Corneal Cytokine Regulation (CCR)

NETRA EYE INSTITUTE
HOLISTIC EYE CARE CENTER

What is keratoconus?

Keratoconus, or KCN, is a progressive eye disease where the cornea thins and bulges into a cone shape, distorting vision. It threatens sight by causing irregular astigmatism, scarring, and even vision loss.

Do you have these KCN symptoms?

Frequent eye rubbing

Blurred or distorted vision

Frequent changes in prescription

Frequent headaches or eye strain

Mild ghosting or double vision

Family history of KCN

Visual impairment despite best corrective lenses

Increased light sensitivity (photophobia)

Early diagnosis and treatment of KCN are crucial to prevent significant vision loss. If detected early, CCR treatment can halt progression, improve vision, and reduce the need for more invasive surgical procedures such as corneal transplants.

KNOW THE FACTS

Inflammation Leads to KCN

KCN is an inflammatory disorder of the eyes, and treating ocular inflammation stops KCN progression and initiates the vision recovery process.

Did you know?

Recent scientific research has clearly shown KCN to be an ocular inflammatory condition due to cytokines produced as part of body's immune response[1,2,3].

By regulating cytokines and reducing ocular inflammation and its associated cofactors, we can stop the KCN progression and reverse the condition.

If your doctor is not treating you for ocular inflammation, you are not addressing the core problem of KCN and may lead to the progression of your KCN.

Treat ocular inflammation to stop KCN progression

1. **Increased lacrimal inflammatory mediators in patients with keratoconus,** Gustavo Souza Moura, Albert Santos et al.
2. **Keratoconus: an inflammatory disorder?** V Galvis, T Sherwin et al.
3. **Tear film inflammatory mediators in patients with keratoconus,** Rana Sorkhabi, Amir Ghorbanihaghjo et al.

Are you treated for inflammation?

Cytokines such as IL-6, IL-8, and IL-1β, as well as TNF-α are inflammatory markers and have been detected in high levels in the tears and corneal tissue of KCN patients.[1]

The presence of these pro-inflammatory cytokines in KCN suggests that the immune system plays a role in the breakdown of corneal integrity.

Inflammation may also contribute to the activation of matrix metalloproteinases (MMPs) and other enzymes that degrade the extracellular matrix (ECM), leading to collagen breakdown and corneal thinning.

The Interleukin-5 (IL-5) and Interleukin-6 (IL-6) cytokines was higher in the cornea of the KCN patients suggesting increased inflammation in the ocular tissues.[1]

1. **Increased inflammatory mediators in ocular surface tissue in keratoconus,** Albert Santos, et al

KCN & Down Syndrome

People with Down Syndrome (DS) have a significantly higher prevalence of KCN compared to general population—studies suggest up to 10–15%, versus about 0.05–0.2% in the general population.

Individuals with DS often have altered immune function and atopic conditions, including overproduction of pro-inflammatory cytokines and chronic low-grade inflammation.

Chronic inflammation can lead to extracellular matrix remodeling, which weakens the cornea.

