Diagnosis and Management of Dry Eyes

Dr. Aravind Roy, MS
LV Prasad Eye Institute
Poll Question 1

What is your position?

1. Ophthalmologist
2. Ophthalmologist-in-training (registrar/resident)
3. Nurse
4. Ophthalmic Technician / Allied Health
5. Medical Student
Figure 3.2 Components of the tear film produced by surface epithelium, lacrimal glands and conjunctival goblet cells that lubricate (MUC 1,4,6), protect from inflammation (TGF-β, IL1-receptor antagonist, tissue inhibitor of matrix metalloproteinase-1 (TIMP-1)), infection (IgA, lactoferrin, defensins), and promote healing (epidermal growth factor). (Reprinted with permission from Pflugfelder SC. Tear dysfunction and the cornea. LXVII Edward Jackson Memorial Lecture. Am J Ophthalmol 2011;152:900-9,e1.)
Poll Question 2

What are the layers of the tear film from surface downwards?

1. Lipid – aqueous – mucin
2. Mucin – lipid – aqueous
3. Aqueous – mucin – lipid
4. Lipid with mucus – aqueous gel
Figure 3.3 Schematic representation of the structure of the tear film. *Left:* Classic: Discrete three layered structure. Contemporary: An aqueous–mucin glyocalyx gel with a mucin gradient has been proposed. (This figure is taken from an article entitled, “McCulley JP, Shine W. A compositional based model for the tear film lipid layer” in the Trans Am Ophthamol Soc 1997; 95:79–88 and republished with permission of the American Ophthalmological Society.)
Tear film dysfunction

Figure 3.5 Alterations in tear film composition due to tear dysfunction include increased osmolarity and inflammatory cytokines, and CD4+ T cells that activate stress signaling pathways and upregulation of cytokines, chemokines, matrix metalloproteinases, and apoptosis induction. (Reprinted with permission from Pflugfelder SC. Tear dysfunction and the cornea: LXVIII Edward Jackson Memorial Lecture. Am J Ophthalmol. 2011;152:900–9.e1.)
Tear Film Osmolarity: Determination of a Referent for Dry Eye Diagnosis

Alan Tomlinson,¹ Santosh Khanal,¹ Kanna Ramaesh,² Charles Diaper,³ and Angus McFadyen⁴

October 2006
Vol: 47, Issue 10
Definition-
Multifactorial disease of the tears and ocular surface that results in symptoms of
- Discomfort
- Visual disturbance
- 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
Dry Eye Classification

Figure 6.5 Etiologic classification of dry eye disease. The list (bottom left) illustrates the environmental risk factors for dry eye disease. The scheme indicates the etiologic classification of dry eye disease into aqueous-deficient or evaporative tear deficiency. (From Krachmer et al., Cornea, 3rd ed, Mosby, Elsevier 2010. Figure 36.1.)
All the following are true of Sjogren’s syndrome except

1. Autoimmune disorder affecting the mucous membranes

2. Associated with dry mouth and dry eyes

3. Dryness of all mucosal surfaces

4. Minor salivary glands are involved

5. Presence of autoantibodies to Ro(SSA) and La(SSB) or both
# Manifestation of Sjogren’s Syndrome

**Table 6.2 Revised International Classification Criteria for Ocular Manifestations of Sjögren’s Syndrome**

I. **Ocular symptoms:** a positive response to at least one of the following questions:
   1. Have you had daily, persistent, troublesome dry eyes for more than 3 months?
   2. Do you have a recurrent sensation of sand or gravel in the eyes?
   3. Do you use tear substitutes more than three times a day?

II. **Oral symptoms:** a positive response to at least one of the following questions:
   1. Have you had a daily feeling of dry mouth for more than 3 months?
   2. Have you had recurrently or persistently swollen salivary glands as an adult?
   3. Do you frequently drink liquids to aid in swallowing dry food?

