COMMUNICATIONS

TREATMENT OF PROLIFERATIVE DIABETIC RETINOPATHY*†

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FEW will disagree with the statement of Lundbaeck (1963) that, from the practical and theoretical points of view, vascular proliferation is the most important element of diabetic retinopathy. If vision is to be preserved, control of vascular proliferation is essential and, in judging the effects of any treatment, the degree of such control is the most important criterion. In an attempt to achieve this control many methods (apart from the fundamental treatment of the diabetes) have been used; *e.g.* a variety of drugs, oxygen under high pressure, and dietary regimes. At the present time the anabolic steroids and the production of pituitary insufficiency by pituitary ablation are the methods most favoured. Light coagulation was first employed for this purpose by Meyer-Schwickerath (1960), who treated four cases in the late proliferative stage but achieved no good effect. He did, however, notice that if microaneurysms were treated associated exudates tended to disappear. Wetsig and Worlton (1963) published a series of 28 cases in which more hopeful results were obtained. In that year I began to use this method and the following is an account of the progress to date of the cases treated.

In proliferative diabetic retinopathy, according to Dobree (1964), the formation of new vessels progresses in three stages:

(1) *Naked Vessels*.—Here the vascular loops and anastomoses are devoid of anything but the finest connective tissue support. This stage lasts for from 6 to 18 months and only towards the end of it do small retinal haemorrhages occur.

(2) *Vascular Proliferation*.—There is a great increase in the number of new vessels and a gradual condensation of connective tissue around them. This stage lasts for from 1 to 2 years and there is a marked tendency to subhyaloid and vitreous haemorrhages from the numerous delicate capillaries.

(3) *Healing*.—At this stage there is a marked decrease in the number of new vessels and a considerable increase in the amount of connective tissue surrounding them. Blood vessels are much less numerous and haemorrhages much less frequent than in Stage 2. This stage appears to represent a form of spontaneous healing and, as Beetham (1963) and others have pointed out, these eyes may retain reasonable vision for years. Nevertheless vision usually suffers seriously from mechanical obstruction formed by fibrous bands and also from retinal tears and detachments due to traction. In the end vision may be lost from these conditions or from secondary glaucoma.

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The evolution of all three stages normally takes about 5 years, but may of course be longer or shorter. The rationale of photocoagulation is that it brings about the advantages of Stage 3 while minimizing its disadvantages. It produces minimal connective tissue reaction with maximal destruction of neo-vascularization while the spontaneous Stage 3 does the opposite. According to Ashton (1961), three conditions govern vessel growth in the eye:

- (1) The presence of living tissue.
- (2) A low oxygen tissue tension.
- (3) A poor venous drainage.

Under these conditions Ashton postulates the accumulation of vasoformative metabolites which lead to neo-vascularization. Photocoagulation reduces the oxygen requirement by decreasing the area of viable, though vascularized retina, and for the same reason it probably reduces the production of the vasoformative metabolites, though this of course, is speculative.

Technique

Light coagulation was applied to all areas of neo-vascularization, to larger aneurysms, and to aneurysmal sacculations in the walls of veins; to venous loops; to areas of flat proliferations and to the base of proliferations which had grown into the vitreous; to micro-aneurysms surrounded by exudates or present in clusters; and to areas of haemorrhage associated with neo-vascularization. Obviously one must keep well away from the macular area and the large vessels must be avoided. (One can, however, coagulate on either side of a vessel without causing occlusion.) The new vessels should not be shut off at the time of coagulation, fibrous tissue will do this later. Only one quadrant or what corresponds to this area should be done at a time. In this connexion it may be noticed that, when one compares retinal photographs showing neo-vascularization before treatment with the same areas after treatment, the coagulations look unduly large; this is because new vessels show up with the coagulator that cannot be seen either with the ophthalmoscope or by retinal photography. About one week is allowed between treatments. The patient is kept in bed with pinhole spectacles for 4 days. Atropine drops and Cortisone ointment are used locally.

Case Reports

Case 1, a woman aged 34, who had had diabetes for 30 years, was first seen in November, 1963.

History.—Vitreous haemorrhages in both eyes for past 2 years, at least six in the right eye and about twelve in the left.

Examination

FUNDUS: Right eye—haemorrhages, exudates, and micro-aneurysms with widespread neo-vascularization in all quadrants. In the temporal area the new vessels were approaching the macular region. Left eye—the same with the addition of massive invasion of the vitreous by new vessels.

VISUAL ACUITY: Right eye 6/6; left eye 6/9 ptly.

