**Introduction**

Dry eye syndrome is defined as follows: a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, 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.\(^1\)

Dry eye syndrome (DES) is also referred to as keratoconjunctivitis sicca, dry eye disease, dysfunctional tear syndrome\(^2\) or just simply dry eye. Although this condition affects a significant proportion of the population, it often goes unrecognised and unattended.\(^3\) It is a symptomatic disease and no single diagnostic test exists to reliably distinguish amongst individuals with and without dry eye. Damage to the cornea and conjunctiva can be the ultimate result of untreated or inadequately treated DES. This can lead to a vicious cycle as the resultant inflammation due to poor tear production damages the eye surface and tear glands which leads to further loss of tear production and even more damage.\(^4\) Symptoms of DES often interfere with daily activities and can impact on quality of life.\(^5\)

**Epidemiology**

The global prevalence of DES ranges from 5% to 50%, increases with age and is higher in women than men.\(^7\) Due to previous research suggesting DES to be more common in the older population, most published estimates pertaining to the prevalence of DES have focused on older age groups. Clinical perception however exists that DES increasingly occurs at younger ages.\(^8\) Data are scarce regarding the prevalence of DES among different races or ethnicity, but may be greater in the Asian population as compared to Caucasians.\(^1\)

**Signs and symptoms**

Dry eye is commonly asymptomatic but may present with the following: foreign-body sensation, ocular dryness, burning, itching, hyperaemia and sensitivity to light. Risk factors include, amongst others, female sex, medicines with anticholinergic activity, hormonal influences and environmental factors. Dry eye syndrome has been classified into aqueous deficient dry eye and evaporative dry eye, but due to the interlinked nature of the causes, it is difficult to distinguish between the two. Dysfunction of the lacrimal functional unit ultimately leads to DES. Treatment of DES should follow a step-wise approach in accordance with the level of severity.

**Risk factors**

Various risk factors for DES, in accordance to the level of evidence, are listed in Table I.

**Causes**

Dry eye syndrome has been classified by the International Dry Eye Workshop (DEWS) into two groups:\(^1\)\(^5\)\(^8\)\(^9\)\(^11\)

- **Aqueous deficient dry eye** involves damaged lacrimal glands, which lead to inadequate tear volume. This type of dry eye can be classified as Sjögren or non-Sjögren. Sjögren syndrome is an autoimmune condition caused by the infiltration of activated T-cells in the lacrimal and salivary glands, causing symptoms such as dry eye and dry mouth. Non-Sjögren aqueous deficient dry eye results from lacrimal gland insufficiency or duct obstruction.\(^11\)

- **Evaporative dry eye** is more common and occurs when there is abnormally rapid tear evaporation. This is usually caused by meibomian gland dysfunction or an insufficient oil layer on the surface of the aqueous layer of tears.\(^8\)\(^11\)
The classification and causes of DES, are presented in Figure 1.

Pathophysiology

The lacrimal and meibomian glands together with the ocular surface (the cornea and conjunctiva) and related innervation make up the lacrimal functional unit (Figure 2).

Lacrimal gland: an exocrine gland similar to the mammary and salivary gland. It is composed of lobules separated by loose connective tissue. Each lacrimal gland lobule consists of many acini and intralobular ducts. Each lacrimal gland lobule consists of many acini and intralobular ducts.

Meibomian gland: a type of sebaceous gland with tubule-acinar structure and holocrine function, located in the superior and inferior tarsal plates of the eyelids. These glands secrete a compound, meibum, made up of polar and nonpolar lipids.

Dysfunction of any of these structures may lead to disturbances in tear volume, composition, distribution and/or clearance, which ultimately results in DES. Dry eye syndrome can thus be attributable to two interlinked causes, tear hyperosmolarity and...

Table I. Risk factors for DES

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Mostly consistent evidence</th>
<th>Suggestive evidence</th>
<th>Unclear evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td>Increased age</td>
<td>Asian race</td>
<td>Hispanic ethnicity</td>
</tr>
<tr>
<td>Female sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td>Antihistamines</td>
<td>Tricyclic antidepressants, selective serotonin reuptake inhibitors, diuretics, beta-blockers, isotretinoin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anxiolytics; antipsychotics; oral contraceptives; botulinum toxin injection</td>
<td></td>
</tr>
<tr>
<td>Supplements and substances</td>
<td>An Omega-6 &gt; Omega-3 fatty acid ratio; vitamin A deficiency</td>
<td>Alcohol; cigarette smoking</td>
<td></td>
</tr>
<tr>
<td>Hormonal influence</td>
<td>Postmenopausal oestrogen therapy; androgen deficiency</td>
<td>Menopause</td>
<td></td>
</tr>
<tr>
<td>Conditions</td>
<td>Connective tissue disease; hepatitis C infection</td>
<td>HIV; diabetes mellitus; sarcoidosis; ovarian dysfunction</td>
<td>Acne; gout; pregnancy</td>
</tr>
<tr>
<td>Procedures</td>
<td>Refractive excimer laser surgery; radiation therapy; haematopoietic stem cell transplantation</td>
<td>Systemic chemotherapy; penetrating keratoplasty</td>
<td></td>
</tr>
<tr>
<td>Environment</td>
<td></td>
<td>Low humidity environments</td>
<td></td>
</tr>
</tbody>
</table>