III. **Ocular signs:** that is, objective evidence of ocular involvement defined as a positive result for at least one of the following two tests:
   1. Schirmer I test, performed without anesthesia (≤5 mm in 5 minutes)
   2. Rose bengal score or other ocular dye score (≥4 according to van Bijsterveld’s scoring system)

IV. **Histopathology:** in minor salivary glands (obtained through normal-appearing mucosa) focal lymphocytic sialoadenitis, evaluated by an expert histopathologist, with a focus score ≥1, defined as a number of lymphocytic foci (which are adjacent to normal-appearing mucous acini and contain more than 50 lymphocytes) per 4 mm two of glandular tissue

V. **Salivary gland involvement:** objective evidence of salivary gland involvement defined by a positive result for at least one of the following diagnostic tests:
   1. Unstimulated whole salivary flow (≤1.5 mL in 15 minutes)
   2. Parotid sialography showing the presence of diffuse sialectasias (punctate, cavitory or destructive pattern), without evidence of obstruction in the major ducts
   3. Salivary scintigraphy showing delayed uptake, reduced concentration and/or delayed excretion of tracer

VI. **Autoantibodies:** presence in the serum of the following autoantibodies:
   1. Antibodies to Ro(SSA) or La(SSB) antigens, or both

(From Krachmer et al., Cornea, 3rd ed., Mosby, Elsevier 2010. Table 36.1.)
Aqueous Deficient Dry Eyes (ADDE)

- Aqueous deficient
  - Sjögren syndrome dry eye
    - Primary
    - Secondary
    - Lacrimal deficiency
    - Lacrimal gland duct obstruction
  - Non-Sjögren syndrome dry eye
    - Reflex block
    - Systemic drugs
Evaporative

Intrinsic
- Disorders of lid aperture
- Low blink rate
  - Meibomian oil deficiency
  - Drug action Accutane

Extrinsic
- Vitamin A deficiency
- Tropical drugs preservatives
- Contact lens wear
- Ocular surface disease, e.g. allergy
Aggravating factors

- Hot climate
- Exposure to chemicals
- Dust
- Smoke
- Prolonged Reading
- Prolonged use of computers
Clinical Signs

Features of blepharitis/meibomitis

- Tear film height is reduced
- Mucous debris or discharge
- Conjunctiva is lusterless
- Keratinisation
- SPKs
- Epithelial defects, plaques & filaments
Clinical Signs

Features of blepharitis/meibomitis
Clinical Signs

Features of blepharitis/meibomitis

Orifice Plugged with White Material
Complications

- Corneal thinning
- Perforation
- Infection
Diagnostic tests in Dry Eye

- Schirmer Test
- Tear film break up time
- Ocular surface staining
- Questionnaires OSDI
- Impression cytology
- Measurement of tear film meniscus
- Esthesiometry
- Ocular surface scraping
- Osmolarity
- Topography & Meibography
Which is the hallmark of dye eye disease

1. Abnormal Schirmer’s and TBUT
2. Staining pattern of Ocular surface
3. Impression cytology
4. Raised Osmolarity of tears
5. Presence of autoantibodies to Ro(SSA) and La(SSB) or both
Schirmer’s Test

- Common office procedure
- Wide variability under different testing conditions 8-33 mm
- In severe dry eyes values below 5 mm are of significance
Tear film break up time (TBUT)

- TBUT - time interval between the complete blink and appearance of the first dry spot
- Wide variability of results
- < 10 seconds suggests tear film instability and < 5 seconds suggests definite dry eyes
Ocular surface Staining

NEI/Industry workshop guidelines

6 areas of conjunctiva

5 areas of cornea
# Ocular surface staining - Grading Schemes

**Other grading schemes**

- Van Bijsterveld
- Oxford

<table>
<thead>
<tr>
<th>Method</th>
<th>Grading Areas</th>
<th>Scale</th>
<th>Maximum Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Bijsterveld</td>
<td>3: nasal bulbar conjunctiva, temporal bulbar conjunctiva, cornea</td>
<td>0–3</td>
<td>9</td>
</tr>
<tr>
<td>NEI/Industry Workshop guidelines</td>
<td>5 areas of cornea, 6 areas of conjunctiva</td>
<td>0–3 for cornea 0–3 for conjunctiva</td>
<td>15 for cornea, 18 for conjunctiva</td>
</tr>
<tr>
<td>Oxford Scheme</td>
<td>Based on comparison to standard panel</td>
<td>0–5 for entire ocular surface</td>
<td>5</td>
</tr>
</tbody>
</table>
Ocular surface Stains

