MANAGEMENT OF CORNEAL DISEASE AND CATARACT

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I would like to disclose the following financial interests or relationships:

- Alcon Laboratories
- Bausch & Lomb
- Kala Corporation
- Mati Therapeutics
- RPS
- Senju Pharmaceuticals
- TearLab
- TearScience
- Wavetec Vision Systems
Quality of vision starts with a healthy ocular surface.

- Tear film: most important refracting surface.
- OSD is most common cause of visual loss in cataract surgery.
WHAT’S IN A TEAR

- A complex mixture of proteins, mucins, oils, and electrolytes
- Antimicrobial proteins: lysozyme, lactoferrin
- Growth factors and suppressors of inflammation: EGF, IL-1RA
- Soluble mucins 1, 4 and 5AC
- Polar and non-polar oils
- Electrolytes for proper osmolarity
- All are to important for homeostasis of the tear film

Image from *Dry Eye and Ocular Surface Disorders*, 2004
TEARS IN CHRONIC DRY EYE

- Lesser concentrations of many proteins
  - e.g. antimicrobial proteins
- Growth Factor concentrations decrease
- Cytokine balance shifted, promotes inflammation
- Soluble mucins 5AC decreased
  - Due to loss of goblet cells
  - Impacts viscosity of the tear film
- Activated proteases
  - Degrade extracellular matrix and tight junctions
STRUCTURE OF THE LIPID LAYER

Two-Phase Lipid Layer Model contains both hydrophobic and hydrophilic groups; interacts with aqueous -mucin layer

HC-Hydrocarbon
WE- Wax Ester
CE-Cholesterol Ester
TG- Triglyceride
F-Free Fatty Acid
C-Cerebroside
P-Phospholipid

NORMAL MEIBOMIAN GLANDS

Orifice of each gland expresses clear lipid
THERE ARE TWO MAIN SUBTYPES OF DRY EYE

DRY EYE

Effect of the Environment
- Milieu Intérieur
  - Low blink rate behavior, VTU, microscopy
  - Wide lid aperture gaze position
  - Aging
  - Low androgen pool
  - Systemic Drugs: antihistamines, beta-blockers, antispasmodics, diuretics, and some psychotropic drugs

- Milieu Extérieur
  - Low relative humidity
  - High wind velocity
  -Occupational environment

Aqueous-deficient
- Sjogren Syndrome Dry Eye
  - Primary
  - Non-Sjogren Dry Eye
    - Lacrimal Deficiency
    - Lacrimal Gland Duct Obstruction
    - Reflex Block
    - Systemic Drugs

Evaporative
- Intrinsic
  - Melbomian Oil Deficiency
  - Disorders of Lid Aperture
    - Low Blink Rate
    - Drug Action Accutane
  - Vitamin A Deficiency

- Extrinsic
  - Topical Drugs Preservatives
  - Contact Lens Wear
  - Ocular Surface Disease eg, Allergy
2007 Dry Eye WorkShop (DEWS) REPORT:

- Documented the expanding role of MGD in dry eye
  - “MGD is a condition of meibomian gland obstruction and is the most common cause of evaporative dry eye.”

MGD may be the leading cause of dry eye syndrome throughout the world

Aqueous and lipid deficient dry eye may not be distinguishable: Low Schirmer score and thin-low lipid layer thicknesses coexist

MGD found in 39% of randomly selected apparently healthy patients

86% of patients with a classified EDE subtype demonstrated signs of MGD
Pure ADDE subtype represented the smallest percentage of patients (~10%)
MEIBOMIAN GLAND DYSFUNCTION
PATHOPHYSIOLOGY

- Caused by terminal duct obstruction with thickened opaque meibum
- Obstruction due to hyperkeratinization of the ductal epithelium and increased meibum viscosity
- Influenced by endogenous factors, such as age, sex, and hormonal disturbances, as well as by exogenous factors such as topical medication
MEIBOMIAN GLAND DYSFUNCTION
PATHOPHYSIOLOGY

- Obstruction may lead to intraglandular cystic dilatation, gland dropout, and decreased secretion

- The consequence of MGD
  - increased evaporation,
  - increased hyperosmolarity
  - instability of the tear film
  - evaporative dry eye
  - ocular surface inflammation and damage
OCULAR SURFACE DISEASE IN CATARACT SURGERY

