



Dry Eye, Assessment and Management

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Approximately 4 million people in UK suffer from Dry Eye Syndrome, mainly women. Dry Eye is actually a group of conditions with a variety of causes. It may result when the eyes produce too little tear fluid, or when tears evaporate from the surface of the eye too rapidly. Many cases are wrongly diagnosed and treated. Generally speaking, my approach is to try to improve the patient's own secretions etc rather than simply finding something to replace them with on a short term basis

The term dry eye covers a variety of conditions with similar symptoms (sore, gritty, burning sensation) and signs (alterations to the tear film and ocular surface). We need to remember that a patient with apparently little corneal staining can suffer a great deal of discomfort due to their dry eye condition. The cornea has more sensory nerve endings than any other part of our body. Conversely, some patients with extensive corneal staining appear to be afflicted with a few symptoms.

Types of Dry Eye

Aqueous deficiency dry eye is most commonly seen in adults, in particular post-menopausal females. It can be caused by lacrimal gland destruction or blockage of lacrimal gland ducts. Aqueous deficiency dry eye includes both Sjögrens syndrome and non- Sjögrens syndrome dry eye conditions.

Sjögrens syndrome is an autoimmune condition affecting both the salivary and lacrimal glands. Primary Sjögrens syndrome denotes dryness of the mouth and eyes; secondary Sjögrens syndrome is when there is also an association with related connective tissue disease such as rheumatoid arthritis.

In primary Sjögrens syndrome there is a focal infiltration of the lacrimal and salivary glands by mononuclear lymphocytes, which destroy the glands and they are replaced by fibrous tissue.

For a diagnosis of Sjögrens syndrome to be made, the patient must be positive for at least one of these following tests¹:

1. Lymphocytic infiltrate on labial salivary gland biopsy
2. Salivary gland dysfunction, as shown by scintigraphy and/or sialography
3. Presence of auto-antibodies (anti-Ro/SS-A or anti-La/SS-B Ab, antinuclear Ab, rheumatoid factor)

HLA-DR3, -DRW52 and -DRW3 are associated with primary Sjögrens syndrome, and HLA-DR4 and -DRW3 are associated with secondary Sjögrens syndrome. The problem is to distinguish between true Sjögrens syndrome patients and those with simple age-related aqueous deficiency dry-eye, so that additional treatments specific to Sjögrens syndrome can be initiated, (e.g. Topical and systemic steroids, NSAIDS, Muscarinic M3 agonists, such as pilocarpine, interferon, methotrexate, azeothiaprime and in severe cases cyclophosphamide).

In secondary Sjögrens syndrome the blood vessels and connective tissue are also affected by lymphocytic infiltration. This results in chronic inflammation, which causes in destruction and deformation of these organs.

The autoimmune diseases associated with can be broken down into 4 groups:-

1. Connective tissue disorders (eg rheumatoid arthritis, Systemic Lupus Erythmatosis, progressive systemic sclerosis, poly myositis, polyarteritis nodosa).
2. Other rheumatic disorders: (eg psoriasis, Bechet's Disease, Giant Cell Arteritis).
3. Autoimmune diseases (eg Hashimoto thyroiditis, primary biliary cirrhosis, chronic active hepatitis, hypothyroidism, hyperthyroidism).
4. Miscellaneous (eg Crohn's disease, celiac disease, myasthenia,, lipodystrophy¹).

Generally, primary Sjögrens syndrome shows more severe ocular involvement than the secondary type.

Non-Sjögrens syndrome tear deficient dry eye can be due to either primary or secondary lacrimal disease, lacrimal obstructive disease and reflex causes, such as decreased corneal sensation as after LASIK refractive surgery.

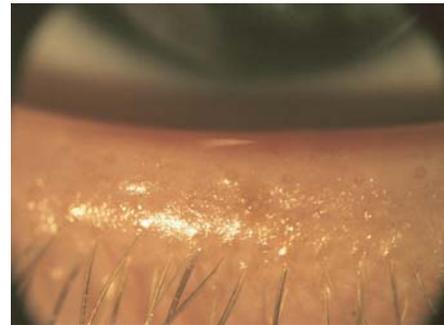
Tear secretion may also be decreased by any condition that decreases corneal sensation, e.g. diabetes & herpes zoster, long term contact lens wear and any corneal surgery that involves incisions or ablation of corneal nerves².

