WORKSHOP A

Ocular Surface Inflammation Detection and Management

COPE Course 44303-AS
Ocular Surface Inflammation Detection & Management

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Financial Disclosures
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Ocular Surface Disease
Dry Eye Disease (DED)
Meibomian Gland Dysfunction (MGD)
Blepharitis
Ocular rosacea
Ocular allergy
Autoimmune origins
Trauma induced
Iatrogenic
Dry Eye Disease defined

Chronic
Multifactorial
Characterized by disturbances in tear film
& ocular surface
Females > male

Environmental conditions
- Arid
- Computer-use
- Contact lens wear
- Systemic disease
  - Sjogren's syndrome
  - Lupus
  - Sjogren-Johnson syndrome

Types of Dry Eye Disease

Evaporative dry eye:
- Caused by Meibomian Gland Dysfunction
- Leading cause of Dry Eye Disease worldwide

Aqueous-deficient dry eye:
- Decreased tear production at the lacrimal gland
- Prevalent in autoimmune disease

http://www.revueph.com/content/d/therapeutic_topics/i/1334/c/25584/
Types of Dry Eye Disease

Evaporative dry eye = 65-86% of cases
Aqueous deficient dry eye = 14-20% of cases

Prevalence in the United states

3.2 million women age 50 and over
1.68 million men age 50 and over

Causes of Ocular Surface Symptoms

Aging
- Lid laxity
- Lagophthalmus
- Floppy eye lid syndrome
Causes of Ocular Surface Symptoms

Gender
- Hormone changes or fluctuations
- Birth control
- HRT

Causes of Ocular Surface Symptoms

Medications
- Oral
  - Antihistamines
  - Anti-depressants
  - Certain anti-hypertensives
  - Decongestants
  - Isotretinoin-type drugs for acne

Causes of Ocular Surface Symptoms

Medications
- Ophthalmic
  - Glaucoma medications
  - Allergy medications
  - Preservative sensitivities
Causes of Ocular Surface Symptoms

Demodex
- Demodex folliculorum
- Demodex brevis

Causes of Ocular Surface Symptoms

Blepharitis affects as many as 70 to 80 million Americans.
Upwards of 80 percent of those patients could have Demodex mites.

Causes of Ocular Surface Symptoms

Demodex
- Men > Women
- The incidence of Demodex infestation increases age
- 84 percent of the population at age 60
- 100 percent of the population older than 70 years of age
Causes of Ocular Surface Symptoms

Trauma/surgical/medical treatment
- Refractive
- Cataract surgery
- Lid procedures
- Burns
- Radiation therapy

Nutritional deficiencies
- Vitamin A
- Omega 3

Systemic Disease
- Diabetes
- Thyroid disease
- Autoimmune disease
Tear Film & Blinking

Blinking influences the tear layer's:
- Structure
- Stability
- Function

11 subjects
Mean age, 21.3 years
Subjects played a computer game for 60 minutes
Blinking was observed by a Web camera
Every 15 min a non-invasive tear break up time was measured

Total blink rate changed very little
Complete and incomplete blink rates fluctuated
Noninvasive [ring] breakup time at 30 min (4.33 ± 2.57 s) was significantly shorter (p < 0.01) than that at baseline before the VDT experiment (8.62 ± 1.34 s)

Tear Film & Blinking

Even if the total blink rate decreases, the tear film remains stable as long as almost all blinks are complete.

The incomplete blinking contributes to tear film instability and is variable with prolonged VDT exposure.

The study indicated that the tear film stability was determined by blinking quality, and the predominance of blinking type relates to tear film stability.

Tear Film & Blinking

Changes in the tear film lipid layer as a function of blinking were investigated using a custom-designed specular reflection monitoring system.

104 subjects’ lipid layers were measured under conditions of normal (‘baseline’) blinking and “forceful” blinking was quantitated on the basis of specific interference colors.

Deliberate, forceful blinking was found to significantly increase the lipid layer thickness (LLT) of the tear film.

The magnitude of increase was found to be correlated with the baseline LLT values.

Individuals with baseline LLT values of 75-150 nm demonstrated a mean increase in LLT of 33 nm following forceful blinking.

Whereas subjects with baseline LLT values < or = 60 nm experienced a mean increase of 19 nm.

