Advanced Diagnostic Testing in Ocular Surface Disease

COPE Course 42288-AS
ADVANCED DIAGNOSTIC TESTING IN DRY EYE DISEASE

WHITNEY HAUSER, OD
ASSISTANT PROFESSOR
SOUTHERN COLLEGE OF OPTOMETRY

DRY EYE DISEASE

LUNCH AND SNOOZE?

DRY EYE DEFINED

1. CHRONIC
2. MULTIFACTORIAL
3. CHARACTERIZED BY DISTURBANCES IN TEAR FILM AND OCULAR SURFACE
4. FEMALES > MALE

DRY EYE DEFINED

1. ENVIRONMENTAL CONDITIONS
   - ARID
   - COMPUTER-USE
   - CONTACT LENS WEAR
   - SYSTEMIC DISEASE
   - SJOGREN'S SYNDROME
   - LUPUS
   - STEVENS-JOHNSON SYNDROME

PREVALENCE IN THE UNITED STATES

1. 3.2 MILLION WOMEN AGE 50 AND OVER
2. 1.68 MILLION MEN AGE 50 AND OVER

THE HISTORY OF DRY EYE

1946 – WOLFF FIRST DESCRIBED THE MULTI-LAYER TEAR FILM
1973 – HOLLY, PH.D., EXPLAINED THAT DEFICIENCY IN SOLUBLE MUCINS CAUSE BREAKS IN OCULAR SURFACE TENSION & NOT ALLOW EVEN SPREADING OF TEARS
1997 – TSENG SHOWED THAT THE OCULAR SURFACE AND TEAR FILM INTERACTED TO PRODUCE A HEALTHY OCULAR SURFACE.

TYPES OF DRY EYE

EVAPORATIVE DRY EYE
CAUSED BY MEIBOMIAN GLAND DYSFUNCTION
LEADING CAUSE OF DRY EYE WORLD WIDE

AQUEOUS-DEFICIENT DRY EYE
DECREASED TEAR PRODUCTION AT THE LACRIMAL GLAND
PREVALENT IN AUTOIMMUNE DISEASE

TYPES OF DRY EYE DISEASE

EVAPORATIVE DRY EYE = 65-86% OF CASES
AQUEOUS-DEFICIENT DRY EYE = 14-20% OF CASES

CAUSES OF DRY EYE SYMPTOMS

AGING
SEX
HORMONE CHANGES OR FLUCTUATIONS
PREGNANCY
BIRTH CONTROL
HRT
MEDICATIONS
ORAL
ANTIHISTAMINES
ANTIDEPRESSANTS
CERTAIN ANTISEPTICS
DECONGESTANTS
ISOTRETINOIN-TYPE DRUGS FOR ACNE

CAUSES OF DRY EYE SYMPTOMS

GENDER
MEDICATIONS
ORAL
ANTIHISTAMINES
ANTIDEPRESSANTS
CERTAIN ANTISEPTICS
DECONGESTANTS
ISOTRETINOIN-TYPE DRUGS FOR ACNE
CAUSES OF DRY EYE SYMPTOMS

• MEDICATIONS
  - Ophthalmic Medications
  - Glaucoma Medications
  - Allergy Medications
  - Preservative Sensitivities

• DEMODEX
  - Demodex folliculorum
  - Demodex brevis

• BLEPHARITIS AFFECTS AS MANY AS 70 TO 80 MILLION AMERICANS
  - UPWARDS OF 80 PERCENT OF THOSE PATIENTS COULD HAVE DEMODEX MITES

• DEMODEX
  - MEN > WOMEN
  - THE INCIDENCE OF DEMODEX INFESTATION INCREASES AGE
  - 64 PERCENT OF THE POPULATION OLDER THAN 70 YEARS OF AGE

• TRAUMA/SURGICAL/MEDICAL TREATMENT
  - Refractive
  - Cataract Surgery
  - lid procedures
  - Burns
  - Radiation Therapy
CAUSES OF DRY EYE SYMPTOMS

- Nutritional Deficiencies
  - Vitamin A
  - Omega 3

CAUSES OF DRY EYE SYMPTOMS

- Diabetes
- Thyroid Disease
- Autoimmune Disease

WHAT DO WE KNOW ABOUT DED?

