The Corneal Dystrophies
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Disclosures:
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- Speakers’ Bureaus: Vistakon, Alcon, VSP; Commission author AMO, A Einstein CyberRounds, SCCO; former Director CL Fellowship previously funded by The Vision Care Institute, LLC, a Johnson & Johnson Company; Research previously funded by NEI (CLEK Study)
- Research funding from SynergEyes, Inc
- COA Board of Trustees
- Emeritus Professor of Ophthalmology, Jules Stein Eye Institute, The David Geffen School of Medicine at UCLA, Los Angeles CA
- Advisor NKCI, Inc
- All comments & errors, however, are completely my own....

Primary references for this discussion:
- Weiss et al. The IC3D Classification of the Corneal Dystrophies. Cornea 2008

Why should we be interested in the corneal dystrophies?
- Study of the CDs will help understand corneal physiology & genetics
- Enhance differential Dx of other corneal diseases, specifically CL complications
- Curiosity
- Historical perspective

“Dystrophy” is currently used to describe an inherited disorder affecting cells, tissues or organs, alone or in combination
- The word dystrophy is derived from the Greek (dys = wrong, difficult; trophe = nourishment) & was introduced into the medical literature by Wilhelm Erb in 1884 to describe a disease of the musculature...
- Arthur Groenouw published 2 patients who had “noduli corneae” 125 years ago
  We now can recognize granular corneal dystrophy in one of these patients, and macular corneal dystrophy in the other...
- About the same time Biber published his thesis discussing what we now recognize as lattice corneal dystrophy
  Groenouw A Arch Augenheilkd 1890
  Biber H A Diggleman Zurich 1890
In Ophthalmology & Optometry, the term “corneal dystrophy” – CD - has been used in reference to a group of inherited corneal diseases that are typically central, bilateral, symmetric, slowly progressive, and without relationship to environmental or systemic factors.

Since Bucklers (Klin Monatsbl Augenheilkd 1949) published the first scheme classifying the corneal dystrophies (granular, lattice, & macular), the most commonly used classification systems have been anatomically-based & phenotypic (aided in some cases by light microscopic histopathology) eg, defined by the involved level of the cornea:

- Epithelial & sub-epithelial
- Bowman’s membrane (ALL)
- Stroma
- Descemet’s membrane (PLL)
- Endothelial

Other CD classification schemes are possible...

- Severity
- Histopathological features
- Biochemical characteristics
- Genetic pattern (genotype)

In particular, the development of genotypic analysis is currently revolutionizing medicine, and especially the study of the CDs.

Genetic characterization of the CDs has revealed both:

Genetic heterogeneity:
wherein different gene abnormalities (genotype) cause a single dystrophic phenotype (eg both KRT3 and KRT12 => the same clinical picture of Meesman’s dystrophy)

And

Phenotypic heterogeneity:
Wherein a single gene (TGFB1) causes different allelic dystrophy phenotypes (eg RBCD, TBCD, granular type 1, and type 2, and lattice type 1)
Most CDs are:

- Autosomal dominant
- Isolated to the cornea, and one layer...
- Bilateral
- Central-Axial (≠ avascularity of the cornea)
- Symmetric
- Stable or slowly progressive
- Early onset (congenital or presents during youth)
- Non-inflammatory

Always consider alternative Dx's

Fabry's disease & other corneal verticillota

Fabry disease is a rare genetic lysosomal storage disease, inherited in an X-linked manner; results from the buildup of globotriaosylceramide in the body's cells, including the cornea.

Other causes of verticillota include systemic medications such as amiodarone, chloroquine, indomethacin, phenothiazines etc.

Fabry disease is a rare genetic lysosomal storage disease, inherited in an X-linked manner; results from the buildup of globotriaosylceramide in the body's cells, including the cornea. Genetic testing now available through Genzyme.

Prevalence of Corneal Dystrophies in the United States: Estimates from Claims Data

David C. Mauck, Leslie M. Nirel, Joshua D. Stern, Roberto M. Karpur, and Alan Segal

Prevalence. To estimate the prevalence of corneal dystrophies, we reviewed claims data from the authors' employer health plan.