- **Preoperative**
  - Recognize and treat preoperative conditions
    - Dry Eye
    - Blepharitis
    - Epithelial Basement Membrane Disease
    - Salzmann’s Nodular Degeneration

- **Intraoperative**
  - Prevent Epithelial Defects

- **Postoperative**
  - Manage Post-Refractive Surgery Dry Eye
  - Manage Complications
**OCULAR SURFACE DISEASE**

Pre-Operative Screening

- Lid Anatomy and function
  - Exposure
  - Lagophthalmos
  - Blepharitis

- Blink rate

- Tear film volume and quality
  - Tear lake at lid margin
  - Foamy tears

- MG Expression

- Tear Break up time


OCULAR SURFACE DISEASE

Pre-Operative Screening

- Corneal Epithelium
- Conjunctival Epithelium
- Surface Staining
  - Rose Bengal
  - Lissamine Green
- Schirmer’s Test
Osmolarity was found to be increased with decreasing tear flow rates. Hyperosmolarity can lead to damage of the ocular surface and is the primary cause of discomfort associated with dry eyes. High osmolarity increases EMMPRIN expression in corneal epithelial cells and is associated with an increase in MMP-9 and loss of epithelial cell-cell junctions. Osmolarity may be the best marker of disease severity across normal, mild/moderate & severe categories.

3. Huet, E et al. AJ of Pathology, Vol. 179 No.3. 2011
TEAR FILM ASSESSMENT WITH LIPIVIEW

- Interferometric technology to evaluate the tear film’s lipid layer
Provides a relative measure of the thickness of the lipid layer of the tear film
LACTOFERRIN AND DRY EYE

- Lactoferrin is a multifunctional protein – part of the transferrin family
- Global marker present in tears
- One of the components of the immune response
  - Demonstrated significant antimicrobial activity
  - Part of the eye’s natural defenses
  - Identified as one of the tear proteins that may be part of the innate defense of the mucosal surface
  - Bactericidal and even fungicidal properties
MMP-9 AND DRY EYE

- MMP-9 - Matrix Metalloproteinase 9
- Dry eye is a multifactorial disease that destabilizes the tear film
- Hyperosmolarity of tears contributes to the inflammatory cascade
  - Distressed epithelial cells produce elevated levels of the cytokine MMP-9
  - Cytokine exacerbates the inflammatory cycle
- MMP-9 increases proportionally with the severity of ocular dryness
- Abnormal levels of MMP-9 (> 40 ng/mL) have been shown to correspond with moderate-to-severe dry eye disease

DEWS Report: The Ocular Surface / April 2007, Vol. 5, No. 2
NEWER POINT-OF-CARE DRY EYE DIAGNOSTICS

- **Osmolarity**
  - TearLab Osmolarity System – TearLab

- **MGD**
  - LipiView Interferometer – TearScience

- **Lactoferrin**
  - Tear Microassay System – Advanced Tear Diagnostics

- **MMP-9**
  - RPS InflammaDry Detector – Rapid Pathogen Screening
**DRY EYE AND CATARACT SURGERY**

- Trauma to corneal nerves
  - Incision cuts corneal nerves at limbus
  - Paracentesis
  - Relaxing Incisions
    - Significantly add to the neurotrophic risk
- Trauma to epithelium
  - With topical fluids
  - Dryness
  - Medications
  - Instruments
**IMPACT OF CORNEAL SURGERY ON DRY EYE**

<table>
<thead>
<tr>
<th>Severity Level</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>Mild to moderate</td>
<td>Moderate to severe</td>
<td>Severe</td>
<td>Extremely severe</td>
</tr>
<tr>
<td>Conjunctival Signs</td>
<td>Mild to moderate</td>
<td>Staining</td>
<td>Staining</td>
<td>Scarring</td>
</tr>
<tr>
<td>Corneal Staining</td>
<td>Mild punctate staining; central staining; filamentary keratitis</td>
<td>Severe staining; corneal erosions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Signs</td>
<td>Tear film; decreased vision (blurring)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Treatment Options**

- Patient education
- Environmental modification
- Preserved tears
- Control allergy

- Non-preserved tears
- Topical steroids
- Secretagogues
- Nutritional support

- Oral tetracyclines
- Oral cyclosporine
- Acetylcysteine
- Moisture goggles
- Surgery (punctal cautery)