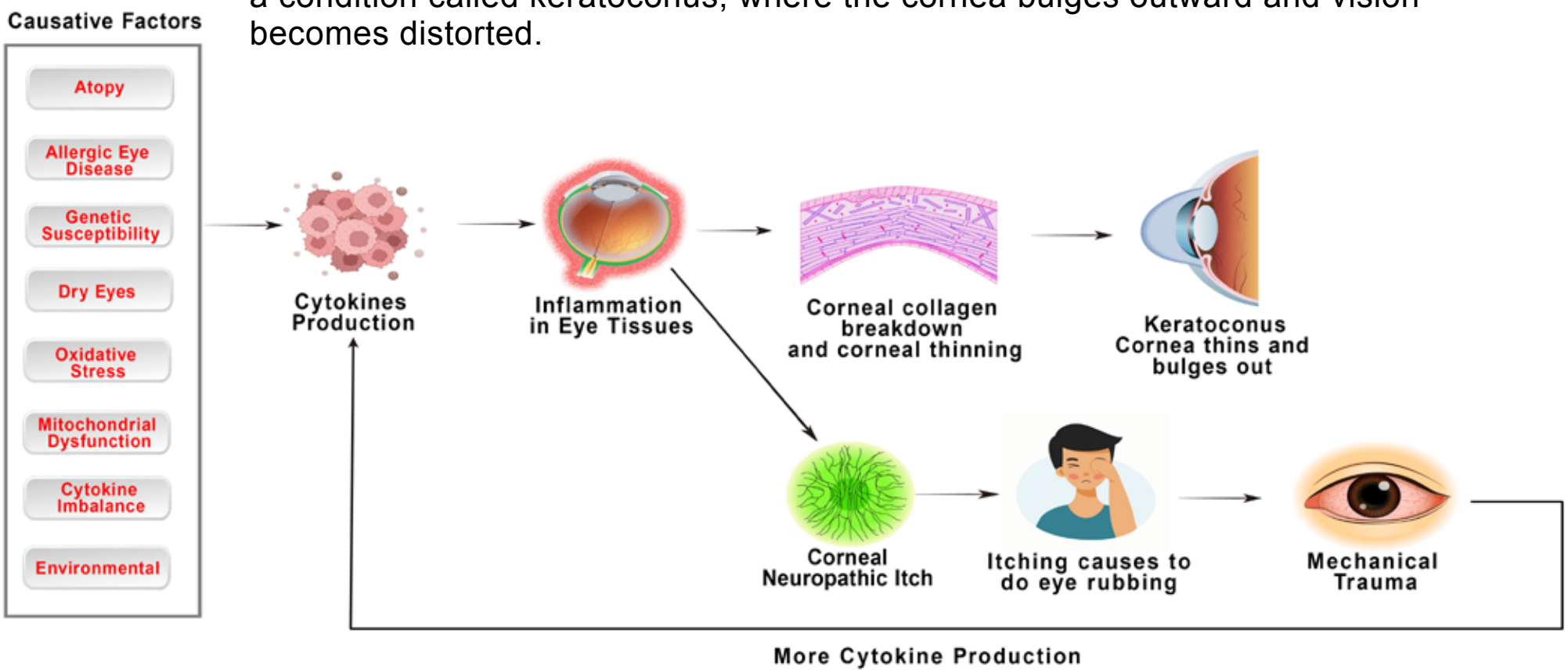
Oxidative stress, commonly elevated in DS, also damages corneal tissue integrity.

Down Syndrome is another strong evidence suggesting how cytokines and chronic inflammation plays a significant role in KCN.

See What's Behind KCN Development

Several factors—such as allergies, dry eyes, genetic tendencies, environmental triggers, and problems with cell function—can disrupt the normal balance of the eye's immune system. This leads to the release of certain chemicals called cytokines, which cause ongoing inflammation in the eye. cornea bulges outward and vision becomes distorted.
Over time, this chronic inflammation can damage important structures in the cornea, especially the collagen that helps keep it strong and properly shaped.

As this collagen breaks down, the cornea becomes weaker and thinner, leading to a condition called keratoconus, where the cornea bulges outward and vision becomes distorted.



Corneal Cytokine Regulation

What is CCR?

Corneal Cytokine Regulation (CCR) is a ground breaking treatment shown to reduce and regulate cytokines and ocular inflammation and its associated cofactors with acupuncture and herbal medicine.

Acupuncture and herbal medicines have shown to reduce ocular inflammation, often associated with elevated levels of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6.

Research studies suggest that acupuncture modulates immune responses by activating the hypothalamic-pituitary-adrenal (HPA) axis and vagus nerve, leading to the downregulation of inflammatory mediators. This immunomodulatory effect contributes to decreased cytokine expression in both systemic circulation and localized ocular tissues.

Similarly, herbal medicines exert anti-inflammatory effects by inhibiting key signaling pathways such as NF-κB and MAPK, which are central to cytokine production. These herbs suppress inflammatory infiltration and oxidative stress, aiding in tissue repair and symptom relief.