If an "average" eye doctor sees 100 pts/week for 50 weeks/yr...

- 5000 pt-visits per year
- 200,000 pt-visits over a 40 year career
- 1000/1,000,000 = 200/200,000

Therefore ~200 CD patients seen over a career. Compare to:

- KC prevalence is 50-250/100,000, or 10/10,000 or ~150,000 KC in USA
- CDs also ~10/10,000 but most (>7/10) FECD & EBMD
- Compared to 16 million diabetics in the USA

The ICD Classification of the Corneal Dystrophies

Data from NIH DRU (2006-2008) and NCHS (2000-2004)

- Epithelial and subepithelial dystrophies
- Hereditary, metabolic, post-traumatic, etc.
- Corneal dystrophies:
  - Epithelial: OPMD, EMD
  - Staphylococcal: MOEM, OME
  - Aniridia: ME, AE
- Genetic, chromosomal, metabolic, etc.
- Corneal dystrophies:
  - Keratoconus
  - Lisch nodules
  - Pigmented dots and plaques
- Corneal dystrophies:
  - Lamellar, arcus, etc.
- Corneal dystrophies:
  - Corneal opacities, arcus, etc.
- Corneal dystrophies:
  - Corneal dystrophies, etc.
- Corneal dystrophies:
  - Corneal dystrophies, etc.
The IC3D Committee developed a series of descriptive, evidential categories:

<table>
<thead>
<tr>
<th>Category</th>
<th>Defining characteristics</th>
<th>Known gene or known gene locus?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Well-defined dystrophy</td>
<td>Known gene</td>
</tr>
<tr>
<td>2</td>
<td>Well-defined dystrophy</td>
<td>Known gene locus; no specific gene identified</td>
</tr>
<tr>
<td>3</td>
<td>Well-defined dystrophy</td>
<td>No known gene or gene locus</td>
</tr>
<tr>
<td>4</td>
<td>Poorly defined dystrophy</td>
<td>No known gene or gene locus</td>
</tr>
</tbody>
</table>

Epithelial and Subepithelial Dystrophies

- **Epithelial basement membrane dystrophy (EBMD)**
  - Also called: Map-dot-fingerprint; Cogan microcystic epithelial; anterior basement membrane
  - The vast majority of cases are degenerative, or related to trauma; although familial cases have been reported related to 5q31 (TGFB1)
  - Presents late in life and usually asymptomatic -- or symptoms of recurrent abrasion and/or blurred vision (due to irregular astigmatism if central lesions)

- **Meesmann corneal dystrophy (MECD)**
  - Also called: Juvenile hereditary epithelial dystrophy
  - Autosomal dominant: heterozygous missense mutation in either Keratin 3 (KRT3) or Keratin 12 (Stocker-Holt variant) 17q12 (KRT12)
  - Can lead to recurrent erosions, blurred vision
  - From irregular surface and/or scarring; Stocker-Holt variant more severe

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**Epithelial basement membrane dystrophy (EBMD)**

**Meesmann corneal dystrophy (MECD)**
Lisch epithelial corneal dystrophy (LECD)
- Also called: band-shaped and whorled microcystic dystrophy of the corneal epithelium
- X-chromosomal dominant: Xp22.3
- Asymptomatic or blurred vision (if pupillary zone involved)

Gelatinous drop-like corneal dystrophy (GDLD)
- Also called: subepithelial amyloidosis; primary familial amyloidosis (Grayson); ~increased epith permeability (to NaF) => inc epithelial lactoferrin from tears => amyloid
- Autosomal recessive: 1p32, Tumor-associated calcium signal transducer 2 (TACSTD2)
- Significant decrease in vision, photophobia, irritation, redness, tearing
- Increased prevalence in Japan (43% consanguineous marriage)
- Can be pigmented (unusual for CDs)
- Tx bandage SCLs (esp post PKP)