The data suggest that, in addition to playing a role in the spreading of lipid across the tear film, the blinking mechanism may be important in the maintenance of the lipid layer by augmenting the expression of lipids from the meibomian glands.
Ocular Surface Disease Detection

Inflammadry
Oculus Keratograph
Lipview
Microscopy

Inflammadry

Rapid Pathogen Screening (Sarasota, FL)
- Detects elevated MMP-9 in tears
- Cost per unit and potential reimbursement
- Studies indicate MMP-9 as a useful biomarker for diagnosing, classifying and monitoring DED

MMP-9

Matrix Metalloproteinase 9
- Proteolytic enzymes
- Produced by stressed epithelial cells
- Vital in wound healing and inflammation
MMP-9

- Increased levels detected in:
  - K sicca (KCS)
  - Corneal ulcers
  - Ocular rosacea
  - Sjogren’s syndrome
  - MGD

Tear MMP-9 Activity in Normal Control and DTS Groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>MMP-9 Activity (ng/mL)</th>
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<tbody>
<tr>
<td>Normal (n = 18)</td>
<td>8.39 ± 4.70</td>
</tr>
<tr>
<td>DTS1 (n = 15)</td>
<td>25.57 ± 17.94</td>
</tr>
<tr>
<td>DTS2 (n = 11)</td>
<td>66.37 ± 57.02</td>
</tr>
<tr>
<td>DTS3 (n = 9)</td>
<td>101.42 ± 70.55</td>
</tr>
<tr>
<td>DTS4 (n = 11)</td>
<td>381.24 ± 42.83</td>
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</tbody>
</table>

*P < 0.008 Compared with normal.
†P < 0.003 Compared with normal and DTS1.
‡P < 0.001 Compared with normal and the other DTS severity groups.


MMP-9

Strong correlation with:
- Survey scores
- Fluorescein staining
- Fluorescein TBUT
Inflammadry

Small applicator touched to the conjunctiva
Snaps into a test cassette
Cassette tip is submerged in solution
Results are obtained in 10 minutes
Similar to adeno-detector

Pros
- Inexpensive
- Fast
- Identifies presence of inflammation

Cons
- Does not quantify inflammation
- Does not identify cause

Oculus Keratograph 5M

- Tear film analysis by non-invasive (non-contact) scanning software
  - NERUT
  - Tear meniscus height
  - Non-contact meibography (meiboscan)
  - Tear dynamics
  - Bulbar redness
  - Topography
Oculus Keratograph 5M

Non-invasive keratograph Tear Break Up time (NIKbut)
- Uses placido disc ring-based corneal topography
- Uniquely objective
- No dye required
- Initial and average break recorded

Non-contact meibography/meiboscan
- Evaluation via infrared photography
- Increased maneuverability compared to K4

Tear meniscus height
- Helps determine tear film quality
- Amount of tears at lower tear meniscus
- White or infrared illumination
- High resolution camera to record images
Oculus Keratograph 5M

**Tear dynamics**
- Interference color pattern and structure evaluation
- Video can record up to 32 images per second
- Evaluating spread of particles in tear film

**Topography**
- Guarantees perfect reproducibility
- Useful in observation and management
  - Contact lenses
  - Refractive errors
  - Contact lens fitting
  - Pre and post-surgical considerations

**Bulbar redness/r-scan**
- 1st instrument to offer fully automatic determination of bulbar redness
- Documents and classifies bulbar & limbal redness objectively
- Detects conjunctival vessels & assesses degrees of redness
Lipiview

- Uses interferometry to measure lipid layer thickness between blinks
- Quantitative assessment in interferometric color units (ICU)

Pilot study: 137 consecutive patients completed SPEED test, then measured ICUs by Lipiview
- **SPEED** > 0: had LLT of 60nm or less
- **SPEED** > 0: had LLT 75nm or greater
- Linear regression analysis found significant correlation between LLT and symptom score
  - As LLT increased, symptom score decreased
Lipiview II

**New Features:**
- Introduced 2014
- Uses Dynamic Meibomian Imaging (DMI)
- High-definition images

**Updated Features:**
- Lipid Layer Thickness (LLT)
- Blink performance

Uses a light-emitting lid-verter
- Allows for selection of images from 3 modes
- High resolution images utilized in patient education

Microscopy

Demodex visible at slit lamp
- Cylindrical dandruff
- Base of lashes

Microscopy for patient education
Microscopy

Epilation maneuver
Movement in a clockwise fashion prior to removal

Microscopy

Place to slide
Observe under lower magnification
Increase magnification
Photograph