WE KNOW:

- WHAT DRY EYE DISEASE IS
- WHO IS AT RISK

PSYCHOLOGY OF DRY EYE

- Extroverts scored higher on Moncrieffe dry eye questionnaire than introverts
- Patients with a greater sense of well-being scored lower

PSYCHOLOGY OF DRY EYE

- 89 Dry Eye Subjects (13 Sjogren’s Patients & 73 Control Subjects)
  - Zung Self-Rating Anxiety Scales (SAS)
  - Zung Self-Rating Depression Scales (SDS)
  - Ocular Surface Disease Index (OSDI)

PSYCHOLOGY OF DRY EYE

- Anxiety and depression scores of the DES group were significantly higher than the control group
- The prevalence of DES subjects with anxiety or depression symptoms was significantly higher in the control group
**PSYCHOLOGY OF DRY EYE**

- SAS scores were found to be correlated with OSDI and educational level. SDS scores were found to be correlated with OSDI.
- Neither SAS nor SDS scores were correlated with age, sex, household income, tear break up time (BUT), Schirmer Test 1 (S1T), corneal fluorescein staining (Fl), or visual acuity.

**CONCLUSION:**

- Anxiety and depression are correlated with DES, demonstrating that DES is an important public health problem that merits increased attention and research.

**PSYCHOLOGY OF THE EXAMINATION**

- Change the “single visit” mentality
- Treatment is a process
- Individualized care

**HOW DOES DRY EYE CARE COMPARE?**

- Eyeglasses Examination: $125-200
- Contact lens examination: $150-200
- Eye examination: $60-225
- Dry Eye Care: $300-800 (upwards of $1600-1800)

*Figures based on one year*

**HOW DOES DRY EYE COMPARE**

<table>
<thead>
<tr>
<th>Medical Office Visit: OSDI Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>99212</td>
</tr>
<tr>
<td>99213</td>
</tr>
<tr>
<td>99214</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medical Office Visit: Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>99212</td>
</tr>
<tr>
<td>99213</td>
</tr>
</tbody>
</table>

If you anticipate three follow-up visits during the year, here's what the revenue would look like:

<table>
<thead>
<tr>
<th>Follow-up Revenue per Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>99212(x3)</td>
</tr>
<tr>
<td>99213(x3)</td>
</tr>
</tbody>
</table>

**FRUSTRATED YET?**
FRUSTRATED YET?

- 55 MILLION AMERICANS SUFFER FROM DRY EYE SYMPTOMS
- 40 MILLION OF THOSE CASES GO UNDIAGNOSED

72% of patients use artificial tears only
62% of patients demand "something better"
97% of patients report condition as "frustrating"


ECONOMIC IMPACT

- $4 BILLION ANNUALLY
- WHEN SOCIETAL COSTS ARE CONSIDERED...
  - MISSED WORK
  - LOSS IN PRODUCTIVITY

THE IMPACT IS...

$55.4 BILLION PER YEAR

SO, WHAT'S A DOCTOR TO DO?

NOW, IT'S TIME TO RALLY

DIAGNOSTIC TESTING
ADVANCED DIAGNOSTICS IN DED

- Tear Osmolarity
- RMS Inflammation
- Oculus Keratograph 5M
- Lipview
- ZoneQuick
- Microscopy

TEAR OSMOLARITY

- Osmolarity vs Osmolality
- Freezing Point Osmometer
- Vapor Pressure Osmometer
- Electrical Impedance Osmometer

TEAR OSMOLARITY

- Tear Lab Osmolarity System (Tear Lab)
- Cost of Unit and Disposables
- Reimbursable
- Single-use Microchip Embedded with Gold Electrodes
- 50 NL Collected

TEAR OSMOLARITY

- Pros
  - Easy to administer
  - Quick results
  - Reimbursable by Medicare
- Cons
  - Cost of unit
  - Cost of disposables
  - Variability of testing

TEAR OSMOLARITY

- Osmolarity Increases with Advancing Dry Eye Disease
- asymmetry of findings

TEAR OSMOLARITY

• DOES IT WORK?
  • IN A STUDY OF 300 PATIENTS, TEARLAB IDENTIFIED:
    • 88% OF NORMAL SUBJECTS
    • 75% OF SUBJECTS WHO HAD MILD-OR-MODERATE DRY EYE DISEASE
    • 95% OF SUBJECTS WHO HAD SEVERE DRY EYE DISEASE USING A DIAGNOSTIC CUT-OFF OF 308MOSMS/L.1

• YOU'RE SURE IT WORKS?
  • TEARLAB DEVICE OUTPERFORMED CORNEAL STAINING AND SCHIRMER'S TESTING IN CORRECTLY IDENTIFYING PATIENTS WHO HAD MILD-TO-MODERATE DRY EYE. (ARVO 2010)