Bowman (ALL) Layer Dystrophies
- Reis-Bucklers corneal dystrophy (RBCD)
  - (Granular corneal dystrophy type 3) C1
  - Also called: Corneal dystrophy of Bowman layer, type 1; geographic corneal dystrophy (Weidle); Superficial granular corneal dystrophy; atypical granular corneal dystrophy; anterior limiting membrane dystrophy, type 1
  - Autosomal dominant: 5q31 (TGFBI)
  - Recurrent corneal erosions and blurred vision
- Thiel-Behnke corneal dystrophy (TBCD)
  - Also called: Corneal dystrophy of Bowman layer, type II; honeycomb-shaped corneal dystrophy; anterior limiting membrane dystrophy, type II; Curly fibers corneal dystrophy: Waardenburg-Jonkers corneal dystrophy
  - Autosomal dominant: 5q31 (TGFBI); 10q24
  - Recurrent corneal erosion and later vision impairment
Grayson-Wilbrandt corneal dystrophy (GWCD)
- Autosomal dominant but unknown gene and genetic locus
- Recurrent erosion and perhaps decreased vision

Stromal Dystrophies
- TGFB1 corneal dystrophies
  - Classic lattice corneal dystrophy (LCD) C1
  - Variants III, IIIA, IIIIB & IV C1
- Granular corneal dystrophy, classic type 1 (GCD1) C1
- Granular corneal dystrophy, type 2 (granular-lattice) (GCD2) C1
- Macular corneal dystrophy (MCD) C1
- Schnyder corneal dystrophy (SCD)
- Congenital stromal corneal dystrophy (CSCD) C1
- Fleck corneal dystrophy (FCD) C1
- Posterior amorphous corneal dystrophy (PACD) C3
- Central cloudy dystrophy of Francois (CCDF) C4
- Pre-Descemet corneal dystrophy (PDCD) C4

TGFB1 dystrophies
- Autosomal dominant; 5q31 (TGFB1)
- Suggests all of epithelial origin
- TGFB1 mutations impair protein secretion, folding, degradation, or interactions with other macromolecules leading to accumulation of deposits

Lattice corneal dystrophy (LCD)
- Also called: Biber-Haab-Dimmer
- Classic Lattice corneal dystrophy (LCD1), TGFB1 type (LCD), and variants
- Autosomal dominant; 5q31 (TGFB1)
- Beware of 2o trauma, 2o CA

Lattice corneal dystrophy, Gelsolin Type (LCD2)
- Also part of: Familial amyloidosis, Finish (FAF); Meretoja syndrome; Amyloidosis V; Familial amyloidotic polyneuropathy IV (FAP-IV)
- Autosomal dominant; 9q34 (Gelsolin GSN)
- Onset in third to fourth decade
Granular corneal dystrophy, type 1 or classic (GCD1)
- Also called: Corneal dystrophy Groenouw type 1
- Autosomal dominant: 5q31 (TGFB1)
- Glare & photophobia, frequent recurrent erosions

Granular corneal dystrophy, type 2 Granular-Lattice (GCD2)
- Also called: Combined granular-lattice corneal dystrophy; Avellino corneal dystrophy
- Autosomal dominant: 5q31 (TGFB1)
- Increased prevalence in Korea & Japan
- Genetic testing available through Avellino Lab USA

Prevalence of Granular Corneal Dystrophy
Type 1 (Avellino Corneal Dystrophy) in the Korean Population
- The prevalence of GCD has not yet been reported. Reports from several countries of the relative frequencies of granular corneal dystrophy type 1, GCD, and lattice dystrophy among "corneal dystrophy" patients show that GCD has the highest prevalence.

Test for gene mutation that causes corneal dystrophy now available in US
- The result is normal, the patient can proceed with LASIK as planned. If the results are not normal, we do not perform LASIK.

