What is Corneal Collagen Crosslinking?

- A chemical reaction that strengthens the connections between corneal collagen fibrils thereby halting the progression of corneal thinning and steepening.
+ Indications
- Forme Fruste Keratoconus
- Keratoconus
- Keratoectasia following corneal refractive surgery
- Pellucid Marginal Degeneration

+ Who is a good candidate?
- Current best corrected vision acceptable to patient
- Absence of significant corneal scaring
- Central corneal thickness > 400 microns

+ When to treat?
- Early in the disease
- Documented progression (risk versus benefit)
- Consider age and disease subtype
  - Keratoconus versus Pellucid Marginal Degeneration
Potential Early Signs

- Autorefraction that recommends more cylinder than in MRx
- Scissoring of reflex on retinoscopy
- Asymmetric refractive error especially if
  - Asymmetric astigmatism
  - Progressive astigmatism
- Ks > 45 D
- Inferior Steepening on topography
- CCT < 530 microns
Patient 2

28 yo c/o monocular vertical diplopia OD x 6 months. Min to mod eye rubbing and occasional snoring.

<table>
<thead>
<tr>
<th></th>
<th>OD</th>
<th>OS</th>
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<tbody>
<tr>
<td>VAsc</td>
<td>20/20</td>
<td>20/20</td>
</tr>
<tr>
<td>ARx</td>
<td>-0.75 + 1.50 x 76</td>
<td>+0.25 + 0.50 x 81</td>
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<tr>
<td>CCT</td>
<td>502</td>
<td>497</td>
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</tbody>
</table>

You need 3 things to crosslink

- UVA light
- Riboflavin soaked cornea
- Oxygen

Riboflavin Sources
WHERE DO CROSS-LINKS OCCUR?

Collagen Interfibrillar Spacing

Multiple studies have shown that standard CXL (epithelium off) will halt or reverse progression in greater than 80% patients.

PHASE III
RANDOMIZED CONTROLLED MULTICENTER TRIAL

- The trials included:
  - Study 1: 58 patients with progressive keratoconus.
  - Study 2: 147 patients with progressive keratoconus.

- Schedule of Assessments:
  - Screening/baseline. Day 0 (randomization/treatment day), 1 day, 1 week, and 1, 3, 6 and 12 months after treatment.

- Primary Endpoint was \( K_{\text{max}} \), as measured by keratometry.

EFFICACY ANALYSIS:
MEAN CHANGE FROM BASELINE KMAX: CXL VS SHAM

<table>
<thead>
<tr>
<th></th>
<th>CXL Group (N=102)</th>
<th>Control Group (N=103)</th>
<th>CXL Group (N=91)</th>
<th>Control Group (N=88)</th>
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</thead>
<tbody>
<tr>
<td>Corneal Opacity</td>
<td>65</td>
<td>9</td>
<td>65</td>
<td>8</td>
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<tr>
<td>Corneal Edema</td>
<td>7</td>
<td>0</td>
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<td>0</td>
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<td>Epithelium Defect</td>
<td>24</td>
<td>1</td>
<td>26</td>
<td>3</td>
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<tr>
<td>Punctate Keratitis</td>
<td>25</td>
<td>8</td>
<td>18</td>
<td>3</td>
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</tbody>
</table>

In 1-2% of patients, corneal epithelial defect, corneal edema, corneal opacity and corneal scar continued to be observed at 12 months.

ADVERSE REACTIONS
PHASE III STUDIES
CONCLUSION

- CXL has revolutionized the treatment of corneal ectatic diseases
  - Graft Failures
  - Dry Eye, Cataract, Glaucoma...
  - Decreased Structural Integrity