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.

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.

- 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

Recurrent Corneal Erosion: Treatment
- If severe enough to cause vision loss or repeated episodes:
  - oral doxycycline with/without topical corticosteroid
    - Day 1: 200 mg bid and FML tid for 6 weeks
  - both meds initial key metalloproteinases important in disease pathogenesis
    - Amniotic membrane transplant
  - debridement,
  - stromal puncture, or
  - PTE
  - Latest development: amniotic membrane transplant
    - e.g. Prokera

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 hypersosmotic ointment at bedtime,
  - bandage contact lens and
  - lubrication.

Stromal Puncture

Amniotic Membrane Transplant
- Amniotic membrane is a biologic tissue with:
  - antitumor, antiscarring, antimicrobial, and anti-inflammatory properties that promote healing of the ocular surface
- Amniotic membrane grafts have been used for a variety of ocular conditions including:
  - Corneal burns
  - Neurotrophic ulcers
  - Sten cell damage
  - Recurrent epithelial defects

Amniotic Membrane Transplant
- Traditionally, amniotic membrane grafts had to be sutured
  - With the advent of tissue adhesives, amniotic transplants can now be sutureless
  - Prokera was approved by the FDA in 2003 as a Class II medical device which has a polycarbonate ring which holds a cryopreserved amniotic membrane
  - Prokera is indicated in the treatment of corneal erosions, neurotrophic corneas, recalcitrant corneal inflammation, acute corneal surface burns, acute Stevens Johnson syndrome, and descemetoceles.

Corneal Debridement
- Soften epithelium
  - 1-2 gtt topical anesthetic
    - 30-30 seconds for 2-3 minutes
  - Use cotton swab, spatula, spud or jeweler forceps
  - Remove flaps by pulling edges toward center
  - Don’t pull directly up or out
  - Remove flaps down to tight, firm edges
  - Te abrasion (>150-100%) = Recurrence rate 10%

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

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).

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.

Macular Corneal Dystrophy

- Surgical treatment usually required by 2nd or 3rd decade of life.
  - PK
  - DALK not indicated as may have damage to Descemets

PTK Treatment for GRANULAR

- 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).

Granular Dystrophy:

- 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

Lattice (Type I)

- Characteristic clinical appearance includes:
  - linear
  - refractile
  - branching deposits within the anterior stroma

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

Penetrating Keratoplasty

PK Surgery: Full Thickness Surgery

Recipient tissue removed

Donor tissue sutured into recipient

Smooth surface with only endothelial disease

Central trephine cut made

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 (approx. 6 months)
  – More tectonic stability as patient keeps own endothelium

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

Abnormal Changes to the Endothelium

• Endothelial cells become more irregular
• Cells secrete collagen towards Descemet’s causing multi-filamentation – guttata
• This breaks down the barrier function and results in stromal and epithelial edema

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
• High density mitochondria - 90% pump
• Lenses produce reversible polymegathism

Abnormal Changes to the Endothelium

• Indicated for patients with
  – Bullous keratopathy
  – Fuch’s
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

- 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

Fuch’s: 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 Dystrophy Endothelial Cell Count: 545 cells/mm

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: 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

DLEK

- Procedure has:
  - minimal affect on refraction,
  - provides rapid visual recovery and
  - maintains structural integrity of the cornea.

DMEK (Descemet Membrane Endothelial Keratoplasty)

- Recipient cornea is stripped of its Descemet’s membrane and endothelium
  - implanted tissue consists of only the donors Descemet and endothelium
  - in comparison, DSAEK has implanted tissue consisting of posterior stroma, Descemet and endothelium
  - implantation of similar tissue “components” without additional posterior stroma has resulted improved visual function and recovery

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 Surgery: Split Thickness Surgery to replace only the diseased tissue

- Procedure: Rimmer technique
- Donor tissue replaced with no sutures, supported by air bubble in anterior chamber.
  - Surface remains smooth with no astigmatism

DMEK (Descemet 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 40-70% 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

DLEK

- Recipient cornea is stripped of its Descemet’s membrane and endothelium
- 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.

DSAEEK

- DLEK refined to DSEK and now DSAEK:
  - compared to DLEK only Descemet’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

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: 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: 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

- 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-Vertical Striae

INTACS FOR KCN

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 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

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

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

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.

C3-R Mechanism

- UVA 370nm
- Riboflavin .1%
- Corneal Collagen Crosslinking
- Biomechanical Stiffness
- Stability

Keratoconus-Hydrops Treatment

- May use hyperosmotics and antibiotics to prevent secondary infections
- PK’s are indicated if resulting scarring limits correction of vision
### Hydrops

**Bilateral corneal disorder hallmarked by a thinning of the inferior, peripheral cornea**

- Corneal thinning begins approx 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 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 Terriers 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

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### Penetrating Keratoplasty

- 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.

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**Keratoconus-Scarring**

**Pellucid Marginal Degeneration**

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**Pellucid Marginal Degeneration**
Pellucid Marginal Degeneration

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 Management

- Need to make sure differentiate:
  - peripheral corneal melt secondary to collagen vascular disease,
  - Mooren’s ulceration,
  - pellucid marginal degeneration,
  - allen, 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.

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 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.
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: 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.