TEAR OSMOLARITY

• CONTACT LENS FITTING
  • MATERIAL SELECTION
  • REDEMPTION FREQUENCY
  • CARE SYSTEM
• GLAUCOMA TREATMENT
  • IOP SELECTION
  • CATARACT AND REFRACTIVE SURGERIES
  • PROPHYLACTIC TREATMENT

TEAR OSMOLARITY

• MICROFLUIDIC ANALYSIS UTILIZING AN INTEGRATED COLLECTION AND ANALYSIS DEVICE
  • HC06111 (EFFECTIVE JANUARY 1, 2011)
  • UNILATERAL TEST
  • THE SECOND EYE SUBMITTED USING A “59” MODIFIER

INFLAMMADRY

• RAPID PATHOGEN SCREENING (SARASOTA, FL)
  • DETECTS SALIVARY AMP 9 IN TEARS
  • COST PER UNIT AND POTENTIAL REIMBURSEMENT
  • STUDIES INDICATE AMP-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

MMP-9

Group MMP-9 Activity (ng/mL)

<table>
<thead>
<tr>
<th>Group</th>
<th>MMP-9 Activity (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (n = 18)</td>
<td>8.39 ± 4.70</td>
</tr>
<tr>
<td>DTS1 (n = 15)</td>
<td>35.57 ± 17.04*</td>
</tr>
<tr>
<td>DTS2 (n = 11)</td>
<td>66.17 ± 57.02* †</td>
</tr>
<tr>
<td>DTS3 (n = 9)</td>
<td>101.42 ± 70.58* ‡</td>
</tr>
<tr>
<td>DTS4 (n = 11)</td>
<td>381.24 ± 42.83*</td>
</tr>
</tbody>
</table>

Data shown are the mean ± SD.
* 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 TBS

INFLAMMADRY

- A 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

INFLAMMADRY

- 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
  - NIKBUT
  - Tear meniscus height
  - Non-contact meibography (meiboscan)
  - Tear dynamics
  - Bulbar redness
  - Topography
OCULUS KERATOGRAPH 5M

- Non-Invasive Keratography Tear Break Up Time (NIKBT)
- Uses Placido Disc Ring-Based Corneal Topography
- Uniquely Objective
- No Dye Required
- Initial and Average Break Recorded

OCULUS KERATOGRAPH 5M

- Non-Contact Meibography / Meiboscan
  - Evaluation via Infrared Photography
  - Increased Maneuverability Compared to K4

OCULUS KERATOGRAPH 5M

- 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

OCULUS KERATOGRAPH 5M

- Topography
  - Guarantees Perfect Reproducibility
  - Useful in Observation and Management
  - Corneal Diseases: Keratoconus, Topographic
  - Constriction Pattern
  - Pre- and Post-Surgical Evaluations

OCULUS KERATOGRAPH 5M

- Bulbar Redness "B-Scan"
  - 1st Instrument to Offer Fully Automatic Determination of Bulbar Redness
  - Documents and Classifies Bulbar & Skirn Redness Objectively
  - Sees Conjunctival Veins & 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 ICU by LIPIVIEW

- Speed >10, 74% had LLT of 60NM or less
- Speed =0, had LLT of 75NM or greater

Linear regression analysis found statistical significance between LLT and symptom score. As LLT increased, symptom score decreased.
ZONEQUICK

- Red cotton thread treated with phenolsulfonphthalein
  - Yellow (acid) = water absorption indicator
  - Red (basic) = tear volume indicator

ZONEQUICK

- Testing Conditions
  - No anesthetics
  - 5 minutes after other drops instilled
  - May be used with contact lenses


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

- Plate to slide
- Observe under lower magnification
- Increase magnification
- Photograph
CASE 1

• 84 YO WF
• (+) SEVERE DRY EYE FOR 1 YEAR
• ORAL MEDS:
  • METFORMIN
  • LISINOPRIL
  • GLYBURIDE
  • LOVASTATIN
  • SERTRALINE
  • ASA
  • GLUCOSAMINE

CASE #1

Dry Eye Complaint
Chronic dryness, increasing for 1 year
Associated symptoms
Fluctuating vision, photophobia
Effect to ADL's
Unable to read, cannot go outside comfortably
Medications for DED
Restasis BID, Non-preserved Systane, doxycycline 100mg BID, Omega 3FA