Table 5. Prevalence estimates

<table>
<thead>
<tr>
<th>Type</th>
<th>Prevalence estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCD1</td>
<td>1/3,000</td>
</tr>
<tr>
<td>GCD2</td>
<td>1/20,000</td>
</tr>
</tbody>
</table>

References:
- Women et al. 2003
- Alkane et al. 2006
- Chaiwarith et al. 2005
- Muster et al. 2002
- Stovar et al. 1999
- Muster et al. 2002
- Johnson et al. 2004
- Chaiwarith et al. 2005
- Muster et al. 2002
- Alkane et al. 2006
- Johnson et al. 2004

Obtained from: COB 1, corneal dystrophy of the Bowman layer type 1; GCD, granular corneal dystrophy; J, lattice corneal dystrophy; TGFB, transforming growth factor β-induced protein.

Anthony J. Alkane, MD, Baris Senmez, MD. Arch Ophthalmol. 2007;125:177-186
Macular corneal dystrophy (MCD)

Macular corneal dystrophy is one of the 3 major corneal dystrophies. The first signs are usually noticed in the first decade of life, and progress afterwards, with corneal opacities, thinning, and attacks of pain. MCD is thought to be caused by the lack or abnormal configuration of KS. Most cases are caused by mutations in the gene coding for carbohydrate sulfotransferase 6.


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**Macular corneal dystrophy (MCD)**

- Also called: Groenouw corneal dystrophy, type II; Fehr spotted dystrophy
- Autosomal recessive: 16q22; Carbohydrate sulfotransferase 6 (CHST6) => enzyme => KS solubility as metabolized
- Corneal thinning (early); dec in MPS => dec collagen spacing => thickening (late) after endothelium affected

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**FIGURE 1**


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**FIGURE 2**


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**FIGURE 3**

Alician blue staining abnl GAG

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**FIGURE 4**

Mucopolysaccharidosis syndromes

- Heterogenous group of rare systemic genetic disorders characterized by accumulation of GAGs in multiple organ systems
- Result from inherited abnormalities of specific lysosomal enzymes involved in degradation of GAGs
- GAGs accumulate intra- and extracellularly distorting cells and extracellular matrix leading to corneal clouding, among other ocular and non-ocular involvement

From Ashworth et al Eye 2006
(cornea opacification esp common in both MPS I* & VI*)

<table>
<thead>
<tr>
<th>MPS type</th>
<th>Enzyme defect</th>
<th>Inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPS I</td>
<td>( \text{\textendash} )</td>
<td>AR</td>
</tr>
<tr>
<td>MPS IIa</td>
<td>( \text{\textendash} )</td>
<td>AR</td>
</tr>
<tr>
<td>MPS IIb</td>
<td>( \text{\textendash} )</td>
<td>AR</td>
</tr>
<tr>
<td>MPS IIH</td>
<td>( \text{\textendash} )</td>
<td>AR</td>
</tr>
<tr>
<td>MPS III</td>
<td>( \text{\textendash} )</td>
<td>AR</td>
</tr>
<tr>
<td>MPS IIIA</td>
<td>( \text{\textendash} )</td>
<td>AR</td>
</tr>
<tr>
<td>MPS III</td>
<td>( \text{\textendash} )</td>
<td>AR</td>
</tr>
<tr>
<td>MPS IV</td>
<td>( \text{\textendash} )</td>
<td>AR</td>
</tr>
<tr>
<td>MPS V</td>
<td>( \text{\textendash} )</td>
<td>AR</td>
</tr>
<tr>
<td>MPS VI</td>
<td>( \text{\textendash} )</td>
<td>AR</td>
</tr>
</tbody>
</table>

Schnyder corneal dystrophy (SCD)

- Also called: Schnyder crystalline corneal dystrophy; Schnyder crystalline dystrophy sine crystals; hereditary crystalline stromal dystrophy of Schnyder; etc
- Autosomal dominant; type L-10 prenyltransferase (inclusion of 1 UBAIAD1)
- Decrease in vision/glow with aging; hyperlipoproteinemia