- Systemic anti-inflammatory therapy

**Plan pre-op and post-op care accordingly**

Cataract Surgery adds 1 severity step

LASIK adds 2 severity steps

If no improvement, add level 2 treatments

If no improvement, add level 3 treatments

If no improvement, add level 4 treatments

## WHEN TO AVOID SURGERY DUE TO OCULAR SURFACE DISEASE

<table>
<thead>
<tr>
<th>Symptoms and Effect on vision</th>
<th>Procede</th>
<th>Caution</th>
<th>Contraindicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>No effect on vision</td>
<td></td>
<td>Symptoms and fluctuating vision</td>
<td>Symptoms and decreased vision due to ocular surface disease</td>
</tr>
<tr>
<td>Supravital conjunctival staining and Central fluorescein corneal staining</td>
<td>No staining</td>
<td>Conjunctiva but not cornea</td>
<td>Conjunctiva and cornea</td>
</tr>
</tbody>
</table>
EPITHELIAL BASEMENT MEMBRANE DEGENERATION

Findings

- Microcysts
- Macrocysts
- BM ridges or lines
- BM sheets or maps

Exam

- Broad beam oblique illumination with Slit Lamp
SALZMANN’S NODULAR DEGENERATION

Findings

- Subepithelial fibrosis
- Fibrotic nodules
- Irregular epithelium
- Basement membrane changes
- Unstable tear film
- Female > Male
Significance in Anterior Segment Surgery

- Visual loss due to
  - Postop stromal scarring
  - Untreated disease
- Inaccurate IOL calculations
- Risk of epithelial defects and postoperative infection
**EBMD/SALZMANN’S NODULAR DEGENERATION**

- **Decision on whether to Tx**
  - Are findings significant enough to
    - Affect preop calculations
    - Reduce postop vision
- **Timing of treatment**
  - Before cataract surgery
  - Combined with Cataract surgery
  - After cataract surgery
EBMD TREATMENT

Moderate/Severe disease

- No associated scarring
  - Superficial keratectomy
- Associated subepithelial fibrosis
  - Phototherapeutic keratectomy

Post- Super K/PTK management

- TSCL until epithelium heals
- Topical Steroids to prevent haze
- Topical NSAIDs for 2-4 days for pain
SALZMANN’S NODULAR DEGENERATION

Treatment

- Superficial keratectomy and/or PTK
FUCHS’ DYSTROPHRY
AND
CATARACT
Assists in the discussion of expectations for patient

- Prognosis for Phaco only
  - Risk of corneal decompensation
    - Immediately post op
    - Long term
- Need for Phaco/EK

DEVELOP A GRADING SCALE FOR THE SEVERITY OF FUCHS
Fuchs Severity Scale

- Mild Guttata
  - no real risk of corneal decompensation

- Confluent Guttata – no evidence of stromal edema
  - Phaco only, discuss possible need for EK
Fuchs Severity Scale

- Confluent Guttata – Possible Stromal Edema
  - May want to re-examine in early morning
  - Definite possibility of EK in near future
  - If no edema still worth the attempt at Phaco only

- Confluent Guttata/Definite Edema
  - Almost always recommend Phaco/EK
Really Take a Patient History
- Hx of blurred vision in the morning
- Open ended question

Endothelial cell count
- Should not be used to determine the need for an EK
- Patients with confluent guttata and no stromal edema can still do well with Phaco only
Pachymetry
- Isolated value not much help
- Common belief that a certain thickness (620 microns) equates to corneal edema
- May be of use in early corneal edema cases
  - Change greater than 10% from AM to PM

Slit lamp exam
- Look for subtle signs of corneal edema
  - Posterior stromal folds
  - Stromal haze
  - Epithelial edema
As a general rule
- For stromal edema and with any level of cataract (or prebysopia):
  - Phaco/DSEK/DMEK is the indicated procedure
- For guttata without evidence of edema:
  - Phaco only

Some exceptions:
- Minimal edema/Dense Cataract/Macularopathy
  - In this case phaco only may be as good as a Phaco/DSEK
  - Mild corneal edema may not be as significant as the maculopathy
  - Not performing the EK will reduce the postop care
- Stromal Edema/Pre-presbyopic/No Cataract
  - EK only