CASE #1

<table>
<thead>
<tr>
<th>Com.</th>
<th>OU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sn</td>
<td>20/100 OD, 20/200 OS</td>
</tr>
<tr>
<td>Sp.</td>
<td>20/150</td>
</tr>
<tr>
<td>CFV</td>
<td>FTFC OD, OS</td>
</tr>
<tr>
<td>Pup.</td>
<td>3.5X</td>
</tr>
<tr>
<td>VSP</td>
<td>26</td>
</tr>
<tr>
<td>GDM</td>
<td>15</td>
</tr>
<tr>
<td>Rim</td>
<td>221 OD, 231 OS</td>
</tr>
<tr>
<td>Inflammability</td>
<td>Negative</td>
</tr>
</tbody>
</table>

CASE #1

• DIAGNOSED WITH GLAUCOMA IN 1970’S
• WAS TAKING 3 GLAUCOMA MEDS FOR YEARS...AND YEARS...AND YEARS
• RECENTLY CHANGED TO NON-PRESERVED ZIOPTAN
CASE #1

• **TREATMENT**
  • **LID HYGIENE** – CLIRADEX WIPES BID X 10 DAYS THEN QHS FOR 20 DAYS
  • **LIPIFLOW TREATMENT** – BEGIN ACUVAIL BID FOR 2 WEEKS, THEN QD FOR 2 WEEKS
  • **RTC 6-8 WEEKS**

• **FOLLOW UP EXAMINATION**
  • “GOOD DAYS AND BAD DAYS”
  • DRYNESS LESS OF A PROBLEM SINCE TREATMENT AND VISION IS IMPROVING
  • ABLE TO READ THE NEWSPAPER

• **CC**
  - DVA
  - 20/60 OD (PH: 20/30) 20/100 (PHNI)
  - EOMs FROM OU
  - CFV FROM OU
  - PAPAS BRIEFLY
  - SPH: 0.5
  - CIL: 0.5
  - OSM: 308 OD   308 OS

Lashes free of debris

Clear secretions

Improved meibomian gland function
CASE #1

SPK persists after treatment
Improved LG staining

CASE #1

CONSULTATION WITH PATIENT'S OD AND OMDO
RTC 4 WEEKS FOR PROKERA OD

CASE #2

52 YO WF
OCCUPATION: WEB DESIGNER
HOBBIES: COMPUTERS, READING, EXERCISE
MEDS: LORAZEPAM, CYMBALTA, FLAX SEED OIL
ADDITIONAL DIAGNOSES: HEMOCHROMATOSIS, ANEURYSM

CASE #2

Dry Eye Complaint
Dry symptoms worsening, "OTC's don't work,
Associated symptoms
Eye fatigue, discomfort, worsening in the evening, often matted
Effect to ADL's
Effects work, limits reading
Medications for DED
Similasan "Dry Eye Relief" (has use "all" artificial tears, warm compresses, cold packs

CASE #2

cc DVA
20/20 OD   20/20 OS

EOMs
FROM OU
Pupils
ERRL(-)APD
SPEED
14/28

OSDI
54/100

Inflammadry
Negative
NIBUT (initial)
4.72 OD   4.33 OS
Osm
294 OD    277 OS

CASE #2

Cylindrical blepharitis
Telangectasias at lid margin
CASE #2

• RECOMMEND BLEPHEX AND LIPIFLOW TREATMENT. PATIENT DECLINES.

CASE #2

• TREATMENT:
  • BEGIN CLIRADEX WIPES BD FOR 10 DAYS THEN QHS FOR 30 DAYS
  • BEGIN SYSTANE BALANCE QID OU
  • RTC in 4 WEEKS

CASE #2

• VISIT #2
  • "LITTLE TO NO IMPROVEMENT NOTED"
  • WORSENING SYMPTOMS AT NIGHT
  • WARM COMPRESSES AT NIGHT WITH RICE BAG
  • REPORTS COMPLIANCE WITH ALL RECOMMENDED TREATMENTS

CASE #2

cc DVA 20/20 OD  20/20 OS
EOMs FROM OU
CVF FTFC OD, OS
Pupils EERL (-) APD
ZoneQuick 30mm OD, OS

CASE #2

• VISIT #3
  • PATIENT REPORTS SIGNIFICANT IMPROVEMENT AND RELIEF
  • ADLS NOT EFFECTED AT THE END OF THE DAY
  • CONTINUING LID SCRUBS AND SYSTANE BALANCE QID

CASE #2

• TREATMENT:
  • BLEPHEX AND LIPIFLOW INDICATED AND RECOMMENDED
  • PATIENT AGREES TO BLEPHEX TODAY