Dry eye disease is a major healthcare problem due to its increasing prevalence as well as its impact on the quality of life of patients, healthcare resources and the economy. It is now becoming evident that this previously unrecognized condition should be regarded as a serious public health problem that is worthy of prompt diagnosis and effective treatment. Thorough evaluation is essential to identify the type of dry eye and decide on the optimal treatment for each patient.

In this article we will discuss the various clinical and laboratory investigations currently in practice for the diagnosis of dry eye and introduce newer diagnostic modalities and also discuss the different treatment options available for the management of dry eye.

Diagnosis

1. Tear film break up time (BUT) – BUT is the time interval between the last blink and appearance of randomly distributed dry spots in a fluorescein stained tear film. < 6 seconds - suggests evaporative dry eye.

2. Schirmer’s test: Test with topical anaesthesia is more reliable in clinical practice. Inference - > 15 mm - normal, 6 to 10 mm - borderline dry, < 6 mm - impaired secretion.

3. Rose Bengal staining – The dye has an affinity for dead or devitalized epithelial cells and for areas devoid of mucus. Van Bijsterveld scoring system – divide the ocular surface into three zones:
   - Nasal bulbar conjunctiva.
   - Cornea
   - Temporal bulbar conjunctiva.

Each zone is then given a score of ‘0’ (no stain) to ‘3’ (confluent stain). Scores in each eye is totaled. A score of 3.5 or greater indicates positive for keratoconjunctivitis sicca. This test can give false negative results in mild or very early cases of dry eye.

Lissamine green stains healthy epithelial cells not protected by mucin (like Rose Bengal) and also degenerated and dead cells (as in fluorescein). There is less discomfort and toxicity but the effect is too transient to appreciate.

4. Tear osmolarity – A hand drawn micropipette or 0.2 microlitre microcap is used to collect 0.1 to 0.2 microlitre of tear from the inferior marginal tear strip by capillary action taking care not to touch the ocular surface, and tested directly on the Osmometer. The normal tear osmolarity is approximately 302 mOsm/L. A reference or cut off value of approximately 312 mOsm/L is indicative of pathology.

5. LipiView ocular surface interferometer¹ – (Figure 1) PRINCIPLE – white light interferometry
   - Provides an interferometry colour assessment of the tear film by specular reflection
   - Measured in interferometric colour units (ICU) (Figure 2).
   - ICU is the colour scale resulting from the interference pattern which occurs at the boundary of the tear film.
   - LipiView uses advanced interferometric technology and captures detailed digital images of the eye’s
tear film to assess the oily lipid layer of tear film (Figure 3).

- LipiView ≤ 70 is considered abnormal (Figure 4).


a) Meibography\(^2\) - shows the morphological changes in the glandular tissue.

b) Non invasive keratograph break up time (NIKBUT) – maps the tear film break up time (Figure 5).

c) Measurement of tear meniscus height using calipers (Figure 6).

d) Evaluating the particle flow characteristics - A video recording with up to 32 images per second enables the observation of the tear film particle flow characteristics and shows the tear film viscosity.

7. Meibomian gland evaluation - Performed with the help of a meibomian gland evaluator which is a hand-held tool used for evaluating meibomian gland secretions. It is designed to deliver consistent gentle pressure, through the eyelid, to the meibomian glands, to mimic the forces of a deliberate blink and to express meibomian secretions. The evaluator is placed onto
the outer lid skin immediately below the lash line and depressed about half way and its position adjusted so that a clear view of the meibomian gland orifices is obtained. Documentation is done as to how many meibomian glands yield liquid secretion during the expression. A total score of < 4 glands secreting clear oil is considered to be a significant blockage of meibomian gland orifices (Figures 7,8,9,10).

8. Tear film cytokines: Increased levels of inflammatory mediators in tears like interleukin (IL)-6,4,10, interferon Y (INF Y), tumour necrosis factor factor α (TNF α) - proves the inflammatory pathology in dry eye. Increased inflammatory mediators are seen with increasing severity of dry eye. This makes the basis for anti-inflammatory therapy in dry eye.

9. Other tests:
   a. Lysosyme assay – normal 1-3mg/ml. Decreased in dry eye disease.
   b. Lactoferrin - normal 2-3mg/ml - has significant antibacterial activity – measured by lactocord solid phase Enzyme Linked Immunosorbert Assay (ELISA) technique. Decreased in Sjogren’s syndrome.
   c. Conjunctival impression cytology -
      • To do quantitative measurement of goblet cells & qualitative assessment of epithelial morphology.
      • To monitor progression of ocular surface change.
      • Nitrocellulose membrane is pressed against bulbar or tarsal conjunctival surface. Three features are observed namely loss of goblet cells, increased nucleo-cytoplasmic ratio and keratinization.

Treatment
Delphi panel consensus for dry eye management

A. Supportive measures
   • Use of room humidifiers.
   • Avoid extreme/harsh environmental conditions.
   • Avoid drugs causing dry eye.
   • Moist chamber spectacles.
   • Contact lens.

B. Medical management
1. Artificial tear substitutes (prefer preservative free) - to be used regularly and frequently (Table 1).
   • Dose: hourly in severe dry eyes, 4-6 times a day in moderate cases. Preservative free drops should be used to prevent epithelial toxicity.
   • Provides only temporary relief and have not been found to reverse conjunctival squamous metaplasia
Ocular Surface Disorder

Figure 8: Normal meibomian gland secretions

Figure 9: Meibomian gland secretions in Meibomian gland disease (MGD)

Figure 10: Meibomian gland evaluation grading
Ocular Surface Disorder

Contains:
- Polymer and preservative
- 0.9% NaCl for tonicity
- Buffers like boric acid

2. Gels (carbomers) require less frequent application than drops.

3. Ointments using petrolatum, lanolin and mineral oil base, dissolve at the temperature of ocular tissue, retained in the cul-de-sac for long - used mainly at night time.