* Omega-6 fatty acids are precursors for arachidonic acid and thus pro-inflammatory. Omega-3 fatty acids block the synthesis of these mediators.1
* If the orbits lie within the treatment fields.
Components of the tear film appear in Figure 3 and Table II.14

**Table II. Tear film components**

<table>
<thead>
<tr>
<th>Component/Layer</th>
<th>Secreted by</th>
<th>Functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid (meibum)</td>
<td>Meibomian glands</td>
<td>Coats the aqueous layer on the ocular surface; provides tear film stability; minimises evaporation; protects against microbial agents and organic matter</td>
</tr>
<tr>
<td>Aqueous</td>
<td>Main and accessory lacrimal glands</td>
<td>Solubilises mucins, electrolytes, proteins, flushes irritants (reflex tears)</td>
</tr>
<tr>
<td>Mucin</td>
<td>Goblet cells, epithelia, lacrimal glands</td>
<td>Lubricant; surfactant between hydrophobic epithelium and aqueous component</td>
</tr>
</tbody>
</table>

Decreased aqueous flow and excessive tear film evaporation lead to hyperosmolar tears, which activate the inflammation cascade and damage to the ocular surface.11 The release of pro-inflammatory cytokines and chemokines cause T helper cell expansion and infiltration to the ocular surface and lacrimal gland leading to inflammation.10 Chronic inflammation may lead to increased evaporation and instability of the tear film. As mentioned, tear film instability can arise from tear hyperosmolality or can arise from lipid layer abnormalities. This in turn results in increased tear evaporation and hyperosmolality.11 Due to the interlinked nature of the causes of dry eye, it is often difficult to differentiate between aqueous deficient dry eye and evaporative dry eye (Figure 4).

**Management**

The ultimate goal in the treatment of DES is to improve the patients’ ocular comfort and quality of life, and to return the ocular surface and tear film back to its normal homeostatic state. Current therapies for DES include tear supplementation (lubricants), tear retention (e.g. punctal plugs), and tear stimulation (secretagogues), biological tear substitutes (non-pharmaceutical fluids e.g. serum), anti-inflammatories (e.g. cyclosporine, corticosteroids), essential fatty acids (e.g. omega-3), and environmental strategies. Treatment should be based on disease severity and are presented in Table IV.1

**Non-pharmacological advice**

Patient education remains the cornerstone of management. Patients should be made aware that symptoms may only be relieved after long-term treatment. It is important for the patient to avoid potential triggers such as cigarette smoke and air conditioning.10,18
The use of humidifiers and avoiding dry environments may also be helpful. The use of glasses to decrease tear evaporation may be suggested to improve symptoms. Patients should be advised to take regular breaks from reading and computer use and increase blink frequency. Dietary modifications, specifically to increase intake of omega 3 fatty acids and to decrease alcohol consumption may be suggested.

**Pointers**

- The use of hypo-osmotic artificial tears is essential. Tears of patients with DES have a higher tear film osmolality. The latter causes morphological and biochemical changes to the corneal and conjunctival epithelium, and is pro-inflammatory.
- Although temporary relief of symptoms and discomfort are obtained with the use of artificial tears, the underlying pathology of DES is not treated.
- Solutions containing electrolytes and ions are beneficial in the treatment of ocular surface damage due to DES. Potassium maintains corneal thickness, while bicarbonate-containing solutions promote the recovery of epithelial barrier function.
- Avoid ophthalmic solutions that contain the preservative benzalkonium chloride as it destabilises the tear film. Benzalkonium chloride can damage the corneal and conjunctival epithelium, which eventually leads to cell necrosis with sloughing of epithelial cells. Preservative-free formulations should be used, especially patients suffering from severe DES.
- Punctal occlusion conserves tears in a useful and practical manner. It is a semi-permanent plug inserted into the punctal orifice and has the advantage of being readily reversible. Permanent punctal occlusion can also be performed using topical anaesthesia. It remains important though to still address the inflammation within the lacrimal functional unit.
- Topically administered corticosteroids pose an increased risk of elevating intraocular pressure, cataract formation, and infection, and should be used in short pulses or minimal doses.

**In summary**

Dry eye syndrome is a common condition, often goes unrecognised, and can ultimately lead to corneal and conjunctival damage. There has been a paradigm shift in the management of this condition. Although lubrication and hydration of the ocular surface remain paramount, various other treatment strategies can be employed. The ultimate goal in the treatment of DES is to improve the patient’s ocular comfort and quality of life, and to return the ocular surface and tear film back to its normal homeostatic state.

**References**