The Latest In Corneal Degenerations and Dystrophies: An OD and MD Perspective.

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CORNEAL DYSTROPHIES
Corneal Dystrophies

• Group of corneal diseases that are:
  – genetically determined and
  – have been traditionally classified with respect to the corneal layer affected

• Emerging molecular science:
  – is redefining traditional thought on the dystrophies and
  – offering potential avenues for therapeutic intervention.
CORNEAL DEGENERATION

• Non-familial, late onset
• Asymmetric, unilateral, central or peripheral
• Changes to the tissue caused by inflammation, age, or systemic disease.
• Characterized by a deposition of material, a thinning of tissue, or vascularization
Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD)

- Primary features of this “dystrophy” are:
  - abnormal corneal epithelial regeneration and maturation,
  - abnormal basement membrane
- Often considered the most common dystrophy, but may actually be an age-related degeneration.
  - large number of patients with this condition,
  - increasing prevalence with increasing age, and
  - its late onset support a degeneration vs. dystrophy.
Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD)

- Not all patients are symptomatic (range 10-69%)
- Most common symptom is mild FB sensation which is worse in dry weather, wind and air conditioning
- Blurred vision from irregular astigmatism or rapid TBUT
- Pain is usually secondary to a RCE (recurrent corneal erosion) in approx 10%
Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD)

• Easy to overlook:
  – typically bilateral though often asymmetric,
  – females>males,
  – often first diagnosed b/w ages of 40-70
Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD)

• Most common findings are:
  – chalky patches,
  – intraepithelial microcysts, and
  – fine lines (or any combination) in the central 2/3rd of cornea
Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD)

• Often referred to as:
  – maps,
  – dots or
  – fingerprints
EBMD-Negative Staining
Epithelial (Anterior) Basement Membrane Dystrophy (EBMD or ABMD): Treatment

- Typically directed towards preventing RCE
- If RCE’s develop:
  - awake with painful eye that improves as day wears on
  - chalky patches/dots in lower 2/3rd of cornea
RCE: Treatment

• Initial treatment includes:
  – use of hyperosmotic ointment at bedtime,
  – bandage contact lens and
  – lubrication.
Recurrent Corneal Erosion: Treatment

- If severe enough to cause vision loss or repeated episodes:
  - oral doxycycline with/without topical corticosteroid
    - Doxy 50 mg bid and FML tid for 4-8 weeks
    - both meds inhibit key metalloproteinases important in disease pathogenesis
    - Azasite (topical azithromycin)
  - debridement,
  - stromal puncture, or
  - PTK
- Latest development: amniotic membrane transplant e.g. Prokera
Stromal Puncture
CORNEAL DEBRIDEMENT

- Soften epithelium
- 1-2 gtt topical anesthetic
- q 15-30 seconds for 2-3 minutes
- Use cotton swab, spatula, spud
- or jewelers forceps
- Remove flaps by pulling edges toward center
- Don’t pull directly up or out
- Remove flaps down to tight, firm edges.
- Tx abrasion (>50-100%)
  – Recurrence Rate 18%
Amniotic Membrane Transplant

- Amniotic membrane is a biologic tissue with:
  - antiangiogenic,
  - antiscarring,
  - antimicrobial, and
  - anti-inflammatory properties that promotes healing of the ocular surface

- Amniotic membrane grafts have been used for a variety of ocular conditions including:
  - Corneal burns
  - Neurotrophic ulcers
  - Stem cell damage
  - Persistent epithelial defects
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ProKera

ProKera Clear:

• has a trephinated 6mm aperture allowing some visual potential

• best suited for chronic inflammatory cases with the limbus being the targeted area of biologic boost and healing e.g. KCS
ProKera

- ProKera
- ProKera Slim:
  - ComfortRing™ Technology was designed with a slim profile that contours to the ocular surface, moves with the eye, and maximizes amniotic membrane contact with the cornea, limbus, and limbal stem cells, providing clinical benefits and maximizing patient comfort
- ProKera Plus:
  - incorporates multiple layers of amniotic membrane that make it suitable for therapeutic applications requiring longer biologic action and durability on the ocular surface. It is recommended for use in severe indications such as chemical burns, Stevens Johnson Syndrome, and severe corneal ulcers.
AmbioDisk

• AmbioDisk™ Amniotic Membrane from IOP Ophthalmics

• AmbioDisk™ is a 4th generation amniotic membrane (AM) technology - a sutureless, overlay AM disk for the office-based or surgical treatment of the ocular surface.

