigens* 1990; 35: 118–27.
- Isaacs JD, Watts RA, Hazleman BL, Hale G, Keogan MT, Cobbold SP, et al. Humanised monoclonal antibody therapy for rheumatoid arthritis. *Lancet* 1992; 340: 748–52.
- Moreault T, Thorpe J, Miller D, Moseley I, Hale G, Waldmann H, et al. Preliminary evidence from magnetic resonance imaging for reduction in disease activity after lymphocyte depletion in multiple sclerosis. *Lancet* 1994; 344: 298–301.
- Watts RA, Isaacs JD, Hale G, Hazleman BL, Waldmann H. Peripheral blood lymphocyte subsets after Campath-1H therapy in rheumatoid arthritis – a 3 year follow-up. *Arthritis Rheum* 1994; 37: S338.

Bilateral hyphaema following diode laser for retinopathy of prematurity

EDITOR,—A number of studies have shown the efficacy of indirect laser photocoagulation in the treatment of retinopathy of prematurity (ROP).^{1–3} The diode laser, in particular, offers advantages of portability and reduced absorption by the tunica vasculosa lentis. A baby who developed bilateral hyphaemas following indirect diode laser treatment for threshold ROP is presented and a possible aetiology discussed.

CASE REPORT

The patient was a male infant born at 24 weeks' gestation, weighing 722 g. At 7 weeks of age, examination revealed stage 3+ retinopathy of prematurity (ROP) extending over 360 degrees in both eyes. No persistent tunica vasculosa lentis was evident. Good pupillary dilatation was achieved with mydriatics and was sustained throughout the procedure. Under sedation, both eyes were treated with a Nidek DC 3000B diode laser and a 28 D lens via an indirect ophthalmoscope delivery system. The estimated minimum spot size with this delivery system is 250 µm. The right eye was treated with 821 burns of 0.1 second in duration and 390 mW power, while the left received 658 burns of 350 mW power.

Twenty four hours after the operation the child was noted to have a total hyphaema in the left eye, with raised intraocular pressure, and a partial hyphaema in the right eye. He was treated conservatively with topical steroids, mydriatics, and hypotensive agents. At review 1 month later, the hyphaemas had resolved, both corneas were clear and the intraocular pressures were normal. Slit-lamp examination revealed

multiple iris transillumination defects. Funduscopy at that time confirmed regression of the ROP from both eyes.

COMMENT

Indirect diode laser photocoagulation is an accepted mode of treatment of retinopathy of prematurity. McNamara *et al*¹ have shown that diode laser treatment is as effective as cryotherapy with no greater morbidity. With an indirect laser conjunctival incisions are unnecessary and anterior segment inflammation is less likely than with cryopexy. An advantage of the diode laser over the argon laser is that the longer wavelength of the diode is not absorbed so readily by haemoglobin. Theoretically, treatment through a persistent tunica vasculosa lentis or vitreous haemorrhage should pose less of a problem than with an argon laser.

We have presented a child who developed hyphaemas and multiple iris defects following diode laser photocoagulation. These findings would indicate that there was significant absorption of laser energy, particularly by the irises, of this baby. We feel that this is the case despite the fact that no miosis occurred during the procedure. This may be the result of 'iris clipping', first described by Woon *et al*.⁴ They noted that the relatively large cone angle of some diode lasers produces a laser beam whose cross sectional area may exceed the area of the pupil. This leads to a reduction in laser delivery to the retina and inadvertent irradiation of the iris which may not be apparent to the treating physician. The

Nidek laser, using a 28 D lens, produces a cone angle of approximately 6 degrees and this is wider than other laser systems which have been used in the treatment of ROP (see Table 1).

Iris clipping is also more likely to occur if the laser beam is not aimed through the centre of the pupil. Since the treatment of ROP involves the ablation of peripheral retina there is an increased likelihood of iris clipping. This would be compounded by the occasional difficulty in dilating the pupils in premature infants (not encountered in our case). In 1993, Benner *et al*⁵ described an infant who suffered a 'non-layering hyphaema and mild vitreous haemorrhage' following diode laser treatment. Unlike our case, however, there was no evidence of iris atrophy. Although it is felt that absorption of laser energy by anterior segment structures is less likely with the diode laser, other authors have described transient lens changes and posterior synechiae following indirect diode laser photocoagulation for ROP.⁶ In conclusion,

Table 1 Comparison of minimum spot sizes and cone angles with different types of laser

Laser type	20 D lens Spot size/ cone angle	28 D lens Spot size/ cone angle
Nidek DC3000B (diode)	180 µm 8.4°	250 µm 5.7°
Iris Medical (diode)	400 µm 6°	500 µm 4°
HGM Litespot (argon)	200 µm 3.3°	300 µm 2.2°

we have described bilateral hyphaemas and iris atrophy occurring secondary to indirect diode laser treatment. We feel that this was due to the phenomenon of iris clipping and that this occurred despite well dilated pupils and the use of relatively modest power levels. We recommend that physicians be aware of this potential complication when treating ROP in this manner.

P RUNDLE
F G MCGINNITY
Department of Ophthalmology,
Royal Group of Hospitals, Belfast

Correspondence to: F G McGinnity, Department of Ophthalmology, Eye and Ear Clinic, Royal Group of Hospitals, Belfast BT12 6BA, Northern Ireland.

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- 1 McNamara JA, Tasman W, Vander JF, Brown GC. Diode laser photocoagulation for retinopathy of prematurity. *Arch Ophthalmol* 1992; 110: 1714-6.
- 2 Hunter DG, Repka MX. Diode laser photocoagulation for threshold retinopathy of prematurity. *Ophthalmology* 1993; 100: 238-44.
- 3 Goggin M, O'Keefe M. Diode laser for retinopathy of prematurity - early outcome. *Br J Ophthalmol* 1993; 77: 559-62.
- 4 Woon WH, flytche TJ, Hamilton AMP. Iris clipping of a diode laser when performing retinal photocoagulation. *Br J Ophthalmol* 1991; 75: 386-90.
- 5 Benner JD, Morse LS, Hay A, Landers MB. A comparison of argon and diode photocoagulation combined with supplemental oxygen for the treatment of retinopathy of prematurity. *Retina* 1993; 13: 222-9.
- 6 Capone A, Drack AV. Transient lens changes after diode laser retinal photocoagulation for retinopathy of prematurity. *Am J Ophthalmol* 1994; 118: 533-5.