Regular Review

Photocoagulation and diabetic retinopathy

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The last survey of blindness¹ in England and Wales cited diabetic retinopathy as the most common cause of blindness in men and women aged 30-64. It accounted for 16% of the 13 242 persons newly registered blind in the years 1963-8, as compared² with only 7% between 1955 and 1962. Roughly 2% of the population is thought to be diabetic (that is, over one million diabetics in England and Wales). The prevalence of blindness due to retinopathy in diabetics has been calculated³ as 1.9%; thus the total of diabetics blind from retinopathy is close to 20 000, a figure over double that estimated by the Committee on Blindness of a Working Party of the British Diabetic Association (1967-9).

Visual loss may, however, be prevented by photocoagulation, and more widespread (and judicious) application of this treatment may well reduce the numbers of diabetics who go blind. All concerned with the care of diabetics need to be aware of the natural history of diabetic retinopathy and the indications for referral for treatment.

Diabetic retinopathy may be divided into background retinopathy and proliferative retinopathy. Some features of the more common background retinopathy, which include micro-aneurysms, hard exudates, and blotchy haemorrhages, are present in 80% of diabetics with a 15-year history of the disease. Background retinopathy has, however, a relatively good visual prognosis: only 3% of eyes with good initial vision and mild lesions lose useful vision in five years.⁴ In some eyes, especially those of elderly patients, when the background lesions affect the macula, vision may be severely reduced by maculopathy—macular oedema caused partly by capillary closure and increased permeability of the adjacent vascular abnormalities.

Proliferative retinopathy has a relatively poor visual prognosis: half the patients affected become blind in five years⁴ from recurrent vitreous haemorrhages and detachment or disorganisation of the retina. Numerically, maculopathy is probably a commoner cause of blindness in diabetics⁵ than proliferative retinopathy, though loss of central vision alone may still leave affected patients with peripheral vision for navigation. In contrast, the blindness of proliferative retinopathy tends to be more disabling, for both central and peripheral vision may be lost as a result of vitreous haemorrhage or intraocular fibrosis.

Photocoagulation has been used in treating diabetic retinopathy since 1959, but only comparatively recently have prospective randomised controlled trials proved its efficacy. Five such trials included patients with two similarly affected eyes, only one of which was chosen by randomisation for treatment.

Let us look first at the results in patients with maculopathy. Patz *et al*⁶ reported a favourable response in a study which included 63 patients, with a follow-up of 9-36 months (average 26). They used the argon laser for treatment, and when visual acuity changed by two lines on the Snellen chart the eye was

considered "better" or "worse." At evaluation the untreated eyes had deteriorated compared with the treated ($P < 0.001$), though the difference was only significant when the initial visual acuity was 6/36 or better. A British multicentre trial using xenon arc photocoagulation for maculopathy largely confirmed these findings.⁷ In this trial 76 patients were seen after one, 44 after two, and 25 after three years. The treated eyes retained significantly better visual acuity than the untreated at each yearly assessment, and in patients with an initial visual acuity of 6/24 or better more untreated eyes deteriorated by more than two lines of Snellen. As Patz's study found, there was no significant difference between treated and untreated eyes with initial visual acuity of 6/36 or less, suggesting that eyes so severely affected have reached a stage unresponsive to treatment. In this trial over a quarter of all eyes which became blind did so from proliferative retinopathy which had developed since entry into the trial, showing that maculopathy and proliferative retinopathy are not mutually exclusive. The results of Patz *et al* seemed to suggest a better result from treatment than those of the British study. Possibly the argon laser is the better choice for treating maculopathy, since the ophthalmologist can obtain a much smaller beam and so can obliterate lesions nearer the fovea.

The evidence in favour of photocoagulation in proliferative retinopathy is more convincing. A multicentre trial⁸ in the United States reported results based on 1732 patients followed from one to two years. Many more of the untreated than the treated eyes had suffered a drop in vision to less than 2/60 (5/200) at two consecutive four-monthly assessments. A decrease in vision of this severity occurred in 129 untreated eyes compared with 56 treated eyes, suggesting that treatment reduces visual loss by roughly 60%.

An analysis of subgroups showed that treatment gave substantial benefits in eyes which had a moderate amount of new vessels on the discs and in eyes with peripheral retinal new vessels, either with or without additional disc new vessels, but which had previously suffered a vitreous haemorrhage. Since both these groups are known to have a poor visual prognosis, the steering committee of the American trial has since modified its protocol to allow for treatment in the control group when these features are present.

This trial also randomly allocated eyes for treatment either with argon laser or xenon arc photocoagulation. No difference was found in the results of treatment in terms of retention of visual acuity, but there was significantly greater field loss in the group treated by xenon arc.

