The CLEK Study “R&R”
Recruitment and Retention

The Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study began enrolling patients on May 31, 1995. Fourteen original clinics were involved with a recruitment goal of eight participants per clinic per month. We anticipated our goals would be met by March 31, 1996. At that time the study would be closed to enrollment. This is the largest, most representative sample of patients with keratoconus to be studied. This is a major milestone in the understanding of this disease.

The recruitment phase of a multicenter clinical study may be considered the most crucial phase of the study. Recruitment goals must be met to insure the continued success of the overall study. It takes the initiative of the individual clinic personnel who dedicate themselves to recruit patients for this study.

Everyone worked hard to recruit – giving talks in the community, newspaper articles, contacting referring eye care givers, website – and in March 1996, with 1,039 patients enrolled, the initial CLEK enrollment goal had been achieved with room to spare. However, an exciting event was to be shared by all when we learned just a week later, on April 30th, 1,189 total participants had been enrolled! The study closed enrollment on June 30, 1996 with a total of 1,210 participants; 20% above our original recruitment objective of 1,000 patients.

Each and every single CLEK participant contributes to the success of this study. Initially, we may get excited about the number of participants enrolled, but let us remind you that the study focus is on education, hopefully prevention, and at best maintenance of the quality of life that, you, the participants ultimately deserve. It is through your support that this research can continue.

We look forward to your continued commitment to this very important project over the next few years. If you find that you are relocating, or you experience other obstacles that might interfere with your participation, let us be the first to attempt to help. Your continued participation is very important to us. Please contact your study office staff members who are always ready and willing to assist in any possible way:

The Ohio State University
College of Optometry
Chairman’s Office
Study Coordinator: Jodi Malone (614) 292-6603

University of Alabama at Birmingham
School of Optometry
Study Coordinator: Maria Voce (215) 934-6734

University of California, Berkeley
School of Optometry
Study Coordinator:
Pamela Qualley (510) 642-5456

continued
Electronic Network for Keratoconus Patients and Eye Care Practitioners

Mark J. Mannis, Director of the Cornea and External Disease Service and Professor of Ophthalmology at the University of California, Davis, and Karla Zadnik, Assistant Professor and CLEK Study Chairman at The Ohio State University College of Optometry co-moderate a network for keratoconus patients called “keratoconus-link.”

The network now has 226 members and is a place to tune into lively discussions about keratoconus in general, contact lens wear, corneal transplant experiences, and a variety of other issues.

To subscribe, new subscriptions should be sent via e-mail to: listproc@ucdavis.edu. In the body of the message, simply type:

subscribe keratoconus-link YOUR NAME

Postings for discussion should be sent to:
keratoconus-link@ucdavis.edu

For more information (other than just to subscribe) Drs. Mannis and Zadnik can be contacted via e-mail at mjmannis@ucdavis.edu or zadnik.4@osu.edu.
1. The fluorescein photographs (how the rigid contact lenses fit) look like this. You can see the fluorescein (green) behind the center and behind the edge of the contact lens. Fluorescein is the yellow-orange fluid the eye doctor instills.

2. This is a photograph of a small corneal scar.

3. This is another photograph of the same corneal scar.

The CLEK Photography Reading Center (CPRC) "reads" all of your photographs to see how your contact lenses fit and if your cornea is scarring. This means a CPRC certified Reader views each slide and evaluates it in a standardized way, entering the pertinent data into a computerized database.

4. This is an example of a corneal map. The oval (red) part at the bottom is the most highly curved area of the corneal surface (the "cone"). The various other colored zones above the cone indicate how the corneal curvature (shape) changes across the corneal surface.
What Is Keratoconus?

