Dry eyes

D Engler, V Abraham

School of Pharmacy, Sefako Makgatho Health Sciences University, South Africa

Corresponding author, email: deirdre.engler@smu.ac.za

Abstract

Dry eye syndrome (DES) affects a significant proportion of the population, and although it is more common in the elderly, this eye condition is increasingly occurring at younger ages. Common symptoms include ocular dryness, a foreign-body sensation, 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.

Keywords: dry eye syndrome, lacrimal functional unit, tear film, severity grading

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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 keratoconjuctivitis 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.[2] 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.[6] 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, ocular irritation, photophobia, mucoid discharge, and blurry vision.[7,8] An accelerated blink rate had been document and permanent visual impairment is rare.[8] The intensity of symptoms is determined by factors such as prolonged visual activity, environmental factors (e.g. wind or dust), as well as the use of certain medications (e.g. antihistamines).[9] Paradoxically, severe corneal damage leads to excessive reflex tearing and increased tear production.[7] Conjunctival scarring can occur in severe cases and can lead to loss of vision.[10]

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]

Table I. Risk factors for DES[1]

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

#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.[9]

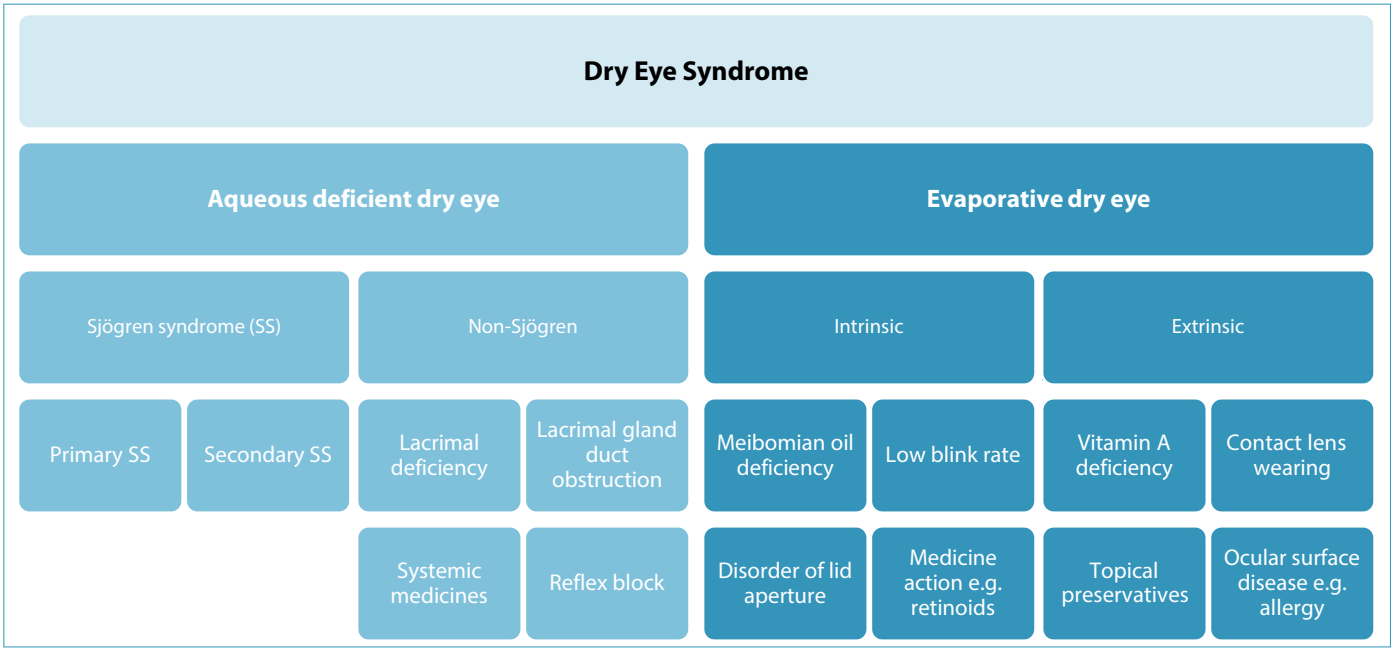

Figure 1. Classification and causes of DES[1,5,8,9,11]

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.[12]

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.[13]

Dysfunction of any of these structures may lead to disturbances in tear volume, composition, distribution and/or clearance,[11] which ultimately results in DES. Dry eye syndrome can thus be attributable to two interlinked causes, tear hyperosmolarity and

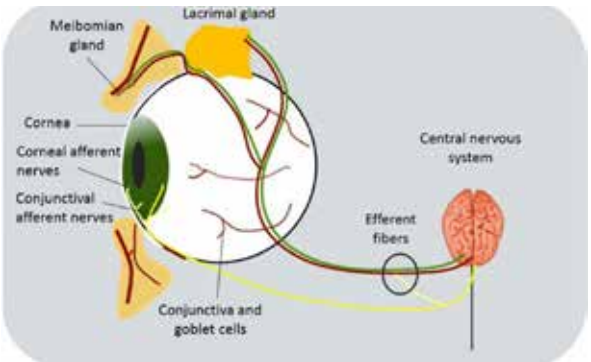

Figure 2. The lacrimal functional unit[15]