- **Fluorescein stain** – Stains surface where cell to cell tight junctions are absent
- **Rose bengal** – Stains dead devitalized cells, causes burning/stinging
- **Lissamine Green** – As rose bengal but without stinging or affecting viability of cells
Ocular surface Stains

Table 7. DTS Panel approach ocular surface fluorescein staining patterns$^{a,b}$

- Severe keratoconjunctivitis sicca
- Moderate keratoconjunctivitis sicca
- Blepharitis
- Exposure keratopathy (thyroid eye disease, less likely, but)
- Medication toxicity (keratoconjunctivitis sicca, especially likely in a rigid gas)
- Contact lens-related keratitis
- Superior limbus keratitis
- Foreign body under lid
- Blepharitis

Ocular surface Stains

Table 8. DTS Panel approach ocular surface lissamine green/rose bengal staining patterns

<table>
<thead>
<tr>
<th>Mild presentation of: Keratoconjunctivitis sicca (classic pattern)</th>
<th>Moderate presentation of: Keratoconjunctivitis sicca (classic pattern)</th>
<th>Severe presentation with filaments (noted in green) of:</th>
<th>Mucus fishing syndrome</th>
<th>Superior limbic keratoconjunctivitis</th>
</tr>
</thead>
</table>

• *Curr. Opinion Ophthal. Vol 28, Supplement 1, 2017*
OSDI questionnaires

Ocular Surface Disease Index® (OSDI®)

Ask your patients the following 12 questions, and circle the number in the box that best represents each answer. Then, fill in boxes A, B, C, D, and E according to the instructions beside each.

<table>
<thead>
<tr>
<th>Have you experienced any of the following during the last week?</th>
<th>All of the time</th>
<th>Most of the time</th>
<th>Half of the time</th>
<th>Some of the time</th>
<th>None of the time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Eyes that are sensitive to light?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2. Eyes that feel gritty?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>3. Painful or sore eyes?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>4. Blurred vision?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>5. Poor vision?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Subtotal score for answers 1 to 5 (A)

### OSDI Questionnaires

Have problems with your eyes limited you in performing any of the following *during the last week?*

<table>
<thead>
<tr>
<th></th>
<th>All of the time</th>
<th>Most of the time</th>
<th>Half of the time</th>
<th>Some of the time</th>
<th>None of the time</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Reading?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>N/A</td>
</tr>
<tr>
<td>7. Driving at night?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>N/A</td>
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<tr>
<td>8. Working with a computer or bank machine (ATM)?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>N/A</td>
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<tr>
<td>5. Poor vision?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>N/A</td>
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**Subtotal score for answers 6 to 9:** (B)
### OSDI Questionnaires

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<th>Half of the time</th>
<th>Some of the time</th>
<th>None of the time</th>
<th>N/A</th>
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</thead>
<tbody>
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<td>10. Windy conditions?</td>
<td>4</td>
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<td>2</td>
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<td>0</td>
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<td>11. Places or areas with low humidity (very dry)?</td>
<td>4</td>
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<td>2</td>
<td>1</td>
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<td>N/A</td>
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<td>12. Areas that are air conditioned?</td>
<td>4</td>
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<td>N/A</td>
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**Subtotal score for answers 10 to 12**

\[(C)\]

Add subtotals A, B, and C to obtain D

\[(D)\]

**Total number of questions answered**

(do not include questions answered N/A)

\[(E)\]
Evaluating the OSDI® Score
The OSDI® is assessed on a scale of 0 to 100, with higher scores representing greater disability. The index demonstrates sensitivity and specificity in distinguishing between normal subjects and patients with dry eye disease. The OSDI® is a valid and reliable instrument for measuring dry eye disease (normal, mild to moderate, and severe) and effect on vision-related function.