Keratoconus is a noninflammatory protrusion of the central cornea characterized by distortion of the front of the eye (the cornea) and irregular astigmatism. Keratoconus affects both eyes in most cases but is often worse in one eye compared to the other. Although the protruding area of the cornea is generally displaced downward, the corneal irregularity disrupts vision, even in the earliest stages. Keratoconus patients are usually treated initially with spectacles, followed by rigid contact lenses when the visual distortion with spectacle correction becomes incapacitating. Typically, 10 to 25 percent of keratoconus patients undergo a corneal transplant, usually because of contact lens intolerance, decreased vision, and/or central corneal scarring.

Keratoconus is characterized by symptoms of visual distortion, observable corneal irregularity that worsens with time, classic signs in the cornea that can only be seen with high magnification, and progressive corneal scarring. Keratoconus has been reported to be associated with general health problems such as hay fever, asthma, and atopic dermatitis, as well as a number of rare syndromes. The role of inheritance in keratoconus has been studied without definitive results to date.

Before the full-scale CLEK Study started in 1995, we conducted a survey of 1,579 keratoconus patients at 38 clinical centers. The average age of these patients was 37 years, with a range of 10 to 89 years. Sixty-eight percent of the patients were white, 21% black, 7% Hispanic, and 3% Asian. Forty-one percent of the sample was female.

The patient reported average age of keratoconus diagnosis was 27 years. Nearly 90% of the sample reported that the diagnosis of keratoconus had occurred between 10 and 39 years of age.

Vision with rigid contact lenses was uniformly quite good, and almost 60% of the patients who were measured for a glasses prescription got some reasonable vision with the appropriate lenses. This may indicate that more contact lens-wearing keratoconus patients should be receiving prescriptions for back-up glasses to wear at the end of the day or when their contact lenses are uncomfortable.

Surgical history data were collected, and 12% of patients had undergone a corneal transplant.

Almost one-third of the patients had a history of hay fever, asthma or atopic dermatitis. Nine percent of the patients reported a positive family history of keratoconus.

These initial results from the CLEK Survey are interesting. They generated many of the questions enrolled CLEK Study patients answered at their annual CLEK Study visits, and they helped the CLEK investigators refine the CLEK Study protocol. Stay tuned for more data on your own keratoconus as full CLEK Study results are reported here.

Want More Information About Keratoconus?

Contact:
Cathy Warren, RN, CRNO
National Keratoconus Foundation
8700 Beverly Blvd. #5069
Los Angeles, CA 90048
Telephone: 310-855-6455
e-mail: nkcf@csmc.edu

If You Head to Eye Surgery...

If you are one of the enrolled CLEK patients who elects to have a corneal transplant during the study, please contact your CLEK doctor and schedule a special Pre-Surgical Visit within one month before your planned surgery date. We are very interested in examining patients before and after a corneal transplant to see how the operation affects vision, contact lens wear, and a variety of other measures.
Ongoing Keratoconus Research in the United States: Your Tax Dollars at Work

Although keratoconus is thought to be a rare condition, there is ongoing research in the United States related to various aspects of keratoconus. Here is a listing of the ongoing research as of 1997:

Beatrice Yue
University of Illinois at Chicago
Biochemical Basis of Keratoconus
Supported by the National Eye Institute, a division of the National Institutes of Health

This research program examines a number of compelling hypotheses in relation to keratoconus: 1) Degradation processes may be one of the mechanisms that are abnormal in keratoconus; 2) The corneal epithelium may play a role in keratoconus, and the disintegration or leakage of the epithelial basement membrane may be a prerequisite for amplified epithelial-stromal interactions and the development of keratoconus. The integrity of the epithelial basement membrane, the expression of hemidesmosome proteins and integrins in keratoconic corneas will be examined by immunohistochemistry and immunoelectron microscopy. 3) The lysosomal enzyme and inhibitor levels may be modulated by cytokines. The modulation of enzymes and inhibitors in normal human, keratoconic, and other abnormal corneas will be studied. 4) Gene alterations of enzymes and inhibitors may affect the extracellular matrix integrity in the cornea. 5) Biochemical abnormalities may exist in conjunctival or other epithelia of keratoconus patients. Through these investigations, the various biochemical and molecular events associated with keratoconus will be better illustrated, and greater insights into the pathogenesis of keratoconus will be attained.