CCR exhibits the following multi-component, multi-pathway and multi-targeted synergistic mechanism of action for treatment of KCN.

- Reduce & Regulating Cytokines
- Reduce Ocular Inflammation
- Reduce Oxidative Stress and Ferroptosis
- Improve Ocular Blood Flow
- Reduce Ocular Excitotoxicity
- Supply Neurotrophins and Antioxidants

CCR offers several compelling advantages for KCN patients compared to conventional treatments.

Halts Progression of KCN

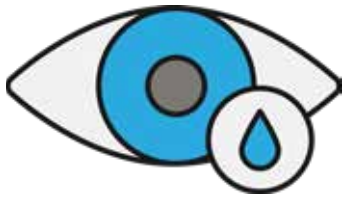
By eliminating ocular inflammation and its co-factors, the progression of KCN can be halted.

Reversal of Keratoconus*

As the cornea heals from ocular inflammation and its associated co-factors are addressed, the cornea starts to heal and reshape*.

Improved Visual Acuity

All KCN patients have shown to have improvement in visual acuity. Our standard of “Normal Vision” is 20/15 - not 20/20.



Dry Eye Improvement

Patients with dry eyes experience improved comfort due to a reduction in dry eye symptoms.

Myopic Improvements

KCN patients with myopia see an improvement in visual acuity and a reduction in prescription power.

Avoid Surgical Complications

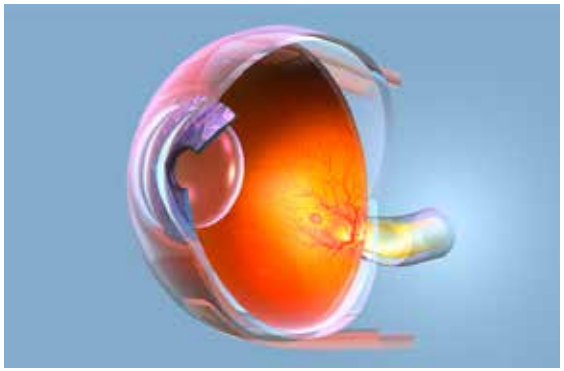
Prevent complications arising from surgical treatments such as corneal rejection, corneal scarring, ulcerative keratitis and glaucoma.

*Reversal may have limitations when there is corneal scarring or hydrops due to anatomical changes to cornea.

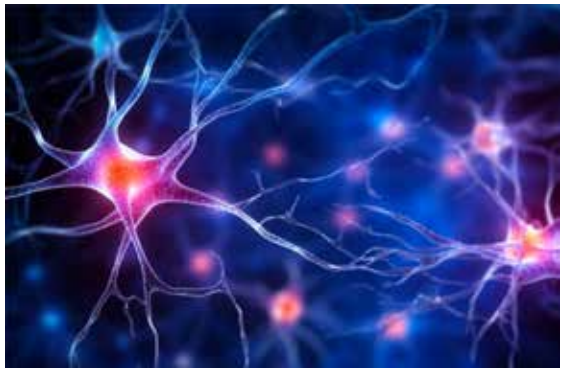
Science Behind Corneal Cytokine Regulation

CCR exhibits multi-component, multi-pathway and multi-target synergistic mechanism of action for treatment of ocular disorders.

