Dry Eye Disease – Simplifying the Complicated

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At the end of this presentation you should:

- Understand normal tear physiology
- Be aware of the impact dry eye has on patients
- Understand the pathophysiology of dry eye
- Understand the differences between different classes of drops
Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.

Redness

Irritation

Stinging

Sandy or Gritty Feeling

Foreign Body Sensation

Sensitivity to Light

Eye Fatigue

Blurriness

Excessive Tearing or Watering

Burning

Eye Fatigue

Eye Fatigue

Eye Fatigue

Eye Fatigue

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Eye Fatigue

Eye Fatigue

Eye Fatigue

Eye Fatigue
72% of Australians report at least one symptom of DRY EYE\(^1\)
Up to 82% of consumers attribute the causes of symptoms/eye problems to lie within their environment or lifestyle.

1. Market Research conducted by Ipsos on behalf of Alcon Laboratories Australia Pty Ltd in 2016. Sample size = 300
Optometrists Drive Recommendation

- Pharmacist recommended it
- Optometrist recommended it
- Online - Google search
- Instore - from a store staff member
- Online - review website
- Friend or family recommendation
- Other healthcare professional recommended it
- Ophthalmologist recommended it
- Conversation with friends or family
- Online - pharmacy website

% of respondents

Ref: Market Research conducted by GfK on behalf of Novartis Australia Pty Ltd in 2016. Sample size = 202
# Dry Eye & Quality of Life

<table>
<thead>
<tr>
<th>Condition</th>
<th>Utility Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild Dry Eye</td>
<td>0.81</td>
</tr>
<tr>
<td>Moderate Dry Eye</td>
<td>0.78</td>
</tr>
<tr>
<td>Moderate Angina</td>
<td>0.75</td>
</tr>
<tr>
<td>Severe Dry Eye</td>
<td>0.72</td>
</tr>
<tr>
<td>Severe Angina</td>
<td>0.71</td>
</tr>
<tr>
<td>Disabling Hip Fracture</td>
<td>0.65</td>
</tr>
<tr>
<td>Complete Blindness</td>
<td>0.33</td>
</tr>
</tbody>
</table>

0 = Death

Adapted from Schiffman

TFOS DEWS II Report (2017)¹

Two years for assembly
• 10 years since TFOS DEWS published

150 Experts From 23 Countries

12 Sub-Committees

11 Reports

650 Pages

The Tear Film & Dry Eye
Tear Film

Layer of lubricating substances that keeps corneal epithelium moist

Three components (2 layers):

- Lipid: prevents tear evaporation
- Aqueous: largest portion of the tear film’s volume that contains oxygen supply
- Mucin: helps to spread tears and stabilise tear film

Tear film functions: maintains health of ocular surface; preserves clear vision; is the primary source of nutrition, waste removal, and antibacterial action

Glycocalyx & Epithelial Cells

Corneal epithelial cell surface is hydrophobic

Glycocalyx

- Long chain ‘bottle brush’ molecules migrate out from microvilli to create a hydrophilic network
- Helps hold mucin to surface
- If damaged tear film is destabilised


Tear Film Instability


- Damaged glycocalyx reduces wettability
- Surface becomes hydrophobic
- Increased tear film instability and evaporation
- Lower TFBUT
The Vicious Cycle of Dry Eye Disease

The Vicious Cycle of Dry Eye Disease

Hyperosmolarity leads to release of inflammatory mediators (IM)

Lower TFBUT exacerbates hyperosmolarity

This causes goblet & epithelial cell loss and damages the glycocalyx

This leads to corneal punctate staining & tear film instability resulting in lower TFBUT

Dry Eye Management

According to the DEWSII 4-Step Suggested Treatment Algorithm
Step One

Lid Hygiene
- Lid Wipes better efficacy in managing blepharitis than baby shampoo

Heat
- >40°C for optimal warm compression

Nutrition
- Essential Fatty Acids

Environmental Changes
- VDU
- Air Conditioning

Ocular Lubricants
- Viscosity Agents
- Lipids

## Step Two: If Step One Inadequate

1. Non-preserved ocular lubricants to minimise preservative-induced toxicity
2. Tea tree oil treatment for Demodex (if present)
3. Tear conservation
4. Overnight treatments (such as ointment or moisture chamber devices)
5. In-office, physical heating and expression of the meibomian glands (including device-assisted therapies)
6. In-office intense pulsed light therapy for MGD
7. Prescription drugs to manage DED (or complications of DED)*
   - Topical antibiotic or antibiotic/steroid combination applied to the lid margins for anterior blepharitis (if present)
   - Topical corticosteroid (limited-duration)
   - Oral macrolide or tetracycline antibiotics

*Please note some of these therapeutic products may not be indicated in Australia for use in dry eye management