4. Tetracyclines are used for meibomitis.

5. Anti-inflammatory agents - As artificial tears do not directly inhibit the ocular surface inflammation in dry eyes, anti inflammatory therapy has to be considered for patients with:
   - A stagnant and unstable tear film who continue to have symptoms that are not relieved by artificial tears.
   - Corneal epithelial disease.
   - Drug used is - Cyclosporine 0.05%-0.1% - two to four times a day.

6. Botulinum toxin injection is given in lagophthalmos, eyelid retraction, exposure and neurotrophic keratopathy.

7. Soft contact lens to be used in conjunction with tear substitutes.

8. Newer treatment modalities -
   - Ocular inserts\(^6\) -
     - Cylindrical rod containing 5mg Hydroxypropyl methyl cellulose (HPMC) placed in the lower cul-de-sac.
     - Imbibes fluid and swells
     - Lasts for 12 -24 hrs
   - Secretagogues
     - Stimulate endogenous tear production
     - Oral pilocarpine (Salagen) 5mg four times a day\(^7\) – cholinergic side effects.
     - Cevimeline – Fewer side effects.
   - Mucolytic agents as acetylcysteine 5% drops used in patients with corneal filaments and mucous plaques.
   - Autologous serum drops [diluted 1:3 with saline] have reported to reduce ocular irritation and conjuntival and corneal dye staining in Sjogren’s syndrome associated aqueous tear deficiency.

C. Surgical management

1. Lateral tarsorrhaphy- reduces evaporation of tears by decreasing the exposed surface area in the interpalpebral fissure.

2. Punctal plugs\(^8\) - (temporary)
   - Description
     - Placement of a silicone or collagen plug into the punctum to prevent tears from draining out of the eyes and into the nose through the lacrimal duct.
   - Correct size plug is selected by the practitioner and inserted either with or without punctal dilation.
   - Indication - Moderate dry eye that is unresponsive to drug therapy
   - Complications
     - Epiphora (excessive tearing) in some patients due to less punctal drainage (early).
     - Possible chronic epiphora if the plug is lost in the canaliculus; dacryocystorhinostomy could be required to restore the patency of lacrimal drainage system (late).

3. Punctal cautery - (permanent)
   - Description
     - Cautery is applied directly to the punctum to destroy the drainage pathways of tears out of the eyes and into the nose.
   - Local anesthetic may be used.
   - Indication - Chronic, severe dry eye that has not improved by lubricants or cyclosporine. Usually, these

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**Table 1: Tear substitutes**

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<tr>
<th>Polymer</th>
<th>Properties</th>
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<tr>
<td>Cellulose esters (Hyperomellose 0.3-1%, Hydroxyethylcellulose, Methylcellulose 0.1-1%, Carboxymethylcellulose)</td>
<td>Increases the viscosity of tears&lt;br&gt;Closely resembles natural tears</td>
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<tr>
<td>Polyvinyl alcohol</td>
<td>Optimal wetting properties at 1.4%</td>
</tr>
<tr>
<td>Povidone 0.6%</td>
<td>Superior wetting when co-formulated with polyvinyl alcohol</td>
</tr>
<tr>
<td>Carbomers (polyacrylic acid)</td>
<td>High molecular polymers of acrylic acid&lt;br&gt;High viscosity when eye is static, shears and thins with eye movement and blinks&lt;br&gt;Increased retention when combined with polyvinyl alcohol</td>
</tr>
<tr>
<td>Hyaluronic acid, Chondroitin sulfate 0.1%</td>
<td>Glycosaminoglycan disaccharide biopolymers&lt;br&gt;Long retention times</td>
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patients would have had punctal plugs that routinely fall out of the punctum, requiring regular replacement by new plugs.

- Complications
- Infection (rare)
- Epiphora

4. Salivary gland transplant\(^9\) - in cases of severe dry eye, transplantation of minor salivary glands or the parotid duct.

5. Treatment of associated conditions
- Blepharitis - Adequate lid hygiene and antibiotic therapy.
- Eyelid malpositions like entropion, ectropion due to aging, eyelid scarring in ocular surface disease and congenital malformations to be treated.
- Ocular surface reconstruction - In Stevens Johnson syndrome, Ocular cicatricial pemphigoid, chemical or thermal burns using:
  - Mucous membrane graft (current gold standard as it has its own epithelium).
  - Amniotic membrane graft.
  - Limbal stem cell graft.
  - Meibomian gland dysfunction - warm compresses, lid massage, lubricants, topical and oral tetracyclines.

6. Newer treatment modality: Lipiflow Thermal Pulsation System\(^10\) (Figure 11, 12).
  - Application of localized heat and pressure therapy in patients with meibomian gland dysfunction (evaporative or lipid deficiency dry eye).
  - Provides controlled, outward directional heat and intermittent pressure therapy to eyelids to facilitate release of lipid from the cystic meibomian glands.

**Summary**

**Step 1.** Evaluation of symptoms and also ask for history of any other systemic disease, allergic status, duration and change in symptoms with day progression, environment, and seasons.

**Step 2.** Make sure to rule out meibomian gland duct obstruction or dysfunction, and any significant lid or ocular pathology.

**Step 3.** Perform the investigations and interpret results so as to reach the right diagnosis and estimate severity of disease.

**Step 4.** Decide the line of treatment.

**References**