Evaporative dry eye is most commonly caused by meibomian gland anomalies, which can be blepharitis associated or obstructive meibomian gland dysfunction/disease. To a certain extent MSD is a normal finding in many people with advancing age.

People with large eyes are also subject to high tear evaporation (eg patients with Thyroid eye disease). This can be due to proptosis and/or lid retraction. It can be also caused by poor eyelid/eyeball alignment (e.g. floppy eyelid syndrome, lagophthalmos) and other causes such as environment contact lens wear, drugs (e.g. BKC toxicity in eye drops or topical B-blockers causing epithelial cell metaplasia and loss of goblet cells³), and allergy⁴. Activities such as driving, watching TV, using a VDU, or reading, all can increase tear evaporation as well due to the reduced blinking that often occurs with concentration on such visual tasks.



Thyroid Eye Disease



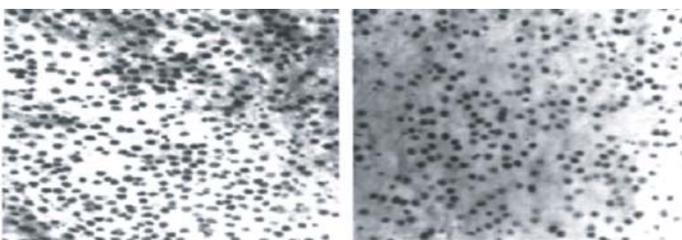
Meibomian Gland Dysfunction

A common feature of both aqueous deficient and evaporative dry eye is increased tear osmolarity. As a result, the tears "pull" water out of the surface of the eye by osmosis, causing the dry-eye symptoms that usually worsen as the day goes on.

Lacrimal gland fluid osmolarity increases as secretory rate declines, independent of the effect of evaporation⁵.

With a defective lipid layer, tears evaporate faster than replaced, hence tonicity increases

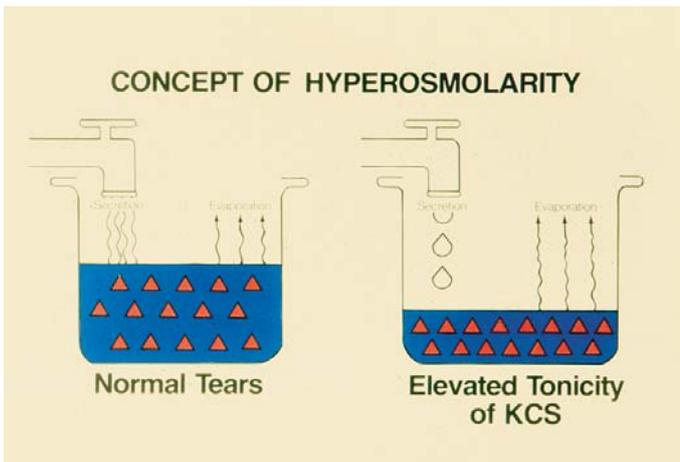
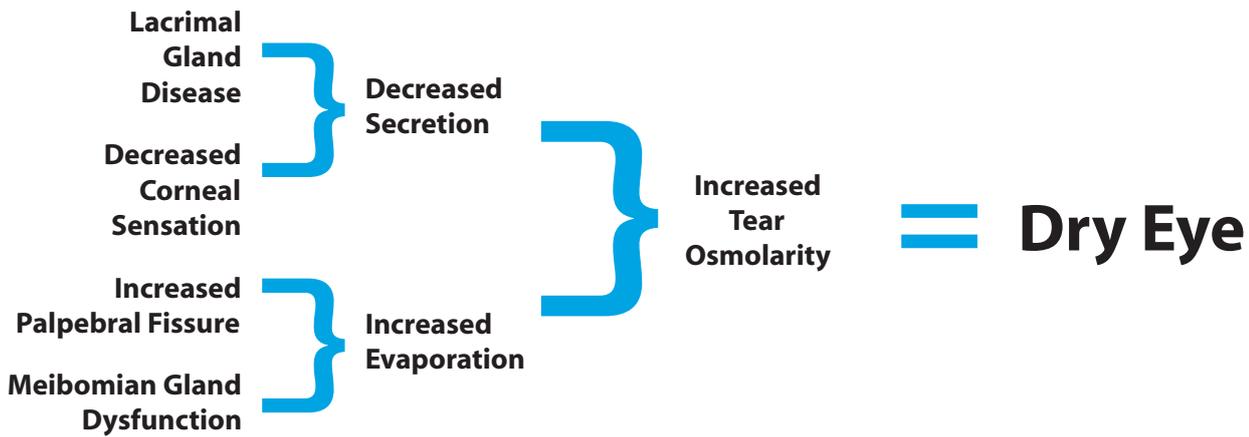
The conjunctiva is the first to suffer, with a reduction in the amount of mucous secreting goblet cells. An intact mucous film is required to hold the aqueous component of the tears in place. The hypotonicity of Theratears drops has been chosen to restore the tear tonicity to a level that encourages goblet cell repopulation of the conjunctiva. This effect is greater if the patient has punctal plugs fitted as the optimised tonicity is maintained for much longer.