Assessing Your Patient’s Dry Eye Disease
Use your answers D and E from side 1 to compare the sum of scores for all questions answered (D) and the number of questions answered (E) with the chart below.* Find where your patient’s score would fall. Match the corresponding shade of red to the key below to determine whether your patient’s score indicates normal, mild, moderate, or severe dry eye disease.

```
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<th>Number of Questions Answered</th>
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<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
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<tr>
<td>D from Side 1</td>
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</tbody>
</table>

*Values to determine dry eye severity calculated using the OSDI® formula.

\[
\text{OSDI}® = \frac{\text{sum of scores} \times 25}{\text{# of questions answered}}
\]
Visante OCT produces accurate measurements of tear height in a non invasive fashion with acceptable sensitivity, specificity, and reproducibility


Figure 7.6 Visante optical coherence tomography images. (A) Dry eye patient. (B) Healthy subject. A vertical 10 mm long scan across the corneal apex obtained immediately after a blink. Upper tear meniscus (UTM) and cornea (CO) are marked on the image. (C) Yellow lines delineate the corneal surface and lower lid margin. The green perpendicular line indicates the tear meniscus height (TMH) processed in the digital image software. Note the difference between the upper and lower TMH between the dry eye subject and healthy control.
Ocular Surface Scraping

(A) Keratinized epithelial cells (note keratin granules) that could be seen in dry eyes, superior limbic keratoconjunctivitis, or exposure keratopathy.

(B) Eosinophil (note bi-lobed nuclei and eosinophilic granules) that could be seen in vernal keratoconjunctivitis, atopic keratoconjunctivitis, or other allergic processes.

Osmolarity

• Increase in tear osmolarity is a hallmark of dry eye disease.

• TearLab Test- The clinician can easily collect and measure osmolarity in a 50 μL tear sample with minimal disturbance to the tear film.
Esthesiometry

• Cochet – Bonnet esthesiometer which consists of a fine nylon filament, the length of which can be adjusted to apply different intensities of stimuli.

• CRCERT – Belmonte esthesiometer- A non-contact air jet esthesiometer
<table>
<thead>
<tr>
<th>Mostly Consistent¹</th>
<th>Suggestive²</th>
<th>Unclear³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Older age</td>
<td>Asian race</td>
<td>Cigarette smoking</td>
</tr>
<tr>
<td>Female sex</td>
<td>Medications</td>
<td>Hispanic ethnicity</td>
</tr>
<tr>
<td>Postmenopausal estrogen therapy</td>
<td>Tricyclic antidepressants</td>
<td></td>
</tr>
<tr>
<td>Omega-3 and Omega-6 fatty acids</td>
<td>Selective serotonin reuptake inhibitors</td>
<td>Anticholinergics</td>
</tr>
<tr>
<td>Medications</td>
<td>Diuretics</td>
<td>Anxiolytics</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Beta-blockers</td>
<td>Antipsychotics</td>
</tr>
<tr>
<td>Connective tissue disease</td>
<td>Diabetes mellitus</td>
<td>Alcohol</td>
</tr>
<tr>
<td>LASIK and refractive excimer laser surgery</td>
<td>HIV/HTLV1 Infection</td>
<td>Menopause</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td>Systemic chemotherapy</td>
<td>Botulinum toxin injection</td>
</tr>
<tr>
<td>Hematopoietic stem cell transplantation</td>
<td>Large Incision ECCE and penetrating keratoplasty</td>
<td></td>
</tr>
<tr>
<td>Vitamin A deficiency</td>
<td>Low humidity environments</td>
<td>Acne</td>
</tr>
<tr>
<td>Hepatitis C Infection</td>
<td>Sarcoidosis</td>
<td>Oral contraceptives</td>
</tr>
<tr>
<td>Androgen deficiency</td>
<td>Ovarian dysfunction</td>
<td>Pregnancy</td>
</tr>
</tbody>
</table>

