#### Management of Dry Eye

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Dry eye is one of the most frequently encountered ocular morbidities, a growing public health problem and one of the most common conditions seen by eye care practitioners.

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The International Dry Eye Workshop (DEWS) defined dry eye as a "multi-factorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage the ocular surface". It is accompanied by note ased osmolarity of the tear film and mammation of the ocular surface."

Female gender, Postmenopausal estrogen therapy, Low dietary intake of mega-3 fatty acids, Systemic diseases as arkinson's disease, sjogren syndrome etc, medications like antihistamines, antimucoma drugs, connective tissue disease, and refractive excimer laser surgery.

The goals of management are:

- Reducing or alleviating signs and symptoms of dry eye.
- Maintaining and improving visual function.
- Reducing or preventing structural damage.

#### Diagnosis

Detailed Ocular history and medical history are mandatory.

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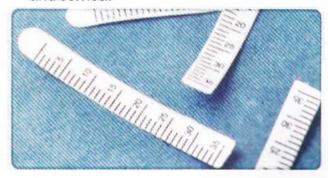
**Symptoms** include irritation, tearing, burning, stinging, dry or foreign body sensation, mild itching, photophobia, blurry vision, contact lens intolerance, redness, mucous discharge, increased frequency of blinking, diurnal fluctuation. symptoms worsen later in the day.

#### Exacerbating conditions:

Wind, air travel, decreased humidity, prolonged visual efforts associated with decreased blink rate such as reading.

#### **Examination:**

- Visual acuity measurement
- External examination: Skin, adnexa, eyelid, proptosis, cranial nerve dysfunction.
- Slit-lamp biomicroscopy: Tear film, eyelashes, eyelids, puncta, conjunctiva and cornea.



### Diagnostic tests:

- Schirmer's test: This is carried out with Schirmer's strip- Whatmann-41 paper 5mm x 35mm whose end is bent to adjust on the lid. Strip is placed between inner 2/3rd and outer 1/3rd of lid.
- Staining: Touch the temporal conjunctiva with a wet stain dipped filter paper and asks thepatient to blink few times and then stop blinking.

Types of Schirmer	Measures	Method	Inferences (based on wetting)
1	Reflex and basic secretion	Strip placed for 5 minutes. The Patient is asked to keep the eye open, look straight and slightly up, blinking is permissible.	<3mm= V Severe, 3-5mm= Severe 5-9mm= Mod, 10mm= Mild >10mm= Normal
2	Reflex secretion	If above test reveals <10mm, ipsilateral nasal mucosa is irritated with a small cotton swab	no wetting or <1mm Sjogren's syndrome >1mm it is non Sjogren's syndrome.
3	Basal secretion	Conjunctival sac is anaesthetised	<5mm= Dry 5-10mm= Equivocal >10mm= Normal

- Tear meniscus height: Height< 0.3 mm is suggestive of dry eye. It is measured with the slit lamp under a cobalt blue filter following instillation of fluorescein.
- 4) Lacrimal gland function test: Lactoferrin is the most abundant tear protein that is secreted by the lacrimal gland.<sup>2</sup> Tear lactoferrin concentrations have been reported to decrease in lacrimal gland dysfunction.
- 5) Other tests:
- i) Slit lamp fluorophotometry:
- ii) Meibometry: It is for noting the mucus gland dysfunction. Direct and indirect

- iii) Ocular protection index: It is TBUT time in seconds divided by inter-blink interval in seconds. OPI <1 = Patient at risk & OPI>1 =Patient not at risk
- iv) Tear Osmolarity: It is measured by taking 0.24 micro litres of tears and measuring the freezing point of dispersion. Normal = 302mOs/litre & in Dry eye = >350mOs/litre
- v) Closed chamber infrared thermometry:
  The temperature is recorded with eye closed and then after opening the eye after five seconds at fixed point & fixed distance from the eye. The temperature increased by 0.1°C after opening the eye is normal. No increase in temperature after opening the eyes seen in dry eye

Stain	Filter		
Fluorescein Stain 2%	Cobalt blue	Time taken between the last blink and appearance of a black in the tear film is the break up time in seconds.  Normal = >10 seconds  Gd-1 = 10 seconds, Gd-2 = 5-10 seconds  Gd-3 = 3-5 seconds, Gd-4 = < 3 seconds	

vi) Closed Chamber humidity of the eye: The humidity is measured with eye closed and then 5 seconds after opening of the eye. The difference in humidity in<1RH%

is normal and in dry eye it is >1RH% (1RH% to 4RH%). It is most reliable test, non-invasive, quick test for early diagnosis of dry eyes even when other tests declare normal values.

