Introduction to dry eyes

What is Dry Eye

Classically, dry eye is described as a disorder of the tear film due to tear deficiency or excessive evaporation, which causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort.

Dry eyes is the commonest eye condition in the world affecting several million people in the UK alone.

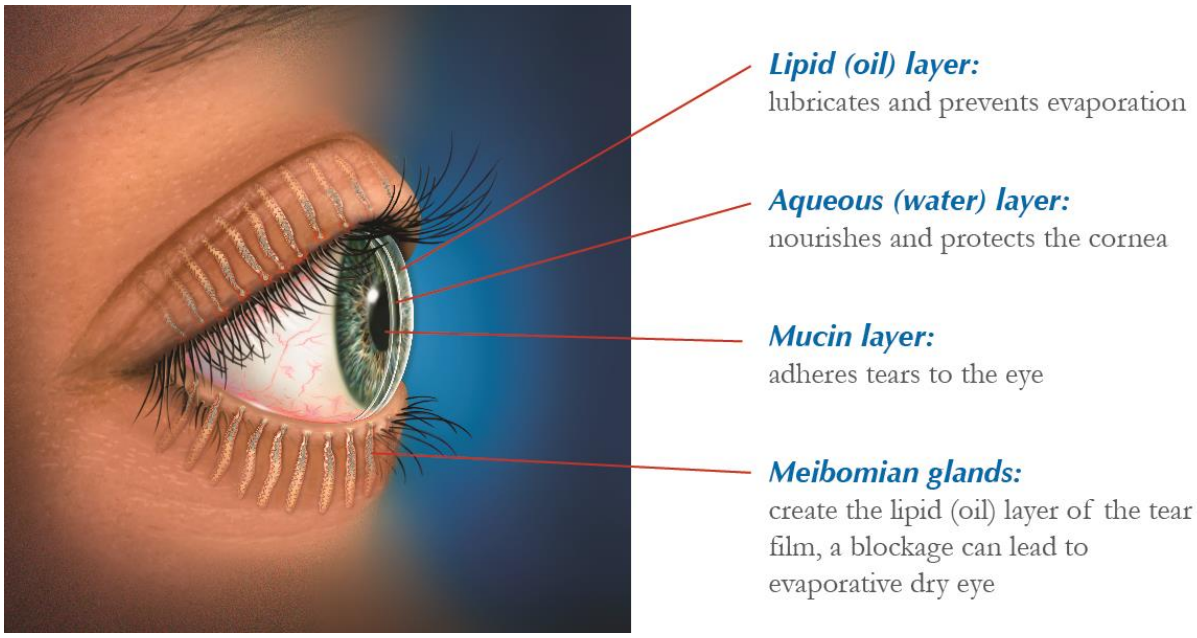
According to the DEWS (Dry Eye Workshop) Definition and Classification Subcommittee, *Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.*

Normal Ocular Surface

The term ocular surface refers to cornea (the front, clear 'window' of the eye) and the bulbar conjunctiva (the mobile, very thin, clear layer, overlying the sclera or 'white' of the eye).

Anterior to, or in front of, this part of the eye is the pre-ocular tear film (POTF).

The POTF has three layers:



i). The meibomian glands found in the lid margins produce most of the outermost (lipid) layer. The Zeiss and Moll glands of the eyelid margin and lashes also contribute to this layer. Oily secretions in this layer are present to contain the aqueous phase of the POTF and also to stabilise the aqueous layer below and retard its evaporation. In the normal healthy eye, the lipid layer's thickness is less than 0.1 micron. Meibomian lipids have particular, important properties for the formation of the tear film; alteration of these properties in conditions such as blepharitis may affect its stability. This alteration in properties may also result in distorted observable interference fringe patterns and this feature can be used diagnostically.

ii). The aqueous (intermediate) layer makes up about 90 percent of the tear film. This layer contains proteins that have antibacterial activity and which may be useful for diagnostic evaluation of the aqueous layer.

iii). The innermost layer of the tear film is known as the mucous layer. This mucous lubricates

the lids and serves as an adsorbing interface between the aqueous layer and the hydrophobic (water-repelling) corneal epithelium, i.e. it keeps the aqueous layer "attached" to the corneal epithelium. In addition, it collects cellular debris from the ocular surface. The traditional concept of rapid tear film breakup is based on disruption of the contact between the lipid and mucous layers, or local breakdown of the mucous layer.

