1. Introduction
The term dry eye syndrome or dry eye disease has been described as a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbances 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 (Dry Eye Work Shop –DEWS,2007). Dry eye represents a disturbance of the lacrimal functional unit, an integrated system composed of the lacrimal glands, ocular surface (cornea, conjunctiva, eye lids and the meibomian glands) with the sensory and motor nerves that connect these structures. The overall function of the lacrimal functional unit is to preserve tear film integrity, ocular surface health, maintaining corneal transparency and surface stem cell population, thereby significantly influencing the quality of images projected onto the retina. Decreased tear secretion, delayed tear clearance from the ocular surface and altered tear composition may compromise tear film stability, sometimes accompanied by ocular inflammation. Disturbances integral to the lacrimal functioning unit are considered to pay an important role in evolution of different forms of dry eye.

2. Disease Definition
Dry Eye Syndrome or Dry Eye Disease refers to a group of disorders of the ocular tear film attributed to reduced tear production or excessive tear evaporation, associated with ocular discomfort and /or visual symptoms with possible disease of the ocular surface.

3. Epidemiology & Prevalence of Dry eye disease
Epidemiological information on dry eye syndrome has been limited by lack of uniformity in its definition and the inability of any single diagnostic test or set of diagnostic tests to confirm or rule out the condition. Dry eye syndrome is a common condition that causes varying degrees of discomfort and disability. While clinic-based studies confirm its frequency (17% of 2127 consecutive new outpatients were diagnosed with dry eye following comprehensive examination), such studies may not reflect the overall population. In a population-based sample of 2520 elderly (65 or older) residents of Salisbury, Maryland, USA, 14.6% were symptomatic, which was defined as reporting one or more dry eye symptoms often or all the time. The combination of being symptomatic and having a low Schirmer test (≤5 mm with anesthesia) or a high rose bengal score (≥5) was seen in 3.5% of the residents. A population-based study of dry eye conducted in Melbourne, Australia, using different diagnostic criteria reported higher percentages of the 926 participants aged 40 to 97 who had a low Schirmer test (16.3% ≤8 mm)or a high rose bengal score (10.8% ≥ 4).There is no population-based study in relation to dry eye disease in India. However, there are three published reports on prevalence of dry eye among hospital-based population from North and Eastern India and the prevalence varies between 18.4% and 40.8%. A study from higher altitudes reported a higher prevalence of 54%. Since these data are hospital based, they are likely to overestimate the prevalence of dry eye.
Section 4 - Recommendations

1. Diagnosis
2. Management
3. Provider & Setting
4. Counseling & Referral
5. Prevention

Clinical Pathway 1
Overview of Dry Eye Disease Management

Quick Reference Guide (QRG) for Dry Eye

1. Patient presenting with Dry Eyes

2. Clinical Assessment
   a. History taking
   b. Visual acuity
   c. Comprehensive slit lamp examination

3. Diagnostic tests
   1. Ocular surface dye staining
   2. Tear break-up time
   3. Aqueous tear production
   4. Fluorescein clearance test/tear function index

4a. Aqueous Tear Deficiency (ATD)

5a. Sjogren’s
   - Primary/Secondary

5b. Non-Sjogren’s
   - Lacrimal deficiency
   - Lacrimal gland duct obstruction
   - Reflex Block
   - Systemic drugs
   - Deficiency

7a. Severe, Resistance to treatment
   Frequent worsening

7b. Mild, Response to Treatment

8a. Treatment
   - Rheumatology consult
   - Salivary gland biopsy
   - Anti-Inflammatory
   - Autologous serum
   - Punctal Occlusion
   - Tarsorrhaphy

4b. Evaporative Tear Deficiency (ED)

6a. Intrinsic
   - Meibomian oil deficiency
   - Disorders of Lid Aperture
   - Low Blink Rate
   - Drug Action e.g. Isotretinoin

6b. Extrinsic
   - Vitamin A deficiency
   - Topical Drugs /Preservative
   - Contact Lens Wear
   - Environmental Factors e.g. humidity, Allergy

7c. Good Response treatment
   Mild/Moderate

8b. Treatment
   - Environmental Modification
   - Warm Compress/Lid Hygiene
   - Tetracycline
   - Tear Substitutes
Prevention of Dry Eye Disease

1. Prevent/Reduce Symptomatology or severity of Dry eye disease
2. Assess risk factors for dry eye disease
3. Educate patients on modification of environmental risk factors
4. Management of dry eye disease based on severity
4.1 Diagnosis of Dry Eye Syndrome