Normal

Dry Eye

The Pathway to Dry Eye



Osmolarity is the concentration of dissolved particles in the tears, without regard to their size, density, electric charge or configuration. It decreases overnight due to decreased tear evaporation, and conversely increases in dry eye⁶. An osmolarity of less than 312 mOsm/kg is physiological, rising to 323 mOsm/kg in moderate to severe dry eye⁷.

Some artificial tear supplements, e.g. Theratears, have a low osmolarity, in an attempt to reverse that found in dry eye. If the lacrimal drainage mechanism is occluded, the effect is longer lived⁸.

Electrolyte Balance

Clinical studies demonstrate that electrolyte balance is crucial for maintenance of conjunctival goblet cells - for example, if sodium levels are too high, or if bicarbonate levels are too low, mucus-secreting goblet cells are lost and the spreading capabilities of the mucous film are impaired.

The ocular surface epithelium is unique in that it does not have a blood supply. It derives its electrolytes and oxygen from the tear film. The tear film, in other words, is a vital fluid and, as such, the electrolyte balance of that fluid is crucial for biological function. The electrolytes in eye drops need to match those of the tear film. Research shows that unless an eye drop has an electrolyte balance that precisely matched that of the human tear film, there is a loss of conjunctival goblet cells (conjunctival goblet-cell density is a very sensitive indicator of ocular surface health, and goblet cells provide the natural lubrication for the ocular surface⁹). The good news is that using better-balanced lubricant eye drops helps to restore the ocular surface. In the 1980s, Wilson, O'Leary and Bachman¹⁰ found they could decrease the corneal desquamation caused by preservative-free sodium chloride by adding certain electrolytes to the solution.

Normal Electrolyte Concentration in Human Tears(mMol/Litre)

Na	132
K	24
HCO	32.8
C	0.8
Mg	0.61

The tears contain water, sodium, potassium, magnesium, calcium, phosphate and bicarbonate ions. The pH of the tears is related to the concentration of hydrogen ions present and averages 7.5, approx the same as serum pH. On awakening, it is lowest due to the acidic products from anaerobic respiration. Bicarbonate is the main buffering agent in the tears, although the protein content also has an influence. It is thought that because potassium and chloride ions are present at a concentration greater than in the blood plasma, this indicates an active secretion rather than simple filtration mechanism¹¹.

The lipid layer

The tear lipid layer, although thin, stabilizes the tear film providing a 25% surface-tension decrease and a 90-95% reduction in aqueous evaporation. The lipid layer is formed from lipids secreted by tarsal meibomian glands and spread onto the ocular surface by blinking. The lipid layer itself is composed of two phases. A thin, deep polar phase, adjacent to the aqueous-mucin layer, has a surfactant role. A thicker and superficial non-polar phase has anti-evaporative properties.