continued
Cristina Kenney  
Cedars-Sinai Medical Center  
Metalloproteinases in normals and keratoconus  
Supported by the National Eye Institute, a division of the National Institutes of Health  

This laboratory will study the specifics of this abnormal enzyme system and is designed to provide valuable information on the etiology of keratoconus. While keratoconus may have multiple etiologies, our studies have demonstrated that approximately 75% are associated with an abnormal enzyme system which can degrade the corneal matrix.

Donna Peters  
University of Wisconsin, Madison  
Assembly of Collagen Fibrils in the Cornea  
Supported by the National Eye Institute, a division of the National Institutes of Health  

The aim of this proposal is the study how fibrils of collagen are assembled in human cornea of normal and keratoconic corneas. The extracellular matrix in the corneal stroma is a highly ordered structure believed to play a major role in maintaining the transparency and rigidity of the cornea. How the components of the extracellular matrix are assembled and what molecular and cellular control mechanisms are involved in the formation of the matrix are only beginning to be understood.

Yaron Rabinowitz  
Cedars-Sinai Medical Center  
Genetic Factors in Keratoconus  
Supported by the National Eye Institute, a division of the National Institutes of Health  

The focus of this project is to develop reliable topographic criteria (corneal shape factors) for detecting subclinical forms of keratoconus to enable us to conduct critical genetic analyses and delineate modes of inheritance of familial keratoconus. These data, combined with cell lines established on the multiple keratoconus families ascertained, will create a unique resource for future molecular genetic studies. Identifying a gene or genes contributing to the pathogenesis of keratoconus may provide insights into devising medical therapy to arrest its progression and prevent the need for multiple contact lens changes and/or cornea transplantation in select individuals.

Sandra Masur  
Mount Sinai School of Medicine  
Keratocyte Collagenase  
Supported by the National Eye Institute, a division of the National Institutes of Health  

Their long-term goal is to determine at the cellular, subcellular and molecular levels how the extracellular matrix and the individual keratocyte interact temporally and spatially in normal and pathological situations such as keratoconus. Normal eye function depends on corneal transparency which, in turn, depends on maintenance of a normal corneal stroma, in part regulated by collagenases. Understanding mechanisms of collagenase regulation will help prevent damage from uninhibited collagenase secretion, as in keratoconus.

The projects described above are in addition to the three federal grants that support the CLEK Study: one to the Chairman’s Office and one to the CLEK Photography Reading Center (both at The Ohio State University College of Optometry) and one to the Coordinating Center at Washington University Medical School, St. Louis, MO.

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collagen fibrils = clear bands of protein that give the cornea its strength  
collagenase = substance which breaks down collagen  
conjunctiva = mucous membrane on front of sclera (white of eye) and on underside of eyelids  
external basement membrane = adhesive substance under the clear corneal “skin”  
extracellular matrix = clear material between the collagen bands  
endothelium = structures which attach cells to the basement membrane  
immunohistochemistry and immunoelectron microscopy = tools to measure cell molecules and structures  
integrins = biomolecules which control cell function  
keratocyte = cells in the corneal stroma
"Wherefore art thou, CLEK Executive Committee?" On the balcony, during the annual meeting of the Association for Research in Vision and Ophthalmology, Left to right: Tim Edrington of the Southern California College of Optometry, Karla Zadnik and Joe Barr of The Ohio State University College of Optometry, Don Everett of the National Eye Institute, and Mae Gordon of Washington University, St. Louis.

CLEK Study Demographics

AGE (years)

AGE

GENDER

EDUCATION

RACE
CLEK: Cumulative Number of Patients Enrolled
June 1, 1995 - June 15, 1996

Month of Enrollment

Patients Enrolled