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## Next Steps

### Step Three

<table>
<thead>
<tr>
<th>Oral secretagogues*</th>
<th>Autologous/allogeneic serum eye drops*</th>
<th>Therapeutic contact lens options</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>• Soft bandage lenses</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Rigid scleral lenses</td>
</tr>
</tbody>
</table>

### Step Four

| Topical corticosteroid for longer duration^ | Amniotic membrane grafts | Surgical punctal occlusion | Other surgical approaches (eg tarsorrhaphy, salivary gland transplantation) |

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*Not currently available in Australia
^Not indicated for the treatment of dry eye in Australia

Eye Drops

Which one and why?
Viscosity–Enhancing Agents

**Cellulose derivative (CMC, HPMC)**
- Viscoelastic\(^1\), non-irritating\(^1\), can cause crusting on lids\(^1\), good ocular retention\(^1\) time but reduced compared to PEG/PG products\(^2\)
- Refresh\(^3\), Xailin\(^3\) Fresh\(^3\), Celluvisc\(^3\), BionTears\(^2\)

**Glycerin-containing**
- Lubricant as well as humectant\(^4\) (retains moisture). Shorter ocular retention time compared to PEG/PG products\(^2\).
- Optive\(^3\) Family\(^3\)

**Sodium Hyaluronate (SH)**
- SH is hypo-osmotic\(^4\), a derivative of hyaluronic acid\(^4\), which is non-Newtonian\(^5\)
- Hylo-Forte\(^6\)/Fresh\(^6\), Xailin\(^3\) HA\(^3\), Blink\(^3\) Family\(^3\), Systane\(^®\) Hydration\(^3\)

**Polyethylene Glycol (PEG) & Propylene Glycol (PG)**
- Intelligent delivery system of Systane\(^®\), balanced osmolarity\(^7\), PG is a humectant\(^4\), the combination forms a protective layer over mucous membranes\(^4\)
- Systane\(^®\) Family\(^3\)  *Systane Hydration not currently available in Australia  `Trademarks belong to their respective owners*

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3. Larson, T. Ocular Lubricants List Optician 2018
7. Dutescue et al Osmolarity of Prevalent Eye Drops Cornea 2015 vol. 34 Issue 5 p 5606

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Business Use Only | 26
Emulsion Products

Emulsions consist of oily droplets stabilised by surfactants or emulsifiers dispersed in an aqueous medium.

Most emulsions contain submicron-sized particles prepared with oils and emulsifiers.

Nano emulsions allow greater spreading.

May or may not contain phospholipids.


Preservatives

Step 1 in the DEWSII Suggested treatment algorithm involves the use of lubricants that can contain preservatives\(^1\), and that contain a lipid component when EDE is present\(^1\).

When Step 1 is insufficient and moving to Step 2 it is suggested to use non-preserved tear supplements\(^1\).

The Systane family of drops that contain preservatives use the preservative POLYQUAD\(^\circledR\)

- POLYQUAD\(^\circledR\) has been shown to have fewer side effects and be much better-tolerated in comparison to the traditional preservative, BAK\(^2\).
- A recent review suggested that when following the DEWSII treatment algorithm and using preserved drops it is best to use non-BAK alternate preservatives, such as POLYQUAD\(^\circledR\)\(^2\)

Dry Eye Management
### Intelligent Delivery System

<table>
<thead>
<tr>
<th>IN THE BOTTLE</th>
<th>Loosely cross-linked droppable gel</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HP-guar loosely cross links with borate</td>
</tr>
<tr>
<td></td>
<td>Sorbitol limits any further cross linking</td>
</tr>
</tbody>
</table>

*PEG isn’t an ingredient of SYSTANE® COMPLETE or SYSTANE® BALANCE*

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SYSTANE® COMPLETE

An all-in-one drop providing optimal coverage for dry eye relief\(^1-3\)

SYSTANE® COMPLETE combines the properties of:

- Systane® HP-Guar technology, which is known to enhance the effect of demulcents\(^4\)
- Nanosized lipid delivery technology\(^1\)

1. Alcon DOF Nanoemulsion for MGD, 2013, available on request.
3. Gokul A. Tear lipid supplement prophylaxis against dry eye in adverse environment 2018
SYSTANE® Ultra Lubricant Eye Drops\textsuperscript{1,2}

Demulcents: Polyethylene Glycol 400 and Propylene Glycol

Viscosity-enhancing agents: HP-Guar/borate, and sorbitol

Preservative: POLYQUAD®

Intelligent Delivery System$^{1,2}$

Summary

Relieve aqueous- and mucin-deficient dry eye
Relieve evaporative dry eye
Relieve multiple types of dry eye

Distribution of Dry Eye by Type

According to data from a cohort of 224 patients with dry eye disease published in 2012

- 10% Aqueous-deficient
- 35% Lipid-deficient
- 25% Combined lipid- and aqueous-deficient
- 30% Symptoms of unknown cause

Alcon