

Strengthening the Cornea

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Could a simple non-surgical technique make the cornea resistant to ectasia in keratoconus and perhaps other corneal ectasias? In this issue of the journal, an article by Wollensak and coworkers, "Collagen Fiber Diameter in the Rabbit Cornea after Collagen-Crosslinking by Riboflavin/UVA," describes the results of crosslinking corneal collagen with riboflavin and UVA light in rabbit eyes. The original hypothesis was that corneal collagen can be crosslinked by riboflavin and UVA light, thereby increasing the cornea's thickness, stiffness, and resistance to subsequent distortion, as well as perhaps to enzymatic digestion. The results of the rabbit studies provide convincing electron microscopic documentation that such crosslinking does, in fact, thicken the collagen fibers of the rabbit cornea.

The results of this study complement a clinical study recently published by these authors in the *American Journal of Ophthalmology*.¹ In that study, the corneas of 22 patients with moderate or advanced progressive keratoconus were treated with topical photosensitizing riboflavin drops and exposed to UVA light for 30 minutes at a distance of 1 cm; follow-up ranged from 3 months to 4 years. During this time, the patients showed no progression of keratoconus, and some, in fact, had a reduction of maximal keratometry. There were no changes in corneal and lens transparency, endothelial cell density, or intraocular pressure.

The current experimental study in rabbit eyes showing a thickening of corneal collagen fibers supports the idea that crosslinking does occur. It does not, however, demonstrate that the cornea really is "stiffer" or that it will be resistant to future ectasia. Furthermore, the clinical study had no controls; it was an open study in which patient and investigator enthusiasm might have affected the results. Thus, the evidence for the idea that riboflavin and UVA crosslinking of corneal collagen makes a cornea resistant to distortion and further ectasia is incomplete, and certainly requires further study.

Nevertheless, the authors are to be commended for a unique approach to progressive corneal thinning—in this case keratoconus, but perhaps applicable to other types of ectasia—which may revolutionize our approach to these diseases. The idea that a safe, inexpensive, and relatively available therapy might stop the progression of a disease which otherwise causes visual distortion and may require corneal surgery with all of its attendant risks offers exciting hope for the future. The precise etiology of keratoconus and other ectasias is unclear. Genetic abnormalities in the collagen and its crosslinking, secretion of matrix metalloproteinases (MMPs) and other lytic enzymes, eye rubbing, allergy, and other factors have been suggested. Whatever the cause or causes, if collagen crosslinking can increase resistance to these distortions, it would be of great importance. The idea that the cornea can be stiffened by this procedure even offers the possibility of a permanent alteration of corneal shape without surgery, a concept that has been explored in various ways in the past without great success.

It is easy to look at the present studies and to realize that both the experimental and clinical results are still very preliminary. On the other hand, the approach is unique, the hypothesis is credible, and should it be proven, the value would be significant. The authors are to be congratulated on providing a novel hypothesis that may be therapeutically beneficial, and on providing the first steps toward evidence that it is really effective. This is important work that deserves our attention and further investigation.

REFERENCE

1. Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-A—induced collagen crosslinking for the treatment of keratoconus. *Am J Ophthalmol*. 2003;135:620–627.

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