*** Only 50% show crystals
Differential Dx of corneal crystals

- Lecithin-cholesterol acyltransferase deficiency (LCAT) & fish eye disease (FED) are rare AR disorders causing anemia, renal insufficiency, atherosclerosis, & cornea opacities similar to non-cystalline SCD & CCDF
- Tangier Dz: AR leading to complete diffuse corneal clouding
- Cystinosis: AR inherited metabolic dz leading to lysosomal storage of cystine => kidney & thyroid dz & fine corneal stroma (including periphery/conjunctiva/TM/periph retina polychromatic crystals
- Also tyrosinemia; Bietti crystalline dystrophy; gold corneal crystals; various drugs; Gout; monoclonal gammopathy of unknown significance (MGUS)-multiple myeloma (corneal crystals are IgG)

Fleck corneal dystrophy (FCD)

- Also called: Francois-Neetens speckled corneal dystrophy
- Autosomal dominant: 2q35; Phosphatidylinositol-3-phosphate (phosphatidylinositol-3-kinase) type III (PIK3C3)
- Congenital, non-progressive
- "constipated keratocytes" at different levels of the stroma; complex lipids & GAGs in membrane-limited intracytoplasmic vesicles

Congenital stromal corneal dystrophy (CSCD)

- Also called: Congenital hereditary stromal dystrophy; congenital stromal dystrophy of the cornea
- Normal corneal thickness
- Autosomal dominant: 12q21.33 (Decodor-DCN)
- Moderate to severe vision loss
- Klintworth (2009) suggests “very rare” with only 4 families reported

Posterior amorphous corneal dystrophy (PACD)

- Also called: Posterior amorphous stromal dystrophy
- Autosomal dominant; with unknown gene
- Probably congenial, possibly slowly progressive
- Usually corneal thinning; flat Ks => hyperopia; endothelial guttata; iris & angle changes
Always consider masquerade diseases

"50 yo WF, asymptomatic except for "itchy-burnies"

Corneal changes phenotypic of PACD, but...

Only one eye involved

"nl corneal curvature & thickness

Only one patch of endo guta (in involved eye)

No iris, angle changes

Upon genetic testing of proband and 5 family members (sister, mother, two daughters, one son) no genetic "hits"

Bierwerth, Tong, Aldave, Edrington, Weissman, unpublished data, 2013

Central cloudy dystrophy of Francois (CCDF)

- Also called: Crocodile shagreen (degeneration), esp if peripheral
- Genetics not yet defined

Pre-Descemet corneal dystrophy (PDCD)

- Some families have been described but unknown genetics
- Asymptomatic
- ?accumulations of cholesterol sulfate

FIGURE 2B. Pre-Descemet corneal dystrophy punctate opacities anterior to Descemet membrane demarcated by inflammation and dhop tanglemen.

Descemet membrane (PLL) & Endothelial Dystrophies

- Fuchs endothelial corneal dystrophy (FECD) C1, C2, or C3
- Posterior polymorphous corneal dystrophy (PPCD) C1 or C2
- Congenital hereditary endothelial dystrophy 1 (CHED1) ?PPCD
- Congenital hereditary endothelial dystrophy 2 (CHED2) C1
- X-linked endothelial corneal dystrophy (XECD) C2
…linkage, association and familial segregation analyses support a role of only one gene in each corneal endothelial dystrophy:

**ZEB1 haploinsufficiency in PPCD3;27 mutations**
- Truncation = loss of function (deletion, decreased protein, improper cell localization)

**SLC4A11 in CHED2**
- COL8A2 in FECD (early onset)

In addition, insufficient evidence exists to consider the autosomal dominant form of CHED (CHED1) as distinct from PPCD…"
Posterior polymorphous corneal dystrophy (PPCD)

- Also called: Schlichting dystrophy
- Autosomal dominant but excl isolated cases: PPCD1 20p1.2-q11.2 (UK gene); PPCD3 10p11.2 (2-handed zinc-finger homeodomain transcription factor 8; ZEB1); 17q12
- May be related to endothelial decompensation & corneal edema. 2° glaucoma: YKC, YCE, abdominal hernia, maldevelopment corpus callosum
- Rarely vision changes but can =>PKP, possible slow progression
- May present unilaterally