Treatment.—In November, 1963, light coagulation was given to the lesions in the right eye in three sessions at roughly weekly intervals. The left eye was not treated.

Follow-up.—No ocular symptoms.

RIGHT: There have been no further haemorrhages in the treated eye. A small fresh area of neo-vascularization associated with a few micro-aneurysms appeared in the upper temporal quadrant

12 months after treatment, but this was easily destroyed with three small coagulations. Since then there have been no fresh lesions for 12 months, apart from a few scattered micro-aneurysms. The visual acuity is 6/5.

LEFT: The untreated eye has had numerous vitreous haemorrhages and the vision is now 1/60.

The total follow-up period is 2 years. The patient has had proliferative diabetic retinopathy for more than 4 years (the onset of vitreous haemorrhage occurred 4 years ago) and the visual acuity in the treated eye is still 6/5.

Case 2, a woman aged 22, who had had diabetes for 14 years was first seen in January, 1964.

History.—She said that the sight had been bad in the right eye for 6 years, and that the left became cloudy 4 months previously and then gradually cleared. Vitreous haemorrhage was diagnosed by Dr. A. Mooney. There had been a number of similar but less severe episodes over the past 4 years.

Examination

FUNDUS: The right eye showed retinal detachment with diabetic retinopathy and retinitis proliferans. The left eye showed haemorrhages, exudates, micro-aneurysms, and areas of neo-vascularization in all quadrants. In the upper temporal quadrant loops of vessels were beginning to invade the vitreous.

VISUAL ACUITY: Right eye 2/60, left eye 6/6.

Treatment.—Right eye: none.

Left eye: light coagulation on four occasions at weekly intervals beginning in January, 1964.

Follow-up.—One year and 10 months after treatment the visual acuity in the left eye was 6/5, and there were no ocular symptoms. The fundus showed no fresh neo-vascularization. The vessels which were beginning to invade the vitreous had been shut off. Apart from one micro-aneurysm and one small haemorrhage in the temporal area just peripheral to the macula, there were no fresh lesions. This patient has been kept on PAS by Dr. A. Mooney. The retinal detachment in the untreated eye has become less.

Case 3, a man aged 48, who had been diabetic for 24 years, was first seen in April, 1964.

History.—There had been a cloud over the left eye for the past 2 months, which had improved. He had had previous slight episodes in both eyes.

Examination

FUNDUS: The right eye showed haemorrhages, exudates, and areas of neo-vascularization. The macula was surrounded with haemorrhages and exudates. The left eye was similar with the addition of a flat area of vascularized proliferation in the upper temporal quadrant and one such area projecting into the vitreous just below the disc (Fig. 1*a* and *b*, overleaf).

VISUAL ACUITY: Right eye 6/9, left eye 6/12.

Treatment.—Two sessions of light coagulation were given to each eye at weekly intervals in January, 1964.

Follow-up.—One year and 8 months later the visual acuity in both eyes was 6/6. There had been no further vitreous haemorrhages and ocular symptoms (Fig. 2*a* and *b*, overleaf).

Examination

RIGHT EYE: A ring of exudates surrounds a number of micro-aneurysms and small haemorrhages in the macular area. There are a few scattered micro-aneurysms in the upper nasal quadrant and in the lower half of the fundus, and no fresh neo-vascularization.

LEFT EYE: There is fresh neo-vascularization on the disc, two small haemorrhages between the disc and the macula, and some scattered micro-aneurysms and haemorrhages in the temporal mid-periphery. There are a few scattered micro-aneurysms and small haemorrhages in the upper nasal and temporal quadrants. The patch of flat proliferation is now avascular and has not increased in size. Those which projected into the vitreous below the disc have remained vascularized, but the supplying vessel at its base is closed.

Case 4, a man aged 57, who had had diabetes for 9 years, was first seen in June, 1963.

History.—The sight of the right eye had started deteriorating 5 years previously and had since become steadily worse.

FIG. 1(a).—Case 3, pre-retinal haemorrhage, exudates, and neo-vascularization before light coagulation.

FIG. 1(b).—Case 3, same area 9 months after light coagulation.

Examination

FUNDUS: Diabetic retinopathy, with retinitis proliferans and retinal detachment in the left eye. Diabetic retinopathy with haemorrhages, exudates, and micro-aneurysms in all quadrants, a cluster of micro-aneurysms at the macula, and a few patches of neo-vascularization in the right eye.

VISUAL ACUITY: Right eye hand movements, left eye 6/5.