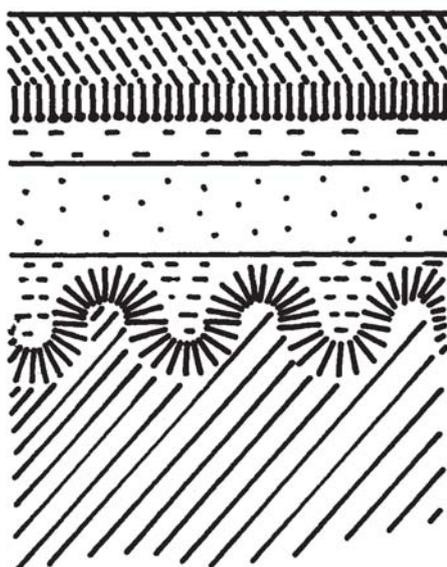
It also reduces the surface tension of the tear film, which holds the tears tight onto the ocular surface. The build up of lipid on the lower lid margin also acts as a hydrophobic barrier, helping to retain the tears between the eyelids and not to overflow down the cheek (Norn 1966). It also may help to prevent skin lipids from migrating into the tear film. This is important as they can destabilise the tear film¹².

Tiffany¹³ showed that there was considerable inter-subject variation in the composition of meibomian lipids. It is made up of both polar and non-polar lipids. 90% of the composition is sterol and mixed wax esters, the remainder being free sterols, free fatty acids, hydrocarbons and phospholipids.

In meibomian gland dysfunction and blepharitis the number of high melting point lipids increases, producing a poor quality tear film with increase evaporation characteristics.

SIX - LAYER TEAR FILM MODEL

(Tiffany 1988)



AIR

Oily layer

Polar lipid monolayer

Adsorbed mucoid

Aqueous layer

Mucoid layer

"Glycocalyx"

CORNEAL

EPITHELIUM

The Mucous Layer

The primary source of the tear film mucous is the goblet cells of conjunctiva, although minor sources also include the corneal and non-goblet conjunctival epithelial cells and the lacrimal gland itself.

There are approx 1.5 million goblet cells present over the conjunctiva, with the greatest density being on the nasal portion of the bulbar conjunctiva¹⁴.

The tear mucins and the glycocalyx render the whole of the ocular surface hydrophilic, allowing the aqueous to spread evenly over the eye. If these are missing epithelial damage can occur due to the non-adherence of the watery layer of the

tears. This can occur even if the tear volume is adequate. The tear mucins from the goblet cells additionally trap foreign matter and expel it from the eye.

It used to be thought that the non-Newtonian characteristics of the tears are largely enabled by the mucins present. This means that the viscosity of the tears to change depending on the shear rate caused during blinking. This means that the tears are more viscous between blinks, becoming runnier during the blink^{15, 16}

We know that the surface tension of water is 72 mN/m, which decreases to 54 if tear proteins are added. Interestingly, if the lipids are removed from the tear film the surface tension also drops to 54, and the tears behave in a Newtonian manner. As we add the lipid back it regains its non-Newtonian properties. As there is no free lipid in the tears, it is assumed that it is complexed, probably to tear lipocalin.

Whatever the intricacies of this exact interaction turn out to be, the non-Newtonian concept is explained in that in the open eye, under low shear forces the tears have high viscosity with its components having intermolecular bonding. Blinking shears the aggregated components apart, in a reversible manner, such that the intra-molecular bonding can re-assert itself between blinks.

The glycocalyx is composed of protein anchored mucins (MUC1) secreted by the corneal epithelium.

The goblet cells secrete MUC5AC, which is secreted in dehydrated form, hydrating in the tears up to a composition of a gel.

The Cornea

The surface area of the adult cornea is approx 1 square cm, approx two thirds to one half of the total exposed ocular surface area. The total surface area of the ocular surface has been estimated as approximately ten times that of the cornea.