Ocular surface disorders can result from a compromise of the structure or function of the cornea, eyelids, conjunctiva, or sclera.

There is a normal, continuous resting tear flow which occurs and, currently, it is considered that waking tear flow is a reflex response to afferent impulses which arise mainly from the ocular surface. Additional sensory input from the nasal mucosa also makes a contribution and this is why strong smells/odours can make our eyes water. Disease or damage to any component of the tear production system (the afferent sensory nerves, the efferent autonomic and motor nerves, and the tear-secreting glands) can destabilise the tear film and lead to ocular surface disease that expresses itself as dry eye. Tear film stability, a hallmark of the normal eye, is threatened when the interactions between the stabilising tear film constituents are compromised by decreased tear secretion, delayed clearance, and altered tear composition. Ocular surface inflammation may then occur as a secondary consequence. Reflex tear secretion in response to ocular irritation is thought to be the initial compensatory mechanism but, with time, inflammation accompanying chronic secretory dysfunction and a

decrease in corneal sensation, eventually compromises the reflex response and results in even greater tear film instability.

Importance of the Tear Film

The term “dry eye” refers to ocular surface disorders in which the common etiology is aqueous deficiency. This can lead to a cascade of secondary disorders. Adequate POTF function is necessary for clear and comfortable vision. In addition, the POTF has other physiologic functions:

• It is the initial refracting (light-bending) surface of the eye.
• It serves as the primary source of oxygen to the anterior cornea.
• It supplements the eye's antibacterial defences.
• It provides lubrication for the eyelids and ocular surface.
• It flushes away metabolic waste products and debris.
• It performs a needed anti-inflammatory function following ocular surface injury.

Drugs Which May Cause Dry Eye

Unfortunately, many of the common medications we take, for one reason or another, may have side effects. There are lots of different medications which may increase the dryness of your eyes. People respond differently to medications whereby one person might have no side effects and another taking the same medication may have several complications. The list which

follows comprises some of the different medications which have been reported to cause dry eye:

Antihistamines - Antihistamines may contribute to a decrease of tear film production.

Antidepressants - Antidepressants are known to cause ocular drying, or the drying of your eyes.

Sleeping Pills - Side effects commonly stated include dizziness, confusion, and also dry mouth and dry eyes. Over-the-counter sleep aids, as well as prescription sleep aids will cause these side effects.

Birth Control Pills - Many pills list dry eye as a side effect, mainly because birth control pills alter your hormones. However, whilst stopping the pills should stop the dryness, pregnancy is also known to cause dry eyes.

Diuretics - These drugs are mostly used to treat high blood pressure.

ACE Inhibitors - Angiotensin-converting enzyme inhibitors are mostly used to treat high blood pressure.

Isotretinoin-Type Drugs - These drugs are mostly used to treat acne conditions, e.g. Roaccutane.

Opiates - Opiate-based medicines such as morphine that help treat extreme pain.

Treatment of Dry Eye – Lubricants

Most of us have heard the term 'artificial tears'. Many of us know someone who is using these products regularly. However, for most products that identify themselves as artificial tears, it is a misnomer because they do not actually mimic the composition of human tears. Most function as lubricants, although some more recent formulations do mimic the electrolyte composition of human tears. Many of the ocular lubricants presently available are not based on clinical efficacy. The description of any given product often specifies permitted active ingredients (eg, emulsifiers, surfactants, and viscosity agents) and concentrations, but may give only limited guidance on inactive additives and solution parameters. Certain inactive ingredients that are used in artificial tears sold over the counter (eg, castor oil in Endura and guar in Systane) are not listed in the product description. It can thus be difficult to prove that any given ingredient in an ocular lubricant acts as the active agent.