• Conventional Uses
  – Non-Healing Epithelial Defects
  – Neurotrophic Ulcerations
  – Corneal Erosions
  – Acute Chemical/Thermal Burns
  – Post-Infectious Keratitis (herpetic, vernal, bacterial)
Diamond Burr Polishing

• Removes abnormal basement membrane
• May also promote scarring
RCE and LASIK

• Patients who have a history of EBMD may not be ideal candidates for LASIK and should be carefully screened for prior to surgery.
Macular (Groenouw Type II)

• Grayish opacities in the superficial stroma

• With age:
  – extension into deeper stromal layers
  – intervening stroma becomes hazy
  – progressive loss of vision,
  – photophobia and ocular discomfort.
Macular Corneal Dystrophy

• Surgical treatment usually required by 2nd or 3rd decade of life.
  – PK
  – DALK not indicated as may have damage to Descemets
Granular Dystrophy: (Groenouw Type I)

• Discrete white granular opacities in central anterior corneal stroma.

• With age:
  – increasing number, density, size and depth of opacities
  – intervening stroma and peripheral cornea remain clear
Granular Dystrophy: (Groenouw Type I)

- RCE are common with associated pain.
- Decreased vision results from subepithelial scarring or dense stromal deposits.
- Surgical treatment includes penetrating keratoplasty or DALK (Deep Anterior Lamellar Keratoplasty).
PTK Treatment for GRANULAR
Lattice (Type I)

- Characteristic clinical appearance includes:
  - linear,
  - refractile,
  - branching deposits within the anterior stroma.
Lattice (Type I)

• The central cornea is progressively opacified resulting in scarring and deterioration of vision while the periphery remains clear.
• RCE’s often present.
• May require surgical intervention with diminished vision.
  – PK
  – DALK
Central Crystalline Dystrophy of Schnyder

- Opacities consist of:
  - small, needle-shaped refractile crystals that are either white or polychromatic
  - may extend into deeper stroma but epithelium remains normal.
Central Crystalline Dystrophy of Schnyder

• Vision is typically mildly affected though there may be associated systemic complications
  – systemic cholesterol should be evaluated
SURGICAL TREATMENTS: PK AND DALK
PK Surgery: Full Thickness Surgery

Central trephine cut made

Smooth Surface with only endothelial disease

Recipient tissue removed

Full thickness block of tissue removed just to get to the endothelium

Donor tissue sutured into recipient

Sutures create an irregular surface with astigmatism and blurring
Corneal Transplant
Penetrating Keratoplasty
Deep Anterior Lamellar Keratoplasty (DALK)

• Removal of all tissue EXCEPT Descemet’s and endothelium
  – Most common rejection seen in PK is endothelial rejection observed in approx 20% of low-risk cases
  – Repeated PK’s increase chance that the graft will be rejected
  – DALK can avoid risk of endothelial rejection with similar optical results as PK
Deep Anterior Lamellar Keratoplasty (DALK)

• Indicated for patients with
  – Keratoconus
  – Corneal scars
  – Corneal stromal dystrophies
  – Basically any pathology that spares the endothelium

• Contraindicated
  – Bullous keratopathy
  – Fuch’s
Deep Anterior Lamellar Keratoplasty (DALK)

• Advantages over PK:
  – No “open sky” during surgery so lesser chance of expulsive hemorrhage
  – Much decreased rejection potential because patient keeps their own endothelium
    • Stromal rejection is rare and easily treated
  – Low to no rejection risk so steroids are tapered more quickly (usually twice as fast)
  – Heals faster as steroids tapered sooner allowing sutures to be removed earlier and more rapid visual stabilization (apprx 6 months)
  – More tectonic stability as patient keeps own endo
Normal Changes to the Endothelium

• Descemet’s layer thickens from 3-17u
• There is a decrease in the # of endothelial cells
  – from 3500 cells/mm2 to 1200
  – this single layer spreads out: lacks mitosis
• High density mitochondria : 90% pump
• Lenses produce reversible polymegathism
Abnormal Changes to the Endothelium

- Endothelial cells become more irregular
- Cells secrete collagen towards Descemet’s causing multilamination = guttata
- This breaks down the barrier function and results in stromal and epithelial edema
Fuch’s Dystrophy