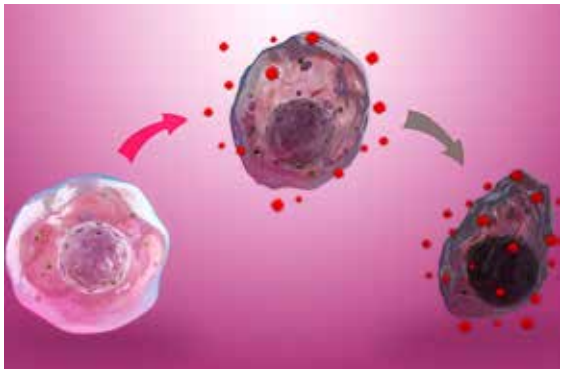
REDUCE OCULAR INFLAMMATION



IMPROVE OCULAR BLOOD FLOW

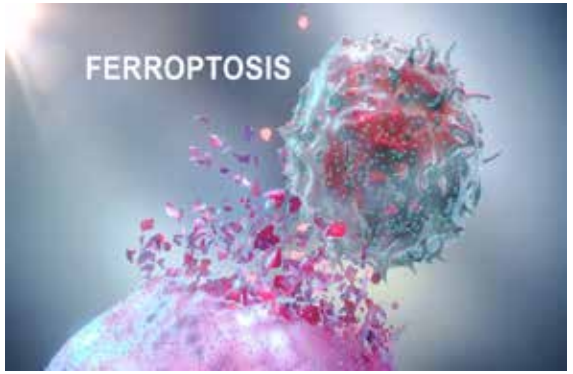


SUPPLY NEUROTROPHINS



REDUCE OXIDATIVE STRESS

SUPPLY ANTIOXIDANTS



REDUCE FERROPTOSIS

“ My vision improved by 8 lines to 20/30 without the need for sclarel lenses. ”

I was surprised to find that I had significant improvement in my vision within 3 weeks of CCR treatment. With both eyes, my vision had improved to 20/30 without the need to use scleral lenses or glasses.

The staff here were very pleasant and made me feel comfortable during the treatment procedure.

VEERAL - STUDENT
KERATOCONUS PATIENT

20/15

Our standard of normal vision is beyond 20/20.

Most patients achieve 20/15 vision after successfully completing their first round of CCR treatment.
About 20% can even read a few letters on the 20/10 line.

CCR revitalizes retinal nerve cells, improving their function and enhancing visual clarity and acuity.

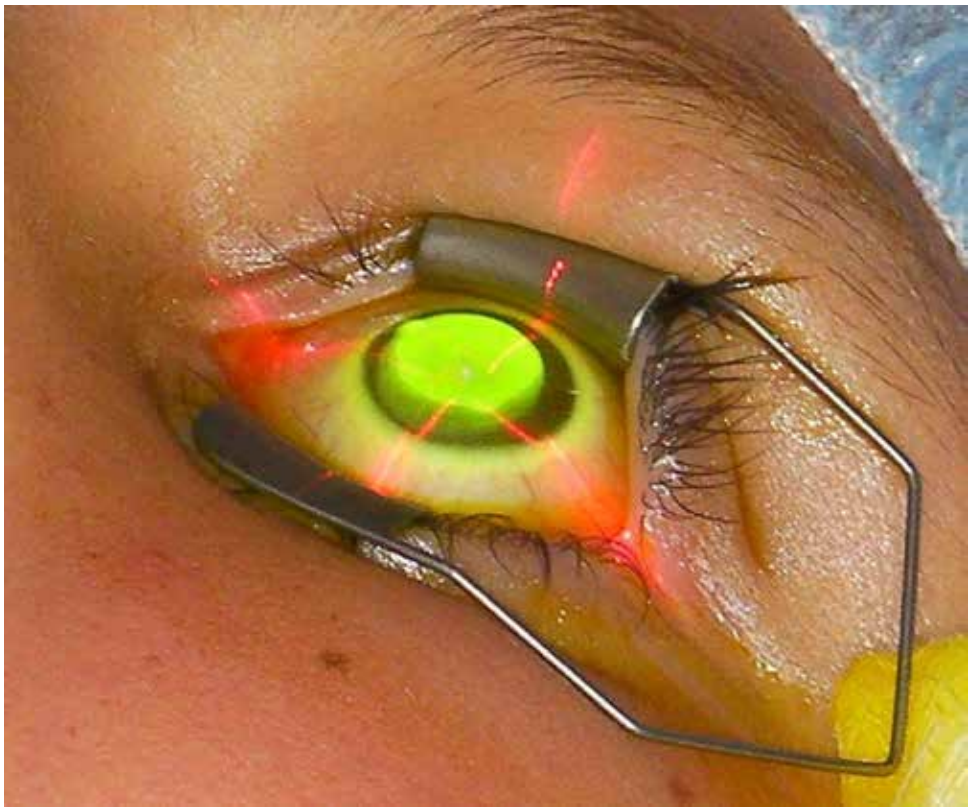
Corneal Collagen Cross-Linking

Corneal Collagen Cross-Linking (CXL) procedure aims to halt the progression of keratoconus by increasing the stiffness of the cornea.
However, while crosslinking can slow disease progression, it does not directly target the inflammatory process or reverse keratoconus.