# Severity grading for dry eyes

<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>Discomfort, severity &amp; frequency*</td>
<td>Mild and/or episodic</td>
<td>Moderate episodic and/or chronic stress</td>
<td>Severe frequent or constant without stress</td>
<td>Severe and/or disabling and constant without stress</td>
</tr>
<tr>
<td>Visual symptoms</td>
<td>None or episodic</td>
<td>Annoying and/or activity limiting, episodic</td>
<td>Annoying, chronic and/or constant limiting activity</td>
<td>Constant and/or possibly disabling photophobia</td>
</tr>
<tr>
<td>Conjunctival injection</td>
<td>None to mild</td>
<td>None to mild</td>
<td>+/-</td>
<td>+/++</td>
</tr>
<tr>
<td>Conjunctival staining</td>
<td>None to mild</td>
<td>Variable</td>
<td>Moderate to severe</td>
<td>Severe, unless cornified</td>
</tr>
<tr>
<td>Corneal staining (severity/location)</td>
<td>None to mild</td>
<td>Variable and inferior</td>
<td>Marked, including central</td>
<td>Severe diffuse, unless cornified</td>
</tr>
<tr>
<td>Corneal/Tear signs</td>
<td>None to mild</td>
<td>Mild debris, ↓ meniscus</td>
<td>Filamentary keratitis, mucus clumping, ↑ tear debris</td>
<td>Filamentary keratitis, mucus clumping, ↑ tear debris, epithelial defect</td>
</tr>
<tr>
<td>Lid/meibomian glands</td>
<td>Variable</td>
<td>Variable</td>
<td>Frequent MGD</td>
<td>Trichiasis, MGD, irregularity, keratinization, symblepharon</td>
</tr>
<tr>
<td>TBUT (sec)</td>
<td>Variable</td>
<td>≤8</td>
<td>≤5</td>
<td>Immediate</td>
</tr>
<tr>
<td>Schirmer score (mm/5 min)</td>
<td>Variable</td>
<td>≤10</td>
<td>≤5</td>
<td>≤2</td>
</tr>
</tbody>
</table>

*Discomfort symptoms may be minimal or absent in levels 3 and 4 due to nerve degeneration.
eviren: environmental; MGD: meibomian gland disease.
Unstable tear film

→ Schirmer test
tear meniscus height

Aqueous tear deficiency

- Level 1
  - Lubricate, hydrate
  - Osmoprotect
  - n-3, n-6 EFA
  - Punctal plugs

- Level 2-4
  - Level 1 therapy + anti-inflammatory, protease
  - (steroid, CsA, TCN, AZM)
  - Serum/albumin
  - Punctal occlusion
  - PROSE

Aqueous normal

- MGD
  - Lid treatments
  - Stabilize tears
  - EFA
  - AZM
  - TCN
  - Steroid
  - CsA

- Altered distribution
  - Treat
  - Chalasis
  - Pinguecula
  - Pterygium
  - Salzmann nodule
  - Lagophthalmos
  - Exposure
Poll Question 5

Which lubricants is best for alleviating symptoms of Dry eye

1. Cellulose derivates - CMC, HPMC
2. CMC + Glycerin
3. Polyols - Polyethylene glycols
4. Polyvinyl alcohol - PVP
5. Hyaluronic acid
6. Oil based emulsions - castor oil and mineral oils
Evidence of superiority

Cochrane Library
Cochrane Database of Systematic Reviews

Over the counter (OTC) artificial tear drops for dry eye syndrome (Review)

Pucker AD, Ng SM, Nichols JJ
Artificial tears

- Artificial tears lubricate the ocular surface.
- Reduce tear osmolarity.
- Protect the ocular surface from desiccation.
- No distinct advantage in ocular surface protection has been found with any particular brand.
- The decision is based on preference and preservative.
Preservatives in artificial tears

- **BAK**
  - Disrupts epithelial tight junctions
  - Accelerates desquamation of epithelial cells
  - Promotes apoptosis in low concentration and necrosis in high concentration
  - Effect is worse in ADDE in presence of punctal plugs

- **Purite**
- **Sodium perborate**
- **Unit dose preservative free**
• Autologous serum contains mediators that support the proliferation, differentiation, and maturation of the normal ocular surface epithelium
• This is attributed to presence of
  – EGF
  – Vitamin A
  – Lysozyme
  – Fibronectin
  – TGF-beta
Autologous serum eye drops for dry eye (Review)

Pan Q, Angelina A, Marrone M, Stark WJ, Akpek EK
Punctal Occlusion

- Punctal occlusion should be considered for patients with aqueous tear deficiency and low tear volume.