• Endothelium:
  – acts as both a barrier and pump function
  – responsible for maintaining corneal transparency by reducing corneal hydration

• Fuch’s:
  – occurs bilaterally,
  – AD inheritance,
  – females 3x more likely to develop condition
Fuch’s Dystrophy: Guttata

• Corneal guttata
  – excessive accumulation of abnormal endo secretions is associated with the disease process
  – usually first noticed in the central cornea in the patients 30’s and 40’s
  – corneal physiology is affected adversely by interference with pump action
  – guttata appear as small refractile “drops” on the corneal endo
Fuch’s Dystrophy: Guttata

- closer inspection with specular reflection reveals an “orange peel-like” dimpling of the endo
- with the decreased pump function, the overlying stroma becomes edematous
- long standing corneal edema may result in corneal scarring and RCE
Fuch’s Dystrophy: Guttata
Normal Endothelial Mosaic
Fuch’s Dystrophy Endothelial Cell Count: 545 cells/mm
Fuch’s Dystrophy

• Patient symptoms vary with degree of guttata and compromised pump function

• Moderate guttata
  – may affect visual function
  – may result in light scatter (haloes)
  – typically noticed upon waking

• With increased disruption to the pump:
  – vision decreases
  – potential development of bullous keratopathy
Stages of Fuch’s Dystrophy

Healthy endo: Cornea Thin and clear
Endo dropout: Cornea swells, mild vision loss
Severe swelling, blisters on surface, Va drops, pain
Chronic swelling, surface scarring
Fuch’s: Bullous Keratopathy
Fuch’s Dystrophy: Treatment

- Treatment in early stages:
  - usually palliative with the goal of improving comfort and function
  - hyperosmotics at bedtime (e.g. muro 128 ointment) may help reduce epithelial corneal edema in the morning
  - bandage CL can be used in the presence of bullous keratopathy
Fuch’s Dystrophy: Treatment

• When visual function deteriorates to the point patient is unduly affected, surgical options are considered including:
  – penetrating keratoplasty (PK)
  – DLEK surgery (deep lamellar endothelial keratoplasty) or
  – newer DSAEK (Descemet Stripping Automated Endothelial Keratoplasty)
  – Latest DMEK (Descemet Membrane Endothelial Keratoplasty)

• Fuch’s is leading reason for PK’s in developed countries
DLEK

• Recipient cornea is stripped of its Descemet’s membrane, endothelium and posterior stroma

• There is transplantation of the posterior stroma and endothelium of the donor cornea through a small incision

• Results in improved:
  – endothelial function,
  – corneal clarity and
  – restoring useful vision.
DLEK

• Procedure has:
  – minimal affect on refraction,
  – provides rapid visual recovery and
  – maintains structural integrity of the cornea.
DLEK Surgery: Split Thickness Surgery to replace only the diseased tissue

Recipient tissue removed

Donor tissue placed into recipient

Scleral incision, deep corneal pocket, and endothelium trephined with Terry Trephine or cut with Cindy Scissors

Just endothelium on posterior stromal disc removed from pocket

Endothelium replaced with no sutures, supported by air bubble in anterior chamber.
Surface remains smooth with no astigmatism
DSAEK

• DLEK refined to DSEK and now DSAEK:
  – compared to DLEK only Descement’s membrane and endothelium is stripped and implanted in DSEK/DSAEK.

• DSEK vs. DSAEK:
  – DSEK has the donor lamellar disc created manually
  – DSAEK facilitated by the use of a blade microkeratome which cuts the donor interface with the corneal button mounted in an artificial anterior chamber
DMEK (Descement Membrane Endothelial Keratoplasty)

• Recipient cornea is stripped of its Descemets membrane and endothelium
  – implanted tissue consists of only the donors Descemets and endothelium
  – in comparison, DSAEK has implanted tissue consisting of posterior stroma, Descemets and endothelium
  – implantation of similar tissue “components” without additional posterior stroma has resulted improved visual function and recovery
DMEK (Descememt Membrane Endothelial Keratoplasty)

• Compared to DSAEK, DMEK may have better clinical potential with 75% patients obtaining 20/25 or better within 1-3 months
  – DSAEK 38-100% patients get 20/40 or better after 6 months
  – PK has 40% patients 20/40 or better after 1 year
• Visual recovering quicker with DMEK with many patients having good vision 1 day post op and best visual recovering by 1-3 months
  – DSAEK slower visual recovery and PK the slowest
• Additionally, may have reduced endothelial cell lost post surgery
CORNEAL DEGENERATIONS
Keratoconus

- Ectatic corneal dystrophy:
  - tends to be bilateral,
  - maybe asymmetric, and
  - generally manifests in the 2nd or 3rd decade.

