Advanced Treatment in Ocular Surface Disease

Douglas K. Devries, O.D.
Eye Care Associates of Nevada

Disclosures

- Douglas K. Devries
  - Consultant or Speakers Bureau for
    - Allergan
    - AMO
    - TearLab
    - NicoX
    - BVI
    - B&L

Chronic Dry Eye – Should I Treat It

- Higher Level of Care to Your Patient
- Expense vs Revenue Center
- Revenue per Patient
- Patients Decide “Cost vs Benefit”

Revenue Potential

<table>
<thead>
<tr>
<th>Re-Appointment Level</th>
<th>Rate</th>
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</thead>
<tbody>
<tr>
<td>Level II</td>
<td>$38.19</td>
</tr>
<tr>
<td>Level III</td>
<td>$60.94</td>
</tr>
<tr>
<td>Level IV</td>
<td>$91.56</td>
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</tbody>
</table>

Will be at least 2 visits and upwards to 8 visits.

Punctal Occlusion OU (one set) $194.84

*Medicare Rates in Nevada

Net Revenue
$341.00 to $800.00 Plus
Per Patient with repeat visits in future years

Ocular Surface Disease

Greatest Opportunity is Yet to Come

Dry Eye – “Greatest Opportunity is Yet to Come” 2010

<table>
<thead>
<tr>
<th>Company</th>
<th>Completed</th>
<th>Status</th>
</tr>
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<tbody>
<tr>
<td>Allergan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TearLab</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NicoX</td>
<td></td>
<td></td>
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<tr>
<td>BVI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B&amp;L</td>
<td></td>
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Company
- Allergan
- AMO
- TearLab
- NicoX
- BVI
- B&L
Sept. 2012 Update

<table>
<thead>
<tr>
<th>Drug</th>
<th>MDA</th>
<th>Company</th>
<th>Stage</th>
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</thead>
<tbody>
<tr>
<td>Lignocaine (1% HCl)</td>
<td>MDI</td>
<td>Johnson &amp; Johnson</td>
<td>Phase 2</td>
</tr>
<tr>
<td>OPI (1% HCl)</td>
<td>ALA</td>
<td>Allergan</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Topical cyclosporine (0.05%)</td>
<td>C5H8</td>
<td>Ciba</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Collagen hydrogel (2% collagen)</td>
<td>MDI</td>
<td>Integra</td>
<td>Phase 2</td>
</tr>
<tr>
<td>Reovirus (NT-II)</td>
<td>Synthesis Vaccine Corp.</td>
<td>Phase 2</td>
<td></td>
</tr>
<tr>
<td>Actoventra</td>
<td>Actoventra</td>
<td>Phase 2</td>
<td></td>
</tr>
<tr>
<td>Rho-endo (5%)</td>
<td>Rho-endo</td>
<td>Phase 2</td>
<td></td>
</tr>
<tr>
<td>Reovirus (1% reovirus)</td>
<td>Actoventra</td>
<td>Phase 2</td>
<td></td>
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What’s New In Ocular Surface Disease

- Possible Paradigm Shift In Methods of Evaluation
- Clinical Lab Testing
  - Osmolarity
  - Inflammation

What Happens When a Patient Doesn’t Respond to Conventional Therapy

- Frustration Sets In
  - Patient
  - Doctor

Multiple Goals

- Recalcitrant Cases of OSD
  - Where do you go from here?
- Compounding Pharmaceuticals
- Mechanical Therapy
Clinical Presentation Can Vary in Severity

Symptom Driven Questionnaire

Tear Function Screening Questionnaire

Standard Patient Evaluation of Eye Dryness (SPEED) Questionnaire

The Healthy Tear Film

**Consequences of Tear Composition Changes in CDE**

- Altered environment for ocular surface tissues
  - Increased osmolarity
  - Imbalanced growth factors and cytokines fail to promote normal epithelial growth
  - Poor viscosity can cause thin spots in tear film and tear breakup
- Ocular surface damage
  - Loss of cornal epithelial integrity
  - Squamous metaplasia of conjunctival epithelium

**Summary:**

- Immune-mediated inflammation of lacrimal glands and ocular surface
  - Cytokines in tears, altered tear composition
- Inflammation disrupts normal neuronal control of tearing
- Multiple triggers and predisposing factors

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**Ocular Surface Disease Testing**

- Evaluate Tear Meniscus
- NaFl Staining & Tear Break Up Time
- Lissamine Green Staining
- Meibomian Gland Expression
- Schirmer’s With Anesthetic or Quick Zone

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**ITF Recommendations: Severity Levels**

- **Dry Eye Severity Level**
  - Signs of Dry Eye

<table>
<thead>
<tr>
<th>Dry Eye Severity Level</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>General symptoms</td>
<td>Mild symptoms</td>
<td>Moderate symptoms</td>
<td>Severe symptoms</td>
<td>Extremely severe symptoms</td>
</tr>
<tr>
<td>Bacterial/ Conjunctival staining</td>
<td>Very mild</td>
<td>Moderate</td>
<td>Severe</td>
<td>Extremely severe</td>
</tr>
<tr>
<td>Corneal erosion</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
<td>Extremely severe</td>
</tr>
<tr>
<td>Tear Woes</td>
<td>Very mild</td>
<td>Moderate</td>
<td>Severe</td>
<td>Extremely severe</td>
</tr>
<tr>
<td>Other</td>
<td>Hydration balance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Example staining</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TFI score</td>
<td>≤ 15</td>
<td>16 to 35</td>
<td>36 to 55</td>
<td>≥ 56</td>
</tr>
</tbody>
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**Dry Eye Severity Level**