*OVS 1989*

**Four Cases of Keratoconus and Posterior Polymorphous Corneal Dystrophy**

OVS 1989

**VSX1: A gene for posterior polymorphous dystrophy and keratoconus**

JAMA 2013

Exclusion of pathogenic promoter region variants and identification of novel nonsense mutations in the zinc finger E-box binding homebox 1 gene in posterior polymorphous corneal dystrophy

Am J Hum Genet 2013

POSTERIOR POLYMORPHOUS DYSTROPHY

*Am J Hum Genet 2013*
Congenital hereditary endothelial dystrophy 2 (CHED2)

- Also called: Maumenee corneal dystrophy
- Autosomal recessive: 20p13 (Solute carrier family 4, sodium borate transporter, member 11 SLC4A11)
- Children of consanguineous marriages (rare in USA, common in other countries)
- CHED1 not real? prev reptd families may be PPCD?

Aldave et al Clin Genet 2013

Molecular bases of corneal endothelial dystrophies
Thore Schmedt e, Maria Grazia Silva, Alireza Ziaei, Ali A. Jarkaman
Experimental Eye Research 95 (2012) 24–34

3.1. Genetics of CHED1
Genetic study of a large British family with autosomal dominant and fully penetrant inheritance of CHED1 served as the basis for identifying the chromosomal locus (Toma et al., 1995). Two-point linkage analysis of this seven-generation family revealed significant linkage to chromosome 20. The identified locus was within the 30 cM region of the same chromosome limited to posterior polymorphous corneal dystrophy (PPCD) (Heon et al., 1995; Toma et al., 1995). The linkage of both disorders to overlapping regions in chromosome 20 has sparked a debate that the two disorders are allelic variants.

Aldave et al Clin Genet 2013
X-linked endothelial corneal dystrophy (XECD)

- X-chromosomal dominant; Xq25
- Congenital onset; males often blurred vision; females asymptomatic
- Variable corneal clouding with “moon-crater” endothelial changes & secondary sub-epithelial band keratopathy

The question of keratoconus…

- Keratoconus (KC)
- Pellucid marginal degeneration (PMD)
- Keratoglobus (KG)

Comparison of characteristics of corneal dystrophies & degenerations (from CLEK Study)

<table>
<thead>
<tr>
<th>DEGENERATIONS</th>
<th>DYSTROPHIES</th>
<th>KERATOCONUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNILATERAL</td>
<td>BILATERAL</td>
<td>MOSTLY BILATERAL</td>
</tr>
<tr>
<td>ASYMMETRIC</td>
<td>SYMMETRIC</td>
<td>ASYMMETRIC</td>
</tr>
<tr>
<td>PERIPHERAL</td>
<td>AXIAL</td>
<td>AXIAL</td>
</tr>
<tr>
<td>- INHERITANCE</td>
<td>+ INHERITANCE</td>
<td>10-20% INHERITED</td>
</tr>
<tr>
<td>LATE ONSET</td>
<td>EARLY ONSET</td>
<td>ONSET @ PUBERTY</td>
</tr>
<tr>
<td>SECONDARY DISEASE</td>
<td>PRIMARY DISEASE</td>
<td>PRIMARY DISEASE</td>
</tr>
<tr>
<td>SOMETIMES INFLAMMATORY</td>
<td>NON-INFLAMMATORY</td>
<td>PERHAPS INFLAMMATORY</td>
</tr>
</tbody>
</table>

After Zadnik & Edrington, 2000

Etiology of Keratoconus

- UNKNOWN, but reports of associations with a large number of diseases (e.g. Down’s, RP, EHLERS-DANLOS SYNDROME ETC); none confirmed at CLEK, but Down’s NOT in Study
- GENETICS: 14% CLEK Pt’s REPORTED A CLOSE RELATIVE WITH KC DX @ BASELINE & 18% yr 7
- EYE RUBBING: MANY HAVE OBSERVED AN ASSOCIATION, but has not been confirmed
- ATOPY: SIMILARLY, MANY HAVE OBSERVED AN ASSOCIATION (ESP VERNAL) BUT NO CONFIRMATION. 53% CLEK Pt’s REPORTED ATOPIC HX @ BASELINE
- RIGID CONTACT LENS WEAR; ALSO NOT CONFIRMED
Familial KC studies => a high degree of genetic heterogeneity, & multiple susceptible-disease loci, suggests that mutations in several different genes, involved in related pathways, acting on common targets, are responsible for disease phenotype