- Likely a multigenic disease:
  - complex mode of inheritance (sporadic, AD and AR reported) and
  - manifestation likely involving environmental factors.
Keratoconus

• Proposed etiology:
  – increased enzyme activities and decreased levels of enzyme inhibitors result in toxic by-products
    • destruction of the normal corneal matrix resulting in thinning and scarring.
Keratoconus: Diagnosis

• SLE findings include:
  – central corneal thinning,
  – Fleischer’s ring,
  – scarring at the level of Bowman’s layer or anterior stroma, and
  – vertical striae (Vogt’s lines).

• Common refractive or topographic effects include:
  – irregular astigmatism and
  – poor best-corrected visual acuity with specs
Keratoconus: Diagnosis

• Keratoconus tends to progress over 7-8 years and then stabilizes

• Severity is variable b/w patients and is often asymmetric

• Thinning can be extensive:
  – resulting rupture in Descemet’s membrane
    • triggers a sudden influx of aqueous into the cornea (Hydrops)
Keratoconus
Central “Nipple” Keratoconus OU
Keratoconus
Keratoconus-Fleischer’s Ring
Keratoconus-Corneal Thinning

- Central Cornea
- Mid-Peripheral Cornea
Keratoconus-Vertical Striae
Keratoconus Treatment

• DALK
• Intacs:
  – Arclike PMMA segments designed to be surgically inserted into deep corneal stroma to flatten the central cornea
  – Indicated for mild to moderate keratoconus with a clear optical zone and contact lens intolerant
  – May delay or eliminate the need for keratoplasty although significant refractive error may remain
  – Refractive stability has been demonstrated up to 5 years post-op in several studies
  – Does have FDA approval for the treatment of keratoconus in the US
TREATMENT OF KERATOCONUS WITH INTACS

• The goal is to improve topography:
  – lift the ectasia to reduce irregular astigmatism
  – flatten the soft tissue to reduce the SE

• These changes should improve the UCVA and increase contact lens or spectacle success.

• The intention is not to cure the disease, but rather to delay need for a corneal transplant.
INTACS FOR KCN
The Future is Here!

• Collagen crosslinking of riboflavin and UVA-light
  – Thought to strengthen the corneal collagen matrix and stabilize the cornea
  – Stops the progression of the condition with the potential of some reversal

• Might become the standard therapy for progressive keratoconus
C3-R Mechanism

UVA 370nm

Riboflavin .1%

Corneal Collagen Crosslinking

Biomechanical Stiffness

Stability
Collagen Cross Linking

• Clinical outcomes seem to follow a reproducible time course after treatment:
  – visual acuity and corneal steepness worsen over the first month
  – resolution to baseline by 3 months with continued improvement thereafter

• Several studies have evaluated the use of CXL in the pediatric population (the most likely group to require a transplant)
  – recommended as a treatment to stabilize the cornea and to limit the progression of the condition
Keratoconus-Hydrops

• Symptoms include:
  – sudden decrease in best corrected vision,
  – foreign body sensation or pain
• Signs include:
  – conjunctival hyperemia/redness,
  – prominent central or inferior corneal edema and
  – clouding along with conjunctival hyperemia
• Tends to be self-limiting
  – in 8-10 weeks the endothelial cells regenerate across
    the ruptured Descemet’s membrane
Keratoconus-Hydrops Treatment

• May use hyperosmotics and antibiotics to prevent secondary infections
• PK’s are indicated if resulting scarring limits correction of vision
Hydrops
Keratoconus - Scarring
Penetrating Keratoplasty
Pellucid Marginal Degeneration

• Bilateral corneal disorder hallmarked by a thinning of the inferior, peripheral cornea
• Corneal thinning begins apprx 1-2 mm above the inferior limbus and is separated by an area of uninvolved, normal cornea between the thinned zone and the limbus.
• Acute hydrops maybe seen in the area of inferior thinning
• Commonly manifests b/w ages of 20-40 with no apparent hereditary transmission and equal gender distribution
Pellucid Marginal Corneal Degeneration
Pellucid Marginal Degeneration
Pellucid Marginal Degeneration