In cases of advanced keratoconus or significant inflammation, adjunctive therapies targeting inflammation may be necessary to halt progression and potentially reverse the condition.

Upto 22% of patients continue to have KCN progression even after CXL since the ocular inflammation remains untreated[1,2].

Corneal Collagen Cross-linking (CXL) does not reverse damage already done by keratoconus; it prevents further deterioration.



1. **Long Term Results of Accelerated Corneal Cross Linking in Adolescent Patients With Keratoconus,** Muhammet Derda Ozer, Muhammed Batur et al.
2. **Corneal Cross-Linking for Pediatric Keratoconus: Long-Term Results,** Daniel A Godefrooij, Nienke Soeters et al.

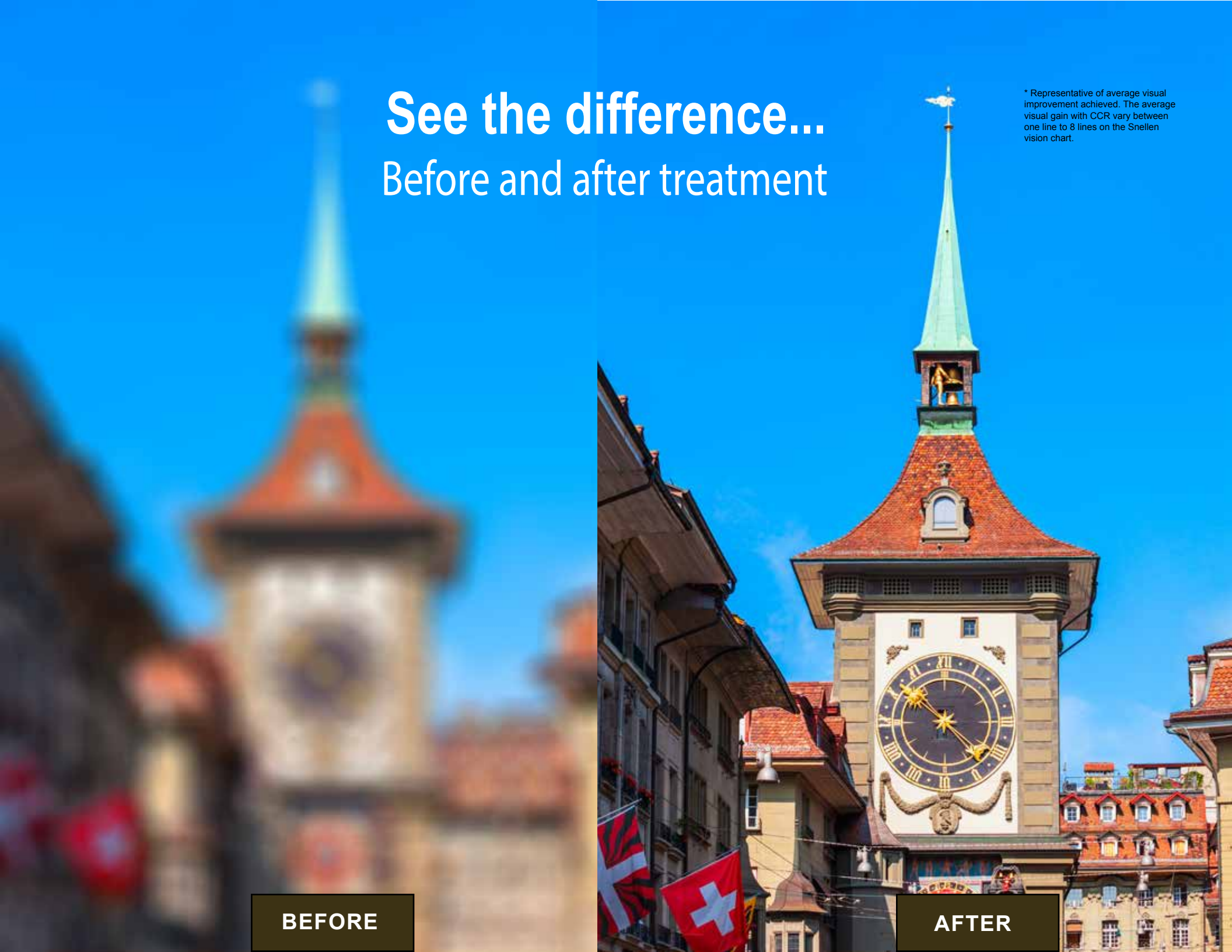
The only treatment shown to stop and improve vision in keratoconus without surgery or corneal cross-linking.