- Dissolvable intracanalicular plugs can be placed into the canaliculus on a trial basis.

- Permanent punctal occlusion is most commonly performed with a disposable thermocautery or with a radiofrequency needle.
Methods

- Surgical
- Thermal
- Tamponade
Thermal

- Cautery
- Diathermy
- Laser

Destroys & shrinks the canalicular walls
Tamponade Methods

- Popular
- No Surgery
- Out patient procedure
Absorbable inserts

- HPMC - 18 hrs
- Collagen - 2 weeks
- Collagen implants
- Reduces outflow - 60 to 80%
Nonabsorbable

- Silicone
- HEMA
- Teflon

Topical anaesthesia

Puncta dilated
Two general styles

Arrow or umbrella

- Vertical portion
- Collar or ring on the top of the plug with narrow neck
- Collar
- Facilities retrograde plug removal
- Decreases the risk of plug migration
Fluted Funnel or Golftea

- Horizontal portion
- Removed in antegrade fashion by
- lacrimal irrigation
- Plugs are notorious for complications
Complications

• Irritation of conjunctiva and cornea
• Pruritis and discomfort
• Rupture of punctal ring
• Suppurative canaliculitis
• Canalicular stenosis
• Pyogenic granulomas
• Dacryocystitis
Complications

- Plug extrusion

- Biofilm formation
Punctal occlusion for dry eye syndrome (Review)

Ervin AM, Wojciechowski R, Schein O
Anti-inflammatory Therapy

- Cyclosporine A
- Corticosteroids
- Tetracycline
- Azithromycin
- Essential Fatty acids
Cyclosporine A (Cs A)

- Cyclosporine prevents T cell activation

- Cs A prevents ocular surface inflammation and apoptosis

- Topical cyclosporine has also been found to increase density of mucus-filled goblet cells in the conjunctiva

- Cs A is administered in twice daily dosing
Corticosteroids

• Potent immuno-suppressors which control ocular surface inflammation

• Low potency steroids are preferred viz. fluorometholone, low dex, loteprednol to avoid raised IOP

• Corticosteroids can be combined to anti inflammatory agents like Cs A
Tetracycline

- Tetracyclines have anti inflammatory effects
- Stabilizes the tear film
- Decreases meibomian gland dysfunction and rosacea
- Treats recurrent corneal erosions
Azithromycin

- Azithromycin applied to the lids may have an antibacterial effect on common agents of anterior blepharitis, including Staphylococcus.
- A number of studies have shown improvement in signs and symptoms of meibomian gland dysfunction.
Essential Fatty Acids

Clinical trials of nutritional supplements containing linoleic acid and/or GLA alone or combined with fish oil for treatment of dry eye have reported improvement in symptoms and/or signs.
Secretagogues

- Pilocarpine 1% Qid stimulates exocrine glands and improves corneal staining

- Less toxic reagents include- Cevimeline
Contact Lenses
PROSE
Prosthetic replacement of ocular system ecosystem

The fluid-filled reservoir hydrates the cornea and shields it from blink trauma, noxious environmental stimuli and inflammatory mediators in the tears.
Figure 3.3: Schematic representation of the structure of the tear film. Left: Classic: Decapitated three-layered structure. Contemporary: An aqueous-mucin glycosal gel with a mucin gradient has been proposed. This figure is taken from an article entitled, "McCulley JP, Sheehy MA. A computational based model for the tear film lipid layer" in the Trans Am Ophthalmol Soc. 1992; 91:79-88 and reprinted with permission of the American Ophthalmological Society.

Figure 4.1: Etiologic classification of dry eye disease. The list (bottom left) illustrates the environmental risk factors for dry eye disease. The scheme indicates the etiologic classification of dry eye disease into aqueous-deficient or evaporative tear deficiency. From McMonnies et al, Cornea, 3rd ed., Mosby, December 2010, figure 36.1.)

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