Bisceglia et al IVOS 50(3)2009

Reduced corneal protein w/ incr degradative enzymes & dese inhibition, incr inflammatory markers => complex disorder with a mix of both genetic and non genetic factors

McMahon GSL1/2009 (rept of Sorbara CLS 3/2009)

Variation in the Lysyl Oxidase (LOX) Gene Is Associated with Keratocan in Family-Based and Case-Control Studies


• Central corneal thickness (CCT) is associated with eye conditions including keratoconus and glaucoma. We performed a meta-analysis on >20,000 individuals in European and Asian populations that identified 16 new loci associated with CCT at genome-wide significance (P < 5 × 10(-8)). We further showed that 2 CCT-associated loci, FOXO1 and FNDC3B, conferred relatively large risks for keratoconus in 2 cohorts with 374 cases and 8,085 controls (rs2721051 near FOXO1 had odds ratio (OR) = 1.82, 95% confidence interval (CI) = 1.4-1.88, P = 2.7 × 10(-9)), and rs4984355 in FNDC3B had OR = 1.47, 95% CI = 1.29-1.68, P = 4.3 × 10(-9)). FNDC3B was also associated with primary open-angle glaucoma (P = 5.6 × 10(-4); tested in 3 cohorts with 2,379 cases and 7,589 controls). Further analyses implicate the collagen and extracellular matrix pathways in the regulation of CCT

Evaluating the Association Between Keratoconus and the Corneal Thickness Genes in an Independent Australian Population

Suzanne Schepens et al. Invest Ophthalmol Vis Sci 2013 Vol 54 No 11

• Genetic Association of COL5A1 Variants in Keratoconus Patients Suggests a Complex Connection between Corneal Thinning and Keratoconus

Nataraj IL, V, Yelena Ylikahri et al. Am J Hum Genet 2013 Vol 93 No 4

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Nataraj IL, Yelena Ylikahri et al. Am J Hum Genet 2013 Vol 93 No 4

• Nielsen et al Acta Ophthalmologica 2013


Reduced corneal protein w/ incr degradative enzymes & dese inhibition, incr inflammatory markers => complex disorder with a mix of both genetic and non genetic factors

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Reduced corneal protein w/ incr degradative enzymes & dese inhibition, incr inflammatory markers => complex disorder with a mix of both genetic and non genetic factors

McMahon GSL1/2009 (rept of Sorbara CLS 3/2009)

Variation in the Lysyl Oxidase (LOX) Gene Is Associated with Keratocan in Family-Based and Case-Control Studies


Evaluating the Association Between Keratoconus and the Corneal Thickness Genes in an Independent Australian Population

Suzanne Schepens et al. Invest Ophthalmol Vis Sci 2013 Vol 54 No 11

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Summary of Assessment & Treatment

- Anterior dystrophies likely to cause recurrent epithelial erosions & decreased vision through irregular corneal astigmatism &/or central opacification.
- Stromal dystrophies likely to eventually decrease vision through opacification; advanced MCD additionally can damage endothelium & lead to increased corneal thickness, epithelial edema, & sub-epithelial scarring.
- Endothelial dystrophies can damage the endothelium & lead to increased corneal thickness, epithelial edema, and sub-epithelial scarring.
- Observation: if minimal symptoms or loss of function.
- Rigid contact lenses can improve vision if corneal irregularity occurs; BSCLs may be particularly protective in GDLD.
- AFTs: lubricants, gels, & hyperosmotics.
- Antibiotics if erosions.
- Corneal transplants (PKP, DSEK, DALK) may be needed in several but not all CDs.