Table 1: Risk Factors for Dry Eye Disease

<table>
<thead>
<tr>
<th>High level of evidence</th>
<th>Moderate level of evidence</th>
<th>Low level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Medications - Tricyclic</td>
<td>Smoking</td>
</tr>
<tr>
<td>Female Sex</td>
<td>antidepressants,</td>
<td>Hispanic ethnicity</td>
</tr>
<tr>
<td>Postmenopausal estrogen therapy</td>
<td>selective serotonin</td>
<td>Anti cholinergic drugs-</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>reuptake inhibitors,</td>
<td>anxiolytics &amp;</td>
</tr>
<tr>
<td>Collagen vascular disease</td>
<td>diuretics, beta blockers.</td>
<td>antipsychotics</td>
</tr>
<tr>
<td>Corneal refractive surgery</td>
<td>Diabetes mellitus</td>
<td>Alcohol</td>
</tr>
<tr>
<td>Irradiation</td>
<td>HIV/HTLV1 infections</td>
<td>Menopause</td>
</tr>
<tr>
<td>Hematopoietic stem cell transplantation</td>
<td>Systemic chemotherapy</td>
<td>Botulinum toxin injection</td>
</tr>
<tr>
<td>Vitamin A deficiency</td>
<td>Cataract surgery with a</td>
<td>Acne</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>large incision</td>
<td>Gout</td>
</tr>
<tr>
<td>Androgen deficiency</td>
<td>Keratoplasty</td>
<td>Oral contraceptives</td>
</tr>
<tr>
<td></td>
<td>Isotretinoin</td>
<td>Pregnancy</td>
</tr>
</tbody>
</table>


4.1.1. Identify characteristics of the causative factors, such as adverse environments, prolonged visual efforts, or ameliorating circumstances, which is helpful in diagnosing dry eye.

4.1.2. Use supporting clinical observations and tests to confirm diagnosis of dry eye.

4.1.3. Question about patient symptoms and signs, exacerbating conditions, duration of symptoms and ocular history to elicit helpful information.

4.1.4. Pay particular attention to the skin, eyelids, adnexa, proptosis, cranial nerve functions, mouth, skeletal system and hands.

4.1.5. On slit lamp biomicroscopy evaluation, focus on the tear film, eye lashes, anterior and posterior eyelid margins, puncta, conjunctiva and cornea. Pay particular attention to Meibomian gland dysfunction in evaluation of tear film.
4.1.6. Test for anti-thyroid and anti-thyroglobulin antibody in dry eye patients suspected of thyroid eye disease.

4.1.7. Order a B-Scan sonogram or other imaging study to assess extra ocular muscle thickness in patients with dry eye who have suspected thyroid eye disease.

4.1.8. Recommend/Perform conjunctival biopsy for dry eye patients who have significant chronic conjunctivitis with a nodular appearance or cicatrisation.

*Figure 1-Severe Blepharitis is a major risk factor for Dry eye disease (See Recommendations 4.1.4 and 4.1.5)*
Figure 2: Filamentary Keratitis in Recurrent Dry Eye Disease

Figure 3 – Severe Dry eye with corneal scarring, vascularization and characteristic Conjunctival folds with significant reduction in tear film

Clinical Pathway 3

Diagnostic Classification of Dry Eye Disease
4.1.9. For patients with moderate to severe aqueous tear deficiency, establish the diagnosis by using one or more of the following tests: Tear break-up time test, ocular surface dye staining and Schirmer test.

4.1.10. Perform these tests in this sequence because the Schirmer test can disrupt tear film stability and cause false positive ocular surface dye staining.

Clinical Pathway 4

Practical Sequence of Dry eye Tests

Figure 4

Schirmer’s Test to assess Tear film. Results less than 10 mm without anaesthesia considered abnormal. Consistently low Schirmer test readings are suggestive of aqueous tear deficiency.

Figure 5- Fluorescein Dye staining of cornea and Conjunctiva in mild to moderate Dry eye disease.
4.1.11. Allow several minutes between the dye testing and the Schirmer test

4.1.12. Assess corneal sensation when trigeminal nerve dysfunction is suspected

4.1.13. Consider a laboratory and clinical evaluation for autoimmune disorders for patients with significant dry eye, other signs and symptoms of an autoimmune disorder or a family history of an autoimmune disorder

4.1.14. Consider testing for an underlying Sjogren Syndrome in patients with moderate punctate staining of the cornea and/or conjunctiva as these patients will require a multidisciplinary approach.

4.1.15. Evaluate aqueous tear production with the Schirmer test. It gives variable results and do not use as the sole criterion for diagnosing dry eye.