The finding that the xenon arc light is equally effective is supported by the results of the British multicentre study on proliferative retinopathy,⁹ which used the xenon arc exclusively. This trial included only 100 patients, but the two eyes of patients were more symmetrically matched according to the type of retinopathy, severity, and visual acuity. Patients in the trial had a one to three year follow-up. There were two

roughly equal groups, 47 patients having disc new vessels in both eyes and 45 having peripheral retinal new vessels only. When disc new vessels were present the treated eyes retained significantly better vision—evident after one, two, and three years. The difference in mean visual acuity between treated and untreated eyes increased with time, suggesting that the beneficial effect of photocoagulation was persisting.

When new vessels are present peripherally but not on the disc, neither the American nor the British trial has so far shown a significant difference between treated and untreated eyes. The progression to decreased vision is slower in eyes with peripheral new vessels and any benefit from treatment would take longer to become apparent.

A third randomised controlled trial for proliferative retinopathy, reported by Hercules *et al*,¹⁰ included eyes with more advanced retinopathy. Only patients with new vessels arising from the optic disc in both eyes were included. The argon laser was used, but the authors specifically decided against direct coagulation of vessels (to avoid causing vitreous haemorrhage) and applied extensive peripheral retinal ablation only. Their patients could be divided into three groups: those whose two eyes had disc new vessels without accompanying fibrous tissue; those with forward disc new vessels or disc new vessels with moderate fibrous tissue; and those with massive disc new vessels with considerable fibrous tissue formation and vitreoretinal traction. Only in the second group and a subgroup of the first group did treated eyes retain significantly better vision, though all three treated groups showed morphological improvement.

The results of these randomised controlled trials suggest that photocoagulation is of considerable benefit when new vessels arise from the disc and in eyes with proliferative changes and a previous history of vitreous haemorrhage. Both these features carry a poor prognosis. The report from Hercules *et al*¹⁰ suggests that treatment may also be effective even when proliferative changes are accompanied by moderate amounts of fibrous tissue—usually a feature of advanced disease. The optic disc can be seen fairly easily during examination with an ophthalmoscope, and detecting new vessels there should be part of the regular routine follow-up of all diabetic patients. Physicians need to be aware of the symptoms of vitreous haemorrhage, and they should look for signs of proliferative retinopathy when patients complain of floaters, especially if accompanied by a drop in visual acuity. While peripheral retinal new vessels pose a less immediate threat, these can still produce visual loss by spread to the macula, and disc vessels are apt to appear as a later feature. Patients with all forms of proliferative retinopathy should be regularly and carefully reviewed in order to assess their suitability for treatment to prevent development of irreversible changes or complete blindness.

The macula is not easily seen without dilatation of the pupil. When, however, there is a drop in visual acuity, either subjective or objective in patients in the older age group, maculopathy should be suspected—especially in the presence of moderate or severe background retinopathy. More use should be made of ophthalmic opticians to provide a refracting service so that the eyes can be tested for corrected visual acuity, but the judicious use of pin-hole testing is an acceptable substitute, especially in a busy diabetic clinic. When visual acuity has dropped to 6/12 or worse, patients must be referred for consideration of treatment, since the controlled trials on maculopathy showed that treatment is most effective before there is appreciable visual impairment.

Are any other forms of treatment effective besides photo-

coagulation? Pituitary ablation has largely been abandoned, though there may still be a place for it occasionally in the rare form of florid retinopathy.¹¹ Treatment with clofibrate was found to clear hard exudates more quickly,¹² but there was no corresponding improvement in visual function, nor is there evidence that long-term treatment with the drug prevents the development of maculopathy. Preliminary results of removal of the opaque vitreous¹³ suggest that vitrectomy may be helpful in patients who have lost vision from long-standing vitreous haemorrhage provided the underlying retinopathy has not reached a stage of traction detachment. The value of this procedure is being tested by a multicentre study in the United States under the sponsorship of the National Institutes of Health.

Fundamental to the whole issue of management of diabetic retinopathy is the influence of the control of diabetes. While there is evidence from animal studies¹⁴ that "good control" is beneficial, there is still inconclusive proof that it lessens complications in man. The important study of Job *et al*,¹⁵ which showed that improved control (by a multiple insulin injection regimen compared with single injections) led to the development of fewer microaneurysms, is being questioned.¹⁶ There is still no general agreement on a definition of "good control" or on the aims of insulin treatment in controlling the glucose concentrations.¹⁷ New ways of achieving normoglycaemia are being tested, and clinical trials are needed urgently to determine whether complications are significantly decreased by a greater approximation to the physiological norm than was achieved in the Job study.

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