Microscopy
Microscopy

Ocular Surface Disease Treatments

- Artificial tears
- Gels, overnight ointments
- Moisture chamber goggles
- Warm compresses
- Lid scrubs
- Punctal plugs
- Lacrissets

- Cyclosporine
- Steroid drops
- Oral medications
- Lipiflow
- Intense Pulse Light (IPL)
- MeiBoFlo
- BlephEx
- Amniotic membrane

Lipiflow

- Thermal pulsation therapy for the treatment of meibomian gland dysfunction resulting in evaporative dry eye disease
  - LipiView
    - Diagnostic instrument used pre- and post-Lipiflow treatment
    - Evaluates lipid layer of tears (measured in interferometric color units, ICU)
    - Evaluates blink quality (duration and completeness)
    - Visual appeal to patient and speaks to advanced testing
Lipiflow

Suture-less amniotic membrane

Inner layer of the placenta avascular connective tissue composed of:
- Basement membrane
- Stromal matrix of collagen
- Fibronectin
- Laminin
- Bio-active components

Suture-less amniotic membrane

Promotes re-epithelialization
Reduces inflammation
Inhibits neovascularisation
Suture-less amniotic membrane

**Methods:**
- ProKera (BioTissue) – cryopreserved
- Ambio2 (IOP Ophthalmics) – dehydrated

The Ambio2 process removes bioburden and potential virulency, but retains the devitalized, cellular components.

Photomicrograph shows intact epithelial and fibroblast cell components – with dense extracellular matrix.

Provided in dehydrated form for room temperature storage; no freezing or refrigeration required.

Activates with sterile saline within minutes; no thawing or soaks required.

Dehydrated using patent-pending DryFlex processing technology to optimize handling characteristics while retaining growth factors, cytokines and collagens inherent in amniotic tissue.

Adheres well to sclera and conjunctiva when placed on the ocular surface. Generally placement does not require suture or glue.

Terminally sterilized, can be stored at room temperature and has a shelf life of 2 years.

**Key components**

Key components responsible for tissue regeneration are retained using the CryoTek™ processing method.

Delivers the unique healing properties of cryopreserved amniotic membrane in a convenient, sutureless, thermoplastic ring set.

PROKERA® is designed to conform snugly to the ocular surface and can be inserted in the office.

Cryopreserved amniotic membrane is the ONLY tissue cleared for wound healing by the FDA.
ProKera

Does PROKERA® replace a BCL?
- No, PROKERA® replaces surgical placement of AMNIOGRAFT®

What sort of topical medications are recommended?
- Routine medications for underlying cause (commonly antibiotics and/or steroids)

Types of topical anesthetics used for PROKERA® insertion?
- 0.5% proparacaine

ProKera Insertion

Hold the upper eyelid

Ask patient to look down
ProKera Insertion

Insert ProKera into the superior fornix

Slide ProKera under the lower eyelid

BlephEx

Disposable
High-speed, rotating surgical-grade micropore
Alger brush-like hand-piece
Strips away accumulated debris & biofilm from the lid margins
- Recommended to be used with surfactant lid cleanser
Clinical Effectiveness of Lid Debridement with BlephEx Treatment

- Single-center, prospective, interventional 4-week clinical trial
- 20 subjects with MGD
  - Evaluated at baseline using OSDI, FTBUT and Efron grading scale for blepharitis and MGD severity
  - Underwent a single BlephEx treatment to all four lids
- Results at 4 weeks:
  - Mean OSDI decreased by 53%
  - Mean FTBUT increased by 65%
  - Mean blepharitis severity and MGD severity both decreased by 54%, respectively

When can BlephEx be used?

- Blepharitis (373.00)
  - Staphylococcal blepharitis
  - Seborrheic blepharitis
- Meibomian gland dysfunction (373.00)
- Excoriatous Dermatitis of Eyelid (373.31)
- Allergic Dermatitis of Eyelid (373.32)
- Demodex blepharitis
  - Parasitic infestation of eyelid (373.4)
  - Demodex folliculorum (133.6)
- Keratoconjunctivitis sicca (370.33)
- Dry eye / Tear film insufficiency (375.15)

Presenting BlephEx to the Patient

Rationale

Risks / benefits / alternatives
Presentation BlephEx to the Patient

Disclosure
  "This is not covered by your insurance."
  Why?

Advanced beneficiary notice?
Informed consent?
Letter of medical necessity?

Thank You