# Dry Eye Disease Treatment Guidelines Based on Disease Severity from the International Dry Eye Workshop (DEWS)<sup>3</sup>

Severity	Description
1	Education     Environmental/dietary modifications     Elimination of offending systemic medications     Artificial tear substitutes gels/ointments     Eye lid therapy
2	If level 1 treatments are inadequate, add  • Anti-inflammatories cyclosporine A topical corticosteroids tetracyclines (for meibomitis, rosacea)  • punctal plugs • secretagogues • moisture chamber spectacles
3	If level 2 treatments are inadequate, add
4	If level 3 treatments are inadequate, add  • systemic anti-inflammatory agents  • cyclosporine A  • Prednisolone  • Methotrexate  • infliximab  • surgery (lid surgery, tarsorrhaphy,mucus membrane, salivary gland, amniotic membrane transplantation)

# 1. Behavioural and environmental strategies

reservation of existing tears by reducing exact about reaction, such as learning to take breaks reading, lowering the computer reactive glasses with side pieces in outdoor and humidification of the entire ment, increasing blink frequency or assignificant process.

#### 2. Eyelid hygiene

Washing the eyelid margin with a gentle soap decreases bacterial colonization. Bacterial colonization is believed to inhibit conjunctival goblet cell proliferation and may also increase the breakdown of meibomian lipid. Reducing colonization, therefore, may improve both the mucous and lipid layers of the tear film.

#### 3. Tear substitutes

Cellulose ethers: Hypromellose, hydroxyethylcellulose, methylcellulose, carboxymethylcellulose (0.5%) - Viscoelastic Polysaccharides: (Just tears, Refresh Liquigel, CCS, SCM).

- Increase viscosity of tears.
- Good retention time on ocular surface.
- Only of benefit in aqueous tear deficiency.





Carbomers: polyacrylic acid- Synthetic polymers: (Viscotears)

- High viscosity when eye is static, shears thin during blinking or eye movement, maximizing thickness of the tear film while minimizing drag.
- Good retention time on ocular surface.
- · But tends to blur vision.

Polyvinyl alcohol- Synthetic polymer: (Liquifilm tears, D-eye, PVA Tears)

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- Low viscosity but optimal wetting characteristics at a concentration of 1.4%.
- Beneficial in lipid, aqueous and mucin layer deficiencies.
- Water soluble, does not cause visual blurring.
- · Has short retention time.

Sodium hyaluronate Mucopolysaccharides: (Lubristil)

- Viscous formulation
- · Good retention time on ocular surface
- Beneficial in corneal wound healing

Povidone (Polyvinyl pyrrolidone) - Synthetic polymer: (D-Eye)

- Co-formulated with electrolytes.
- Beneficial in mucin layer deficiency





Acetylcysteine:

· Breaks down mucin molecule.

- Can be co-formulated with another lubricant such as hypromellose.
- Useful in severe dry eye for complications resulting from dense mucus.
- · Not commercially available.

Electrolyte composition. Products that mimic the electrolyte composition of natural tearspotassium and bicarbonate appear to be the most important.<sup>4</sup>

Preservatives. Preservatives are added to artificial tears to reduce the risk of bacterial contamination in multidose containers, and to prolong shelf life.

There are 2 main types of preservatives: detergent and oxidative.<sup>5</sup>

Detergent preservatives act by altering bacterial cell membrane permeability. Detergents have toxic effects on the ocular surface epithelium and, with frequent use, can cause epithelial irritation and damage.

Patients with a compromised tear film are at higher risk. E.g. Benzalkonium chloride. 4.5

Oxidative preservatives penetrate the bacterial cell membrane and act by interfering with intracellular processes. They are sometimes referred to as "vanishing" preservatives because they dissipate on contact with the eye and, therefore, are less likely than detergents to cause ocular damage.<sup>5</sup> However, they may not always dissipate completely in DED patients because of decreased tear volume.<sup>2</sup> e.g. Stabilized oxychloro complex.

4. Anti-inflammatory therapy

Due to a newer understanding of the pathogenesis of dry eyes, use of anti-inflammatory medications is a paradigm shift in the treatment of dry eye.

 Cyclosporine (0.05%) (Restasis, Cyclomune)- Well known immunomodulator.

Preservatives	Advantages	Disadvantages
1) Benzalkonium chloride	<ul> <li>Chemically stable.</li> <li>Effective and fast acting against many micro-organisms.</li> <li>Does not degrade easily even at high temperature.</li> </ul>	<ul> <li>Can accumulate in ocular tissues causing cell death with frequent dosing.</li> <li>So frequency of use must not exceed 4-6 times daily.</li> </ul>
2) Sorbate	Useful for sensitive eyes and contact lens wearers due to infrequent adverse reactions	Limited antimicrobial activity     May cause punctate keratitis
3) Chlorobutanol	Antimicrobial action	Causes irritation in more than 50% users
4) Sodium perborate	<ul> <li>Low levels have good antimicrobial activity.</li> <li>Changes to oxygen and water on contact with tear film.</li> </ul>	Causes cell death within minutes even at low concentration
5) Polyquaternium-1	Has lesser effect on corneal epithelium than BKC.	Causes superficial epithelial damage
5) Stabilised oxychlorocomplex	<ul> <li>Oxidative preservative that is converted in to natural tear components in the eye.</li> <li>Antimicrobial activity.</li> <li>Safe and well tolerated.</li> </ul>	Least cytotoxic effects



FDA approved to increase tear production in patient whose tear production may be reduced by inflammation of the eye associated with kerato conjunctivitis sicca.