- Subjective symptoms are visual secondary to a dramatic increase in against-the-rule astigmatism.
- Area of thinning is free of vascularization or lipid infiltration which differentiates this condition from Terriens marginal degeneration of Mooren’s ulceration.
- Corneal mapping demonstrates inferior mid-peripheral zones of corneal steepening at 4-8 o’clock producing “butterfly wing-like” pattern which is diagnostic.
Pellucid Marginal Degeneration
Pellucid Marginal Degeneration

- Management includes specs, CL and surgery
- Spectacle correction is often satisfactory in the early stages due to the minimal degree of induced astigmatism
- In more advanced stages, CL are the suggested mode of treatment
- CL management can be difficult because of the high degree of ATR and asymmetrical astigmatism
- Surgical intervention involves PK, a kidney-shaped PK or an inferior lamellar patch graft.
Pellucid Marginal Degeneration
Terrien’s Marginal Degeneration

- Rare, bilateral, asymmetric disease of unknown etiology.
- Peripheral cornea, predominantly superiorly, undergoes lipid deposition, vascularization, opacification and stromal thinning leading to gutter formation, ectasia and eventual corneal perforation. Epithelium remains intact.
Terrien’s Marginal Degeneration

• May occur at any age, though typically occurs in middle-aged males.
• The eyes are typically not injected and there is little if any pain, photophobia or anterior chamber reaction
• Increased regular and irregular astigmatism, which may produce visual changes though patients are usually asymptomatic.
Terrien’s Marginal Degeneration

- Degeneration often progresses in a circumferential pattern
- Perforation is usually only a complication of trauma.
- Etiology poorly understood though chronic inflammatory skin conditions and autoimmune mechanisms maybe possible etiology factors.
Terrien’s Marginal Degeneration
Terrien’s Management

• As most patients are asymptomatic, management is largely supportive.
• May suffer from periodic episodes of red, irritated eyes which are quickly resolved with steroids (Pred forte, Lotemax)
• Early refractive treatment includes:
  – spectacles (polycarbonate),
  – CL an option though difficult to fit due to irregular astigmatism (RGP over piggyback),
  – and when vision uncorrectable surgical intervention includes PK.
Terrien’s Management

• Need to make sure differentiate:
  – peripheral corneal melt secondary to collagen vascular disease,
  – Mooren’s ulceration,
  – pellucid marginal degeneration,
  – dellen, etc.
Mooren’s Ulcer

• A painful, relentless, chronic ulcerative keratitis that begins peripherally and progresses circumferentially and centrally.

• It is idiopathic; occurring in absence of any diagnosable systemic disorder that could be responsible for the progressive destruction of the cornea (e.g. peripheral corneal melt secondary to RA).
Mooren’s Ulcer

- Mooren’s divided into 3 distinct varieties:
  - Unilateral Mooren’s: painful progressive corneal ulceration in elderly
  - Bilateral Aggressive Mooren’s Ulcer: occurs in younger Px, progresses circumferentially than centrally in the cornea and
  - Bilateral Indolent Mooren’s Ulceration: occurs in middle-aged Px presenting with progressive peripheral corneal guttering in both eyes, with little inflammatory response.
Mooren’s

• Pathophysiological mechanism remains unknown but there is evidence suggesting an autoimmune process.
• Px typically present with redness, tearing, photophobia, but pain is the most outstanding feature. The pain is often incapacitating and may be out of proportion to the inflammation.
• Maybe visual disruption secondary to associated iritis, central corneal involvement, irregular astigmatism due to peripheral corneal thinning.
Mooren’s Ulcer
Mooren’s Ulcer
Mooren’s: Management

• Initial therapy includes intensive topical steroid Tx: Pred Forte hourly is association with cycloplegics (e.g. Homatropine 5%) and topical antibiotics (moxifloxacin).

• Pulse oral therapy (Prednisone 60-100 mg daily) can be considered when topical therapy ineffective after 7-10 days.

• If ulcer continues to progress, conjunctival resection should be performed.

• For those Px that continue to progress, immunosuppressive chemotherapy is required to halt the progression.

• After active ulceration halted, PK maybe performed.