Scientifically Evaluated Treatment Using Natural Treatment Methods

See the difference...

Before and after treatment

* Representative of average visual improvement achieved. The average visual gain with CCR vary between one line to 8 lines on the Snellen vision chart.



REFERENCES

1. **Increased inflammatory mediators in the ocular surface tissue in keratoconus,** Albert Santos, José A P M Filho et al.
Summary: The Interleukin-5 (IL-5) and Interleukin-6 (IL-6) cytokines was higher in the corneal epithelium of the keratoconus group which might indicate increased inflammation in the ocular tissues. There was also greater immune activity in the corneal and conjunctival epithelial cells of patients with keratoconus based on IL-5 and IL-6 gene expression.

2. **Increased lacrimal inflammatory mediators in patients with keratoconus,** Gustavo Souza Moura, Albert Santos et al.
Summary: Inflammatory activity seems to be involved in the development of keratoconus. Out of 21 cytokines, 14 were more concentrated in the tears of keratoconus patients than healthy subjects. Interleukin-6 (IL-6) cytokine was significantly higher in keratoconus patients' tears and was related to disease severity.

3. **Keratoconus: an inflammatory disorder?** V Galvis, T Sherwin et al.
Summary: This review highlighted increased levels of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and matrix metalloproteinase-9 (MMP-9) in the tears of keratoconus patients, suggesting an inflammatory component to the disease. Eye rubbing, a known risk factor for keratoconus, was associated with elevated tear levels of MMP-13, IL-6, and TNF-α, indicating that mechanical trauma may contribute to the inflammatory response.

4. **Tear film inflammatory mediators in patients with keratoconus,** Rana Sorkhabi, Amir Ghorbanihaghjo et al.
Summary: The study found that patients with keratoconus had significantly higher levels of Interleukin 6 (IL-6), Interleukin 1 beta (IL-1β), and Interferon-gamma (IFN-γ) in their tear film compared to normal controls.

5. **Cytokine Expression in Keratoconus and its Corneal Microenvironment: A Systematic Review,** Robert Wisse, Jonas Kuiper, Renze Gan et al.
Summary: The review identified increased levels of pro-inflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and matrix metalloproteinase-9 (MMP-9), in the tear film and corneal tissue of keratoconus patients.

6. **Serum inflammatory biomarkers are associated with increased choroidal thickness in keratoconus,** João Pinheiro-Costa, Mário Lima Fontes et al.
Summary: The study suggests a relationship between increased choroidal thickness and inflammatory mechanisms in keratoconus patients. Elevated serum inflammatory indices neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and systemic immune inflammation index (SII) provide additional evidence of systemic inflammation's role in the development of keratoconus.

7. **The Role of Atopy in the Choroidal Profile of Keratoconus Patients,** Ana Filipa Moleiro, Ana Francisca Aires et al.
Summary: The study compared choroidal profiles (e.g., thickness, vascular density) between KCN patients with atopy and non-atopic KCN patients. Results indicated that atopic KC patients exhibited significantly thinner choroids and reduced vascular perfusion compared to non-atopic KC patients. These findings suggest that atopy-related inflammation may contribute to choroidal thinning, possibly through systemic immune dysregulation or local inflammatory mediators.

