

## The evolution of photocoagulation



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Today's diabetes world is fast-moving and exciting; knowledge is accumulating at an astonishing rate. To help understand the present, however, it sometimes helps to examine the past.

In this instalment of *Tattersall's Tales*, Robert Tattersall describes the advances made in diabetic retinopathy treatment during the 1960s and 70s, as well as the risks associated with the new photocoagulation technique.

In my last Tales I described how hypophysectomy was developed as a desperate treatment for blinding retinopathy in the 1950s and 60s. It was always controversial and even its most enthusiastic supporters agreed that it had serious and often life-threatening side effects. Fortunately, a procedure was being developed which would supplant it.

The long known danger of looking directly at the sun during a solar eclipse was the stimulus for the development of light coagulation by Gerd Meyer-Schwickerath (1921–1992) of Essen, Germany. His experiments began in the spring of 1946 after he had seen many patients with macular damage after the eclipse of 9 July 1945. It was known that retinopathy was usually improved or even prevented by conditions which reduced the oxygen supply to the retina such as high myopia, optic atrophy or disseminated choroiditis and this suggested that photocoagulation might work by 'destruction of normal retinal tissue thereby reducing the metabolic activity of the retina'.

Initially, the aim was to prevent recurrent haemorrhages of new vessels but, because these haemorrhages were often very frequent, treatment had to be repeated many times. A surprising finding from later trials was that, even in those who had received several hundred burns, the subjective effect on the visual field was surprisingly small.

Meyer-Schwickerath's first trials showed that the intensity of light needed to treat the human retina was greater than that for his experimental animal – the rabbit. He took this information and used it to develop an instrument that used the sun as its light source. However, to create significant burns a fivefold magnification of the retinal image of the sun had to be produced and, given the weather in Northern Europe, this was never going to be practical!

In 1949 Meyer-Schwickerath tried using a high-intensity carbon arc light source. This worked, but the gases liberated in the reaction, saturated as they were with soot and carbon particles, were a nuisance. The next attempt involved a high-pressure xenon lamp – when xenon is made to glow by high-intensity currents, the spectrum of light emitted is similar to ordinary daylight. His first paper reporting this technique detailed four cases of late proliferative retinopathy and revealed disappointing results (Meyer-Schwickerath, 1959). Only one patient with microaneurysms and exudates experienced partial disappearance of the exudates on coagulation of the microaneurysms. But this was enough to encourage him to continue.

Between 1959 and 1964 the value of the treatment was repeatedly questioned or, as Meyer-Schwickerath himself put it, 'when I introduced photocoagulation 20 years ago, there were many listeners but few believers'. What he considered crucial was his own first use of fundus photography in 1954 (made possible by development of the electric flash), followed by adopting the Zeiss fundus camera developed in 1955 by Littmann (Meyer-Schwickerath, 1968). Much of the scepticism was dissipated by a 1965 paper by K Schott reporting the results in 58 patients treated by Meyer-Schwickerath (Schott, 1965). In the 33 who had been followed for a reasonable length of time, serial photographs showed a gradual diminution of hard exudates and disappearance of retinal oedema. Another important observation was that new vessels often regressed even if they had not been directly photocoagulated. Visual acuity also improved in many cases.

By 1968 Meyer-Schwickerath and Schott had reported a follow up of 73 eyes treated with photocoagulation in 'the early non proliferative stage' (Meyer-Schwickerath and Schott, 1968). After up to 13 years proliferative retinopathy had only developed in one participant – a figure markedly lower than the natural history reported in many other papers could suggest. Thus, the pair concluded the following.

- The signs and symptoms of diabetic retinopathy can be reversed if treatment is carried out in the early stages.
- Photocoagulation in the early stages can prevent the late complications of proliferation, haemorrhage and retinal detachment.

The authors advocated 'early photocoagulation in all cases of diabetic retinopathy showing progression.'

### Photocoagulation further afield

Adoption of light coagulation was relatively slow because there was no absolute proof of its efficacy. Before and after photos were all very well but there was a suspicion that in many publications only the most dramatic ones were selected. There was also a suspicion that destroying the most alarming appearances of retinopathy was simply cosmetic. Nevertheless, the technique was attractive because it did not have the drastic side-effects of pituitary ablation. There were many reports of uncontrolled studies in the late 1960s but it was probably the enthusiasm of the respected Boston ophthalmologist William Beetham and his ruby laser that convinced the US of the value of the procedure (Beetham et al, 1970).

The most important driver of further research was a 1968

meeting organised by the United States Public Health Service at Airlie House, Virginia, where a large group of experts from all over the world were brought together to discuss the problem of retinopathy and its treatment (Goldberg and Fine, 1969). Airlie House was a conference centre in a rural setting with no possibility of evening entertainment – except discussing diabetic eye disease! The original idea had come from two fellows who did not want to go to fight in the ongoing war in Vietnam and succeeded, with the help of Matthew Davis (a well-known ophthalmologist), to enter employment at the National Eye Institute in Bethesda. Their idea was that the people who actually did the work rather than heads of department would be invited. No individual papers were given but circulated beforehand was a proposed classification of retinopathy which in effect told participants to do their homework.

A standard classification of retinopathy was thought to be particularly important because in the absence of one no conclusions could be drawn from the 1200 pituitary ablations and 1600 photocoagulations undertaken in the previous 10 years. The leitmotiv of the meeting was the alarming growth of the problem and the lack of effective therapy, particularly for proliferative retinopathy. Participants agreed on the importance of randomised controlled trials, defined maculopathy and decided on the importance of stereo pictures and standard photos. Their work and collaborations dominated research and treatment of retinopathy for the next 20 years (Goldberg and Jampol, 1987)

The American Diabetic Retinopathy Study (DRS) was planned as a direct result of the 1968 meeting and began in 1971 under the sponsorship of the National Eye Institute. When the first report came out in April 1976, it clearly showed that photocoagulation reduced the rate of severe visual loss in proliferative retinopathy (The Diabetic Retinopathy Study Research Group, 1976). A year earlier, preliminary results of a UK multicentre trial showed that photocoagulation delayed the progression of maculopathy with a mean difference between treated and untreated eyes after 3 years of 1.2 Snellen lines (Cheng et al, 1975).

Of course, photocoagulation was not a panacea but merely a way of stopping retinopathy getting worse. It also had unavoidable side effects in the form of reduced visual fields and night vision and, in the hands of careless or unlucky operators, excessive or misdirected burns on the macula, for example. Even in the best hands there was still a 10 % or greater risk of progression of visual loss. However, from my standpoint as an observer in the clinic, the biggest problem was one which was hardly ever discussed – operator variability. The ophthalmologist whose results were best in my locale was someone who never wrote any papers or had any national acclaim!

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