Table 2-Classification of Dry Eye Severity

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discomfort</td>
<td>Mild/ Episodic</td>
<td>Moderate, episodic or chronic with or without stress</td>
<td>Severe, frequent, or constant without stress</td>
<td>Severe and/or disabling and constant</td>
</tr>
<tr>
<td>Visual Symptoms</td>
<td>None or episodic</td>
<td>Annoying and/or limiting activity episodic</td>
<td>Annoying, chronic/constant Limiting activity</td>
<td>Constant, possibly disabling</td>
</tr>
<tr>
<td>Clinical Signs</td>
<td>None to mild</td>
<td>None to mild, may or may not have staining, reduced tear meniscus, TBUT &lt; 10</td>
<td>Moderate to marked conjunctival staining, marked central corneal staining, filamentary keratitis, TBUT &lt; 5, Schirmer score &lt; 5</td>
<td>Conjunctival injection &amp; marked staining, severe punctate erosions, scarirng, almost immediate TBUT, Schirmer Score &lt; 2</td>
</tr>
</tbody>
</table>
Based on 2007 International Dry Eye Workshop (DEWS) Report
Clinical Pathway 5

Treatment Algorithm for Dry Eye Syndrome Management

1. Artificial Tears with preservative, 4 times a day
2. Preservative Free Ointment Qhs With Patch During Sleep For Nocturnal Lagophthalmos
3. Preservative free Tear Substitute Increase in frequency as needed
4. Occlusive spectacles, side shields, Goggles, Vaporizer / Avoid heat, wind,
5. 10% Acetylcystein in case of Excess mucus
6. Topical Corticosteroids or Cyclosporine to treat inflammation
7. Temporary Punctal Occlusion
8. Autologous Serum Tears
9. Contact lenses
10. Permanent Punctal Occlusion
11. Lateral Tarsorrhaphy
4.2. Management of Dry Eye

Clinical Pathway 6 - Overview of Dry Eye Management
Treatment of Mild Dry Eye

4.2.1. Place patients who have suggestive symptoms without signs on trial treatments with artificial tears when other potential causes of ocular irritation have been eliminated.

4.2.2. For patients with a clinical diagnosis of mild dry eye, address potentially exacerbating exogenous factors such as anti histamine or diuretic use, cigarette smoking and exposure to second hand smoke, and environmental factors such as air drafts and low humidity environments.

4.2.3. Suggest measures such as lowering the computer screen to below eye level to decrease lid aperture, scheduling regular breaks, and increasing blink frequency to decrease the discomfort associated with computer and reading activities.

4.2.4. Prescribe emulsions, gels and ointments to treat dry eye symptoms.

4.2.5. Increase use of artificial tears as required, but recommend frequent tear instillation depending on the lifestyle or manual dexterity of the patient.

4.2.6. Prefer Nonpreserved tear substitutes; however, you may recommend tears with preservatives for patients with mild dry eye and otherwise healthy ocular surface.

4.2.7. Prescribe non preserved tears when tear substitutes are frequently and chronically used.

4.2.8. Use Systemic Doxycycline in patients with evidence of Meibomian gland dysfunction.

4.2.9. Correct eye lid abnormalities resulting from blepharitis.

4.2.10. Correct eye lid abnormalities resulting from trichiasis.

4.2.11. Correct eyelid abnormalities resulting from lid malposition.
Clinical Pathway 7
TREATMENT RECOMMENDATIONS FOR DRY EYE SYNDROME BY DISEASE SEVERITY LEVEL
(Adopted from AAO Preferred Practice Pattern 2013, Dry Eye Syndrome


Mild Dry Eye

Moderate Dry Eye

- In addition to above treatments:
  - Anti-inflammatory agents (topical cyclosporine and corticosteroids),
  - Punctal plugs
  - Spectacle side shields

Severe Dry Eye

- Systemic anti-inflammatory agents
- Mucolytic agents
- Autologous serum tears
- Contact lenses
- Permanent punctal occlusion
- Tarsorrhaphy

Â Education and environmental modifications
Â Elimination of offending topical or systemic medications
Â Aqueous enhancement using artificial tear substitutes, gels/ointments
Â Eyelid therapy (warm compresses and eyelid scrubs)
Â Treatment of contributing ocular factors such as blepharitis or meibomianitis
Â Correction of eyelid abnormalities

**Treatment of Moderate Eye Disease**

4.2.12. Use low dose topical corticosteroid therapy at infrequent intervals for short period of time (i.e., several weeks) to suppress ocular inflammation

4.2.13. Monitor patients prescribed corticosteroids for dry eye for adverse effects such as increased intraocular pressure and cataract formation

4.2.14. Do not routinely recommend omega-3 fatty acid supplements for dry eye treatment since there is no evidence of their efficacy

4.2.15. Consider punctual occlusion for patients with aqueous tear deficiency when medical means of aqueous enhancement are ineffective or impractical

4.2.16. Punctal plugs are not routinely recommended for dry eye management in India owing to their relatively high cost. Punctal occlusion by thermal cauterization is preferred for patients with aqueous tear deficiency resistant to medical and conservative measures of treatment