Progress.—Light coagulation was refused, but 10 months later he returned, having had six episodes of haemorrhage into the vitreous of the better eye. The left fundus now showed an increased number of haemorrhages, exudates, and micro-aneurysms, and numerous micro-aneurysms, haemorrhages, and exudates in the macular area. There were areas of flat proliferation in the nasal and temporal quadrants of the retina, and the amount of neo-vascularization had increased. The visual acuity was now 6/6 ptly.

Treatment.—Light coagulation was given in two sessions in April, 1964. For 7 months he had no further trouble but a routine visit to his ophthalmologist showed a large haemorrhage along the superior nasal vein and a ring of neo-vascularization close by. There were also fresh areas of neo-vascularization below, but there were no micro-aneurysms or exudates in the macular or temporal area and the visual acuity was 6/5. The fresh lesions were coagulated in November, 1964.

FIG. 2(a).—Case 3, vascularized retinitis proliferans projecting into the vitreous before light coagulation.

FIG. 2(b).—Case 3, same area 21 months after light coagulation.

Follow-up.—One year and 6 months later there was no vitreous haemorrhage and the visual acuity was 6/5. There were two rather large aneurysms just below the optic disc and these were coagulated with a 1.5 diaphragm in September, 1965. There have been no fresh lesions since.

Case 5, a man aged 66, who had had diabetes for 21 years, was first seen in February, 1965.

History.—For a number of years he had had occasional cloudiness of vision in one eye or the other. During the past year he had had three haemorrhages into the right vitreous, and two into the left.

Examination.—There were lens opacities and hazy vitreous in both eyes.

FUNDUS: Both eyes showed micro-aneurysms and exudates in the macular area, haemorrhages, exudates, and micro-aneurysms in profusion over all quadrants, and widespread neo-vascularization. There was a mass of organized tissue below.

VISUAL ACUITY: Right eye 6/24, left eye 6/18.

Treatment.—Two sessions of light coagulation were given to each eye in February, 1965.

Follow-up.—6 months later there were no ocular symptoms or vitreous haemorrhage. The fundi showed a few scattered micro-aneurysms and small haemorrhages, but no fresh neo-vascularization. The vitreous was much clearer. The visual acuity was 6/12 in the right eye and 6/18 in the left.

Case 6, a man aged 52, who had had diabetes for 18 years was first seen in November, 1964.

History.—He was referred by his oculist because of diabetic retinopathy.

Examination

FUNDI: The right eye showed scattered haemorrhages, exudates, and micro-aneurysms, especially surrounding the macular area. There were a few small patches of neo-vascularization. The left eye was similar, but the neo-vascularization was more widespread and there were a number of venous loops.

Treatment.—Light coagulation was given twice to each eye in November, 1964.

Follow-up.—10 months later the visual acuity was 6/6 in both eyes. I have not seen him again but his oculist reports a small fresh area of neo-vascularization below the left disc, which will need further light coagulation. Otherwise he has had no trouble.

None of these patients has noticed any change in dark adaptation or any visual field defects. There have been no complications.

Fields of Vision

Case 1 showed a slight concentric contraction of the central isopters. Case 3 showed a lower nasal sector defect in the right eye and a smaller nasal loss in the left. As the fields were not estimated before treatment, it is not known whether the light coagulation produced these defects. A puzzling feature in all these cases was the inability to elicit scotomata on the Bjerrum screen corresponding to the coagulations, but no doubt special methods using low illumination would reveal them.

Summary

In five patients (7 eyes) who experienced repeated vitreous haemorrhages, the haemorrhages have ceased after light coagulation. (Three of these have lost the vision in one untreated eye through proliferative diabetic retinopathy). In all cases the visual acuity has been maintained or has improved. Apart from one patient with lens opacities (in whom the vision has improved to 6/12 in the right eye and remained at 6/18 in the left), all have been maintained at 6/6 or 6/5. The shortest period of follow-up was 6 months, the longest 2 years. In the one case of proliferative diabetic retinopathy which did not have vitreous haemorrhages (Case 6), the progress of neo-vascularization has stopped in one eye and only one small fresh area has appeared in the other in a period of 10 months. Contrary to what Schott (1964) found in his series, the two young diabetics did particularly well.

It is recognized that it is difficult to assess the value of any treatment owing to the great variability in the progress of this disease. In this series the number of cases is small and the follow-up is rather short in some. Nevertheless it is felt that the results are sufficiently encouraging to make the report worth while.

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