8. **Choroidal thickness assessment in keratoconus patients treated with cross-linking compared to healthy population,** Antonio Ballesteros-Sánchez, Concepción De-Hita-Cantalejo et al.
Summary: The study suggests that choroidal thickness is significantly thicker in keratoconus patients treated with cross-linking than in healthy individuals. This finding could be associated with inflammatory choroidal mechanisms in keratoconus patients.

9. **Evidence of Oxidative Stress in Human Corneal Diseases,** Rajeev Buddi, Brian Lin et al.
Summary: The study is to investigate the presence of oxidative stress markers in various human corneal diseases, including keratoconus, Fuchs' dystrophy, and normal corneas. The study identified increased levels of malondialdehyde (MDA), nitrotyrosine (NT), and inducible nitric oxide synthase (iNOS) in diseased corneas, indicating oxidative damage. The study suggests that oxidative stress plays a significant role in the development of various human corneal diseases, with each disease exhibiting a distinctive oxidative stress profile.

10. **Oxidative Stress in the Pathogenesis of Keratoconus and Fuchs Endothelial Corneal Dystrophy,** Katarzyna A Wojcik, Anna Kaminska et al.
Summary: The study observed elevated levels of reactive oxygen species (ROS) in both keratoconus and Fuchs endothelial corneal dystrophy corneas, indicating heightened oxidative stress. There was a noted decrease in the activity of antioxidant enzymes, such as superoxide dismutase and catalase, in the corneal tissues of patients with these conditions. The study suggests that oxidative stress plays a significant role in the development of both keratoconus and Fuchs endothelial corneal dystrophy, potentially contributing to the development and progression of these corneal diseases.

11. **Increased systemic oxidative stress in patients with keratoconus,** I Toprak, V Kucukatay et al.
Summary: The study found that patients with keratoconus have higher levels of systemic oxidative stress compared to healthy individuals. This oxidative stress is believed to contribute to the cellular damage in the cornea, leading to its weakening. The findings suggest that managing oxidative stress could potentially be a therapeutic target for slowing the progression of keratoconus or improving its treatment outcomes.

12. **Long Term Results of Accelerated Corneal Cross Linking in Adolescent Patients With Keratoconus,** Muhammet Derda Ozer, Muhammed Batur et al.
Summary: This retrospective study followed 35 eyes of 23 patients aged 14 or younger, treated with epi off accelerated corneal collagen cross linking (A CXL) for progressive keratoconus and monitored for an average of 56 ± 8 months (about 4.5 years). Preoperatively, keratoconus severity ranged from stages I to IV. At one year, central corneal thickness (CCT) and thinnest point pachymetry (TTPC) decreased significantly; by the second year only TTPC remained reduced. At final follow up, CCT had increased significantly above baseline. Despite treatment, 20% of eyes showed disease progression, and factors such as baseline K1/K2 keratometry readings, CCT, TTPC, and younger age were associated with progression.

13. **Corneal Cross-Linking for Pediatric Keratoconus: Long-Term Results,** Daniel A Godefrooij, Nienke Soeters et al.
Summary: In this prospective cohort of 54 eyes from 36 pediatric patients with progressive keratoconus (aged up to 18 years), standard "epi off" corneal cross-linking was performed and eyes were monitored for up to 5 years post-treatment. The study documented a significant mean reduction of −2.06 diopters in maximum keratometry (Kmax) at 5 years ($P = 0.01$), along with improvements in average keratometry, uncorrected distance visual acuity (UDVA), and corrected distance visual acuity (CDVA)—though not all reached statistical significance at every time point. Despite treatment, 22% of eyes exhibited keratoconus progression by at least 1.0 D at final follow-up; regression analysis suggested that decentralized cone location.

Book Appointment or Have questions?

Call (732) 503-9999

to speak with a patient care coordinator.

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