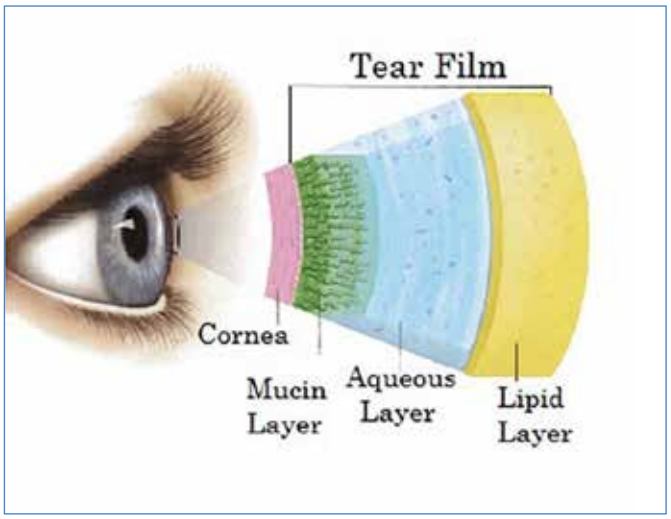

Figure 3. The tear film[16]

tear film instability.[11] Components of the tear film appear in Figure 3 and Table II.[14]

Table II. Tear film components[12-14]

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

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

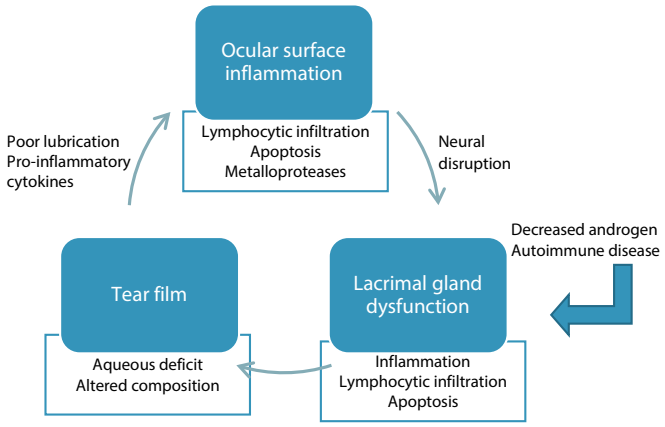

Figure 4. Interconnection within the lacrimal functional unit[14]

evaporation and instability of the tear film. As mentioned, tear film instability can arise from tear hyperosmolarity or can arise from lipid layer abnormalities. This in turn results in increased tear evaporation and hyperosmolarity.[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.[1] Current therapies for DES include tear supplementation (lubricants), tear retention (e.g. punctal plugs), and tear stimulation (secretogogues), 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]

Table III. DES severity grading[1]

Severity level	1	2	3	4
Discomfort, severity and frequency	Mild and/or episodic; occurs under environmental stress	Moderate episodic or chronic; stress or no stress	Severe frequent or constant without stress	Severe and/or disabling and constant
Visual symptoms	None or episodic mild fatigue	Annoying and/or activity limiting episodic	Annoying, chronic and/or constant; limiting activity	Constant and/or possibly disabling
Corneal staining	None to mild	Variable	Moderate to marked	Marked
Corneal/tear signs	None to mild	Mild debris; decreased meniscus	Filamentary keratitis; mucus clumping; tear debris	Filamentary keratitis; mucus clumping; tear debris; ulceration
Lid/meibomian glands	Meibomian gland disease variably present	Meibomian gland disease variably present	Frequent	Trichiasis; keratinisation; symblepharon
Fluorescein tear break-up time#	Variable	≤ 10 sec	≤ 5 sec	Immediate
Schirmer score*	Variable	≤ 10 mm/5 min	≤ 5 mm/5 min	≤ 2 mm/5 min

#Measures the interval between instillation of fluorescein and appearance of the first dry spots on the cornea;
*To determine whether the eye produces enough tears to keep it moist

Table IV. Recommended treatment according to level of severity[1,14,17,18]

Severity grading	Recommended treatment according to severity
Level 1	• Patient education • Environmental and dietary modification • Minimise or eliminate the use of medicine which may decrease tear production e.g. antidepressants, diuretics and antihistamines* • Artificial tear substitutes, gels/ointments • Eye lid therapy
Level 2	Should Level 1 be inadequate, step-up by adding: • Topical anti-inflammatories • Tetracyclines (for melbomianitis; rosacea) • Punctal plugs • Secretogogues • Moisture chamber spectacles
Level 3	Should Level 2 be inadequate, step-up by adding: • Serum • Contact lenses • Permanent punctal occlusion
Level 4	Should Level 3 be inadequate, step-up by adding: • Systemic anti-inflammatory agents • Surgery

*This should be done in consultation with a health care practitioner

The use of humidifiers and avoiding dry environments may also be helpful.[8] 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.[17,19] 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 osmolarity. The latter causes morphological and biochemical changes to the corneal and conjunctival epithelium, and is pro-inflammatory.[1]
- Although temporary relief of symptoms and discomfort are obtained with the use of artificial tears, the underlying pathology of DES is not treated.[14]
- 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.[1]
- 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.[1,18]
- 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.[14]
- 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.[14]

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.

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