It reduces inflammation by preventing T cells from releasing cytokines.

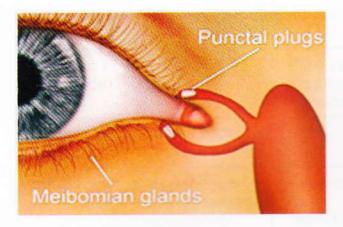
Cyclosporine therapy appears to address all three tear film components (aqueous, oil, and mucin). Unit dose vials (0.4 ml).

dosing=1 drop 2x daily.

- Topical corticosteroids are approved by the FDA and prescribed for corticosteroidresponsive inflammatory conditions of the conjunctiva, cornea and anterior globe—including DED.<sup>4</sup> Prednisolone is almost as potent and penetrates ocular tissues well. Other steroids, like loteprednol etabonate and fluorometholone, are less potent and have better safety profiles.
- Tetracycline: Oral doxycycline can be used in all patients with dry eyes who have significant component of meibomian gland disease.
- Essential Fatty Acids: necessary for complete health. 18 carbon omega-6 and omega-3 fatty acids.

#### 5. Punctal plugs

 Absorbable (collagen / various polymers) last for variable periods of time (3 days to 6 months).





- Non absorbable (silicone or hydrophilic)
- Thermoplastic (thermo sensitive, hydrophobic acrylic polymer)
- Hydrogel Plugs

Punctal plugs are indicated in patients who are symptomatic of dry eyes, have a Schirmer test (with anaesthesia) result less than 5mm at 5 minutes.

Contraindications to the use of punctal plugs include allergy to the materials used in the plugs to be implanted, punctal ectropion, and pre-existing nasolacrimal duct obstruction

Intracanalicular plugs-more invasive.



Surgical occlusion of punctum can be done using electro-cautery or laser.

#### 6. Tear stimulation Secretagogues:

They are cholinergic agonists that stimulate endogenous tear production by the lacrimal glands and/or ocular surface epithelia (e.g. oral pilocarpine). Diquafosol (one of the P2Y2 receptor agonists), rebamipide, gefarnate, ecabet sodium (mucous secretion stimulants),

and 15(S)-HETE (MUC1 stimulant).

7. Moisture spectacles/goggles:

Increase humidity around eye.

## 8. Autologous serum:

Serum and plasma contain many antiinflammatory factors which include inhibitors of inflammatory cytokines and inhibitors of MMPs and mediators of the ocular surface inflammatory cascade of dry eye.<sup>7</sup>

### 9. Silicone hydrogel lenses:

have high oxygen permeability and relatively low water content, may be used in severe dry eye or when other therapy has failed. Highly oxygen permeable materials enable overnight wear in appropriate circumstances.<sup>8</sup>

The Boston scleral lens is indicated for management of severe dry eyes due to Sjögren's syndrome & autoimmune diseases. Boston Scleral provides an oxygen permeable optical shell that fits under the lids and over the front surface of the eye. It fits on the sclera and immerses the eye in a pool of artificial tears. The fluid reservoir of the device masks the distorted surface of the cornea to improve vision and provides a protective cushion that reduces pain and photosensitivity caused by inflamed and irritated corneas.

There is a small risk of corneal vascularisation and possible corneal infection associated with the use of contact lenses by dry eye patients.

Scleral Lens

Liquid reservoir
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Transitional zone
Transitional zone

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For severe or refractory DED. Methods include:

- Short-term tarsorrhaphy- tape, adhesive glue (lasts a few days), or botulinum toxin (lasts an average of 16 days).
- Temporary tarsorrhaphy (4-6 weeks).9
- Permanent tarsorrhaphy. The lid margins are excised and sutured so that they heal together. The procedure can be reversed.<sup>9</sup>

Amniotic membrane transplantation is recated in persistent epithelial defects responsive to medical treatment.

#### Salivary Gland Auto transplantation

scapable of replacing deficient mucin and the aqueous tear film phase. This procedure equires collaboration between an approach almologist and a maxillofacial surgeon.

#### Parotid duct transplantation

Should be considered in dry eyes especially caused by Stevens-Johnson syndrome.

The early detection and timely management of this syndrome is important, as they can

help prevent long-term sequelae and sightthreatening complications.

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Human eye blinks on average of 4,200,000 times each year.



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