Although certain artificial tears have demonstrated more success than others in reducing symptoms of irritation, or in reducing ocular surface dye staining, in head-to-head comparisons, there have been no large scale, masked, comparative clinical trials to evaluate the wide variety of ocular lubricants.

That said, the main objectives in caring for patients with dry eye disease are to improve the patient's ocular comfort and quality of life, and to return the ocular surface and tear film to the normal homeostatic state. Whilst symptoms can rarely be eliminated, they can often be improved, leading to an improvement in the quality of life. It is more difficult to demonstrate that

topical lubricants improve the ocular surface and the tear film abnormalities associated with dry eye. Until agents are developed that can restore the ocular surface and tear film to their normal homeostatic state, the symptoms and signs of dry eye disease will continue.

Ocular lubricants are characterized by hypotonic or isotonic buffered solutions containing electrolytes, surfactants, and various types of viscosity agents. In theory, the ideal artificial lubricant should be preservative-free, contain potassium, bicarbonate, and other electrolytes and have a polymeric system to increase its retention time.

Preservatives

The single most important advance in the treatment of dry eye has come with the elimination of preservatives, such as benzalkonium chloride, from lubricants. Because of the risk of contamination of multidose products, most either contain a preservative or employ some mechanism for minimising contamination. Preservatives are not required in unit dose vials that are discarded after a single use.

The widespread availability of nonpreserved preparations allows the administration of lubricants much more frequently without concern about the toxic effects of preservatives. For patients with moderate-to-severe dry eye disease, the absence of preservatives is of more critical importance than the particular polymeric agent used in ocular lubricants. The ocular surface inflammation associated with dry eye is exacerbated by preserved lubricants.

Preservative-free formulations are crucial for patients with severe dry eye with ocular surface disease and impairment of lacrimal gland secretion, or for patients on multiple, preserved topical medications for chronic eye disease.

Nonpreserved, single unit-dose tear substitutes are more costly for the manufacturer to produce, more
costly for the patients to purchase, and less convenient to use than bottled ocular lubricants. For these reasons, re-closable unit dose vials were introduced.

Ocular ointments and gels are also used in treatment of dry eye disease. Ointments are formulated with a specific mixture of mineral oil and petrolatum. Some contain lanolin, which can be irritating to the eye and delay corneal wound healing. In general, ointments tend not to support bacterial growth and, therefore, do not require preservatives.

Gels containing high molecular weight crosslinked polymers of acrylic acid (carbomers) have longer retention times than artificial tear solutions, but have less visual blurring effect than petrolatum ointments.

The stability of the tear film depends on the chemical and physical characteristics of that film interacting with the conjunctival and corneal epithelium via the membrane spanning mucins. In the classical three-layered tear film model, the mucin layer is usually thought of as a surfactant or wetting agent, acting to lower the surface tension of the relatively hydrophobic ocular surface, thereby rendering the corneal and conjunctival cells wettable.

The tear film is probably best described as a hydrated, mucin gel whose mucin concentration decreases with distance from the epithelial cell surface. This may explain why most of the available water-containing lubricants are only minimally effective in restoring the normal homeostasis of the ocular surface. In addition to washing away and diluting out irritating or toxic substances in the tear film, artificial lubricants hydrate gel-forming mucin. While some patients with dry eye have decreased aqueous lacrimal gland secretion, alterations or deficiencies involving mucin will also cause dry eye.

Although many topical lubricants, with various viscosity agents, may improve symptoms and objective findings, there is little evidence that any agent is superior to another.
Most clinical trials involving topical lubricant preparations will document some improvement (but not resolution) of the patient's symptoms and improvement in some objective measures.

However, the improvements noted are not necessarily any better than those seen with the vehicle or with other non-preserved artificial lubricants. The elimination of preservatives and the development of newer, less toxic preservatives have made ocular lubricants better tolerated by dry eye patients. However, ocular lubricants, which have been shown to provide some protection of the ocular surface epithelium and some improvement in patient symptoms and objective findings, have not been demonstrated in controlled clinical trials to be sufficient to resolve the ocular surface disorder and inflammation seen in most dry eye sufferers.