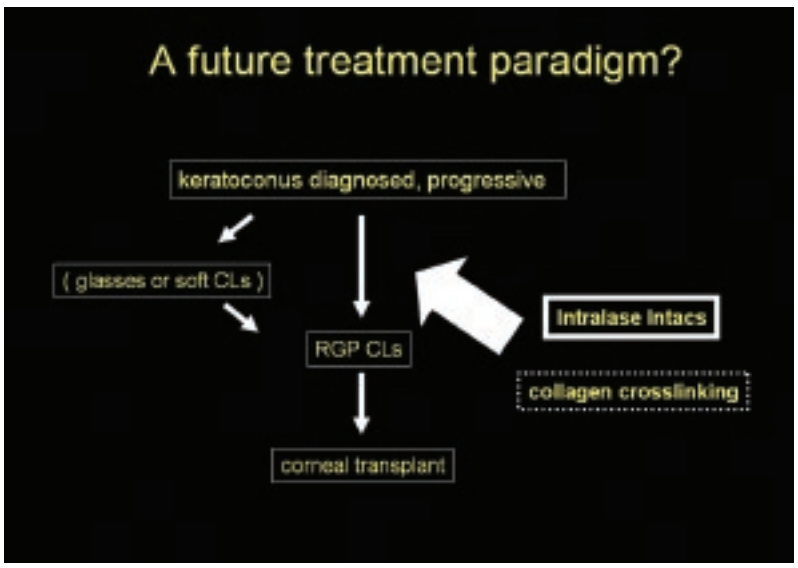
Collagen crosslinking for keratoconus – halting progression

*By Dr Adam Watson**

More and more evidence is accumulating that keratoconus progression is halted by corneal collagen cross-linking treatment. This means that our traditional approach to keratoconus treatment is likely to change.

In New Zealand, a country with a high prevalence of keratoconus and the highest reported rate of corneal transplant surgery for keratoconus in the world1, collagen cross-linking has the potential to become a very important sight-preserving treatment.



The cornea before and after the cross-linking treatment.

UVA cross-linking treatment.

Properly known as corneal collagen cross-linking with riboflavin ("C3R", "CCL" and "CXL" are shorthand terms), the procedure causes stiffening of the cornea so that it resists further deformation. In keratoconus, the cornea weakens, thins and steepens with development of irregular astigmatism. C3R causes enhanced cross-linking between collagen microfibrils in the cornea, and between and within the molecular building blocks of these microfibrils. This is achieved by applying non-toxic riboflavin (vitamin B2) to the cornea to act as a photosensitiser, then using a measured dosage of Ultraviolet-A radiation (UVA) to generate free radicals within the cornea with chemical cross-links resulting.

In practical terms for the patient, the procedure is straightforward and comfortable. Local anaesthetic drops are given before removal of the central 8-9mm of corneal epithelium. Riboflavin solution is then applied for 30 minutes to saturate the corneal stroma before the UV-A treatment is carried out using a precisely calibrated instrument such as the UV-X system, again for 30 minutes. Aftercare is much the same as for PRK excimer laser treatment, with a bandage contact lens applied and topical treatment to improve comfort and epithelial healing over the next three days.

The increased cross-linking within the cornea leads to a stiffening effect, akin to the corneal stiffening that occurs with natural ageing. The biomechanical strength of human cornea may be increased by a factor of 3 or more2. This increased corneal rigidity appears to be responsible for slowing or halting of corneal ectasia.

The C3R process, using riboflavin solution combined with UVA exposure, was developed in Germany from 1993 onwards with the first patients treated in 1998. The treatment has been steadily gaining momentum as clinical results have become available with clinical trials continuing in several centres around the world and the FDA in the USA recently approving a trial of C3R.

Published evidence uniformly shows no progression of keratoconus in the follow-up period3-5. For example, in the Dresden study of 60 eyes with 5 years follow-up, no eyes had progression and about half of eyes demonstrated some flattening of keratometry values3. A slight mean improvement of 1.4 lines in best corrected visual acuity was also found. Early results of a randomised trial in Melbourne, reported at the RANZCO Congress in November 2007, also showed flattening of steepest keratometry values with a small improvement in best corrected visual acuity5. The untreated control eyes in the same 3 month period showed steepening of keratometry (mean 1.45D).

C3R is also likely to have a complementary effect with intrastromal corneal implant surgery (Intacs, Kerarings). The procedures have been performed both simultaneously and with intrastromal rings preceding C3R by a few months (C3R potentially "locking in" the flattening effect of intrastromal rings). Studies thus far suggest additive effects6,7.

Potential candidates for C3R are those with demonstrated progression of keratoconus or other corneal ectasias (pellucid marginal degeneration, iatrogenic cases). A minimum corneal thickness of 400 microns after epithelium removal is a requirement to protect the endothelium from potentially toxic UVA levels8. This is measured before treatment is commenced – if the cornea is too thin, a hypotonic riboflavin solution may be applied to cause corneal swelling, sufficient to enable safe treatment. No sight-threatening side effects have been reported from worldwide experience.

In the last issue of (*NZ Optics* March 2008), a speaker at the Global Keratoconus Congress in Las Vegas, Dr Kenneth McCandless, talked of a paradigm shift in our approach to the management of keratoconus, with intrastromal corneal implants being the preferred choice for contact lens intolerant patients, resulting in deferment of, or avoiding the need for, corneal transplant surgery. The exciting twin developments of C3R and intrastromal implants, together with their excellent safety profile so far, may mean that the standard treatment paradigm shifts again – from intervention following contact lens intolerance to intervention much closer to initial diagnosis with demonstrated progression. The outlook for treatment of keratoconus and other ectasias is brighter now than ever before.

Dr Adam Watson and technician Catherine Cruz with Eye Institute's UV-X cross-linking system.

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