- **Symptoms of Dry Eye**

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<td>Severe symptoms</td>
<td>Extremely severe symptoms</td>
</tr>
<tr>
<td>Symptoms: sticky, sandy, gritty, dry</td>
<td>Never</td>
<td>Sometimes</td>
<td>Frequent</td>
<td>Always</td>
</tr>
<tr>
<td>Discomfort, swelling, burning, pain</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Vision Blurring, mismatched</td>
<td>No</td>
<td>No</td>
<td>Sometimes</td>
<td>Usually</td>
</tr>
<tr>
<td>Use of artificial tears</td>
<td>Less than 3 times per day</td>
<td>Several times per day</td>
<td>Several times per day</td>
<td>Several times per day</td>
</tr>
</tbody>
</table>

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*Photos courtesy of M. W. Belin, MD.*

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*INFLAMMATION*
### Progression of DTS Severity Levels

<table>
<thead>
<tr>
<th>LEVEL 1</th>
<th>Moderate to severe symptoms, no signs</th>
<th>Mild to moderate conjunctival signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEVEL 2</td>
<td>Marked corneal punctate staining</td>
<td>Central corneal staining</td>
</tr>
<tr>
<td>LEVEL 3</td>
<td>Severe symptoms</td>
<td>Marked corneal punctate staining</td>
</tr>
<tr>
<td>LEVEL 4</td>
<td>Extremely severe symptoms/ altered lifestyle</td>
<td>Severe corneal staining, erosion</td>
</tr>
</tbody>
</table>

### What is Dry Eye Disease?

**Official Definition:**

Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.

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### Need for a More Objective Dry Eye Test

- The importance of osmolarity
- The trend in point-of-care diagnostics
- Needs to be quick
- Needs to allow for minimal tear volume patients
- Needs to be easy for staff and patients

### Possible Paradigm Shift

- **Objective Lab Measurements of Ocular Surface Disease**

### Osmolarity as a Gold Standard

The measurement of tear film osmolarity arguably offers the best means of capturing, in a single parameter, the balance of input and output of the lacrimal system. It is clear from the comparison of the diagnostic efficiency of various tests for DED, used singly or in combination, that osmolarity provides a powerful tool in the diagnosis of DED and has the potential to be accepted as a gold standard for the disease.

Alan Tomlinson - Glasgow Caledonian University, UK

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### Hyperosmolarity in Dry Eye Diagnosis

**Dry Eye Diagnosis**

Scotch Bhains, Alan Tomlinson, Angus McIntyre, Charles Dickson, and Kevin Rumens

### Dry Eye Diagnosis

[Graph showing hyperosmolarity in dry eye diagnosis]
Hyperosmolarity & Ocular Surface Damage

Hyperosmolarity-Induced Apoptosis in Human Corneal Epithelial Cells Is Mediated by Cytokine c- and MAPK Pathways

Osmolarity Severity Analysis

Osmolarity is the only sign to become stable after Rx.

Osmolarity & Tear Film Instability in DED

Osmolarity in the Diagnosis of Dry Eye Disease

- Osmolarity is the "gold standard" test for Dry Eye
- 45 years peer reviewed research
- Osmolarity has been added to definition of Dry Eye
- Global marker of Dry Eye, indicating a concentrated tear film

Osmolarity Testing

Tear Film Instability in DED

Utility of TearLab™ in Clinical Trials & Disease Management

Testing for Inflammation

What is MMP-9?

Detecting Elevated Levels of MMP-9
InflammaDry

- Detects elevated levels of MMP-9 in tear fluid
- 10 minute in-office results
- Easy to use – can be performed by technicians or nurses
- Disposable – no additional equipment required

Limit of Detection: the normal level of MMP-9 in human tears ranges from 3-41 ng/ml

- Positive test result = MMP-9 ≥ 40 ng/ml
- Negative test result = MMP-9 <40 ng/ml

InflammaDry is CE Marked and commercially available in Europe. At this time, InflammaDry is pending 510(k) review by FDA and is not commercially available in the U.S.

How to Use InflammaDry: Four-step Process

1. Gently dab the Sample Collector in 6-8 locations on the palpebral conjunctiva (lower eyelid) to collect a tear sample. Do not use a dragging motion.
2. Snap the sample collector into the test cassette and press firmly where indicated.
3. Dip the test cassette into the provided buffer vial for 20 seconds. Replace the cap.
4. Read the results: 2 lines (1 red, 1 blue) = positive, 1 line (blue) = negative

Place for Conventional Testing?

- Value of Educational Testing
- Chronic and Progressive Disease Process
- Multiple Etiologies
- Multiple Modalities in Treatment

Evaluate Tear Meniscus