4.2.17. Use non invasive therapies like Eye glass side shields and moisture chambers
Clinical Pathway 8- Artificial Tear Substitutes in Management of Dry Eye Disease

<table>
<thead>
<tr>
<th>Mild Dry Eye Stage I</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Low viscosity eye drops based on Polyvinyl Alcohol (PVA), Polyvinyl Pyrrolidine (PVP) with Preservative</td>
</tr>
<tr>
<td>• Frequency of application &lt; 4 times daily</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Moderate Dry Eye Stage Ia</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Low viscosity eye drops with PVA without preservatives</td>
</tr>
<tr>
<td>• PVP without preservatives</td>
</tr>
<tr>
<td>• Low viscosity cellulose derivatives</td>
</tr>
<tr>
<td>• Hyaluronic Acid 0/1%</td>
</tr>
<tr>
<td>• Osmoprotection</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Moderately Severe Dry Eye Stage IIb</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Higher viscosity cellulose derivatives without preservatives, frequency of application &gt;4 times daily</td>
</tr>
<tr>
<td>• Hydrogels (Carbomers), with preservative, frequency &lt; 4 times daily</td>
</tr>
<tr>
<td>• Hyaluronic Acid 0.3%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Severe Dry Eye Stage III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydorgels without preservatives combined with unpreserved PVA, PVP</td>
</tr>
<tr>
<td>Combined with Hyaluronic Acid 0.3%</td>
</tr>
</tbody>
</table>
Treatment of Severe Dry Eye

4.2.18. Hydroxy Propyl Cellulose eye drops, emulsions, gels are frequently used in moderate to severe dry eye. Punctal occlusion may be attempted in patients who are unable to use frequent artificial tears.

4.2.19. Prescribe autologous serum drops to improve ocular irritation symptoms as well as conjunctival and corneal dye staining in patients with Sjogren syndrome and Graft versus host disease.

4.2.20. Treat filamentary keratitis with debridement of the filaments or application of topical mucolytic agents, such as acetylcysteine 10% four times a day.

4.2.21. Perform debridement of filaments with a cotton-tip applicator, dry cellulose sponge, or a non-toothed forceps.

4.2.22. Avoid treatment with contact lenses in patients with associated neurotrophic keratopathy.

4.2.23. Perform thermal cautery if permanent punctal occlusion is to be accomplished.

4.2.24. Perform a stepwise punctal occlusion so that no more than one punctum is cauterized in each eye at a treatment session.

4.2.25. Perform a limited tarsorrhaphy to decrease tear evaporation in patients with severe dry eye who have not responded to other therapies.

4.2.26. Recommend Boston Scleral Contact lenses in treatment of severe dry eye.
4.3. Provider & Setting

4.3.1. If you are a health care provider other than an ophthalmologist, refer patients with dry eye who have moderate or severe pain, lack of response to therapy, corneal infiltration or ulceration, or visual loss to an ophthalmologist.

4.4. Counseling & Referral

4.4.1. Educate patients with dry eye about the chronic nature of the disease process and provide specific instructions for therapeutic regimens.

4.4.2. Periodically reassess the patients’ compliance and understanding of the disease, the risks for associated structural changes and re inform the patient as necessary.

4.4.3. Caution patients with pre-existing dry eye that kerato-refractive surgery, particularly LASIK may worsen their dry eye condition.

4.4.4. Treat dry eye, when present, prior to considering kerato-refractive surgery.

4.4.5. Refer patients with moderate to severe dry eye unresponsive to treatment or when systemic disease is suspected to an ophthalmologist who is experienced in management of these entities.

4.4.6. Refer patients with systemic immune dysfunction or those who require immunosuppressive therapy to an internist or rheumatologist.

Clinical Pathway 9- Treatment of Dry Eye Disease based on Level of Care

[Diagram showing the pathway]
4.5 Recommendations for Prevention of Dry Eye Disease

Suggest the following recommendations to those at risk of dry eye disease:

4.5.1 Avoid excessive movement and windy conditions

4.5.2. Avoid hot, dry environments since both heating and air conditioning can worsen dry eye disease

4.5.3. Use humidifier to keep the air moist. Adding moisture to the air reduces dry eye symptoms

4.5.4. Wear wrap around glasses to reduce effect of wind on ocular surface to reduce evaporative dry eye symptoms.

4.5.5. Recommend taking frequent breaks while reading, seeing television and using mobile phone or computer devices.

4.5.6. Position computer screen below eye level to reduce lid aperture and minimize tear evaporation

4.5.7. Recommend refraining from smoking and exposure to secondary smoke

4.5.8. Recommend use of hot compresses and eye massage

4.5.9. Recommend use of artificial tears and lubricating gels as soon as symptoms of dry eye disease appear