The cornea is one of the most highly sensitive areas, having the greatest density of sensory nerve endings found anywhere in our body. Most of these are sensory nerves derived from the long ciliary nerves from the ophthalmic branch of the trigeminal nerve. The ciliary nerves form a perilimbal nerve ring, from which nerve fibres enter the deep peripheral stroma radially, losing their myelin sheaths, before coursing anteriorly to form a sub-epithelial plexus. From here they penetrate Bowman's layer to form sensory nerve endings at the level of the wing cells in the epithelium. This is why epithelial cell loss can result in severe ocular discomfort.

The cell membrane of the epithelial cells is a hydrophobic lipid bi-layer, containing numerous glycoprotein and glycolipid particles that are covered with oligosaccharides, collectively called the glycocalyx. The glycocalyx is responsible for the hydrophilic properties of the ocular surface. It interacts with the mucins in the innermost section of the tear film to maintain tear stability. If either the epithelial glycocalyx or the mucin secreting conjunctival goblet cells are abnormal or missing, then tear film instability results, usually with ensuing corneal desiccation damage. A good example of glycocalyx damage is that caused by frequent instillations of eye drops containing Benzalkonium Chloride preservative, and of goblet cell damage as occurs with the Stevens-Johnston Syndrome. In both cases the tears no longer are held in place in front of the epithelium, and damage follows.

Dry Eye Assessment

1. Assess the quantity and quality of the tears both invasive and non-invasive TBUT and lipid quality
2. Assess the tear meniscus
3. Examine the cornea and bulbar conjunctiva for staining using fluorescein and lissamine green, using appropriate filters
4. Examine the lid margin for blocked non-expressible meibomian glands, notching of the lid margin and signs of inflammation and infection
5. Examine the tarsal conjunctiva for abnormalities such as allergic papillae, cysts, concretions etc
6. monitor subjective progress with a questionnaire



The Fluorescein TBUT

A dry Eye patient will usually have a reduced tear break up time as assessed using the Tearscope (<23secs) or modified fluorescein (reduced instillation) technique (<10 secs)
A reduced tear meniscus height is a useful indicator of tear volume (less than 1mm, using slit-lamp magnification with a reduced slit height, so as not to impinge upon the pupil).



The Tearscope



The Lipid layer as seen by the Tearscope (photo A Matheson)
Blocked Meibomian Glands (photo A Matheson)



Grid showing NITBUT



Why isn't the Schirmer test more helpful?



- Decreased tear production or increased evaporation decreases Schirmer test result.
- Meibomian gland dysfunction increases Schirmer - less oil on the paper improves wettability¹⁷
- The test can produce increased tearing due to mechanical irritation

Corneal Staining

In dry eye disorders the corneal and conjunctival epithelial surfaces, and/or the intra-cellular junctions are damaged, altered or compromised¹⁸. The use of stains allows us to view these changes directly and immediately. It is thus extremely important to be able to assess this damage if the diagnosis is to be made and any treatment evaluated for effectivity. Although several techniques have evolved to assess the extent of this damage, ocular surface staining with dyes such as fluorescein, rose bengal and lissamine green is the most practical clinically.

Fluorescein staining seems to offer the best clinical means of diagnosing the presence of corneal epithelial surface defects, particularly those of less severity than would exhibit staining with rose bengal. There is some controversy as to whether the dye is staining compromised or damaged cells or areas where cells are missing or intracellular junctions are weak^{19,20}

The apparent fluorescence of fluorescein is considerably enhanced if in addition to the cobalt blue excitation filter with the slit lamp illumination on max intensity, a yellow barrier filter is used (Wratten no12, see below) in the viewing system

Although fluorescein staining is usually associated with corneal desiccation, it may occur with other causes, such as ocular rosacea, insult from staphylococcal exotoxins, infections and allergies amongst other causes. It is important to consider these are considered before arriving at a diagnosis of dry eye.

According to Korb¹⁸, the optimal technique for viewing staining is to instil the drop, blink three times, wait 1-2 minutes, so that the stain has had enough time to penetrate the damaged epithelial cells, but also to leach out of the tear film, so as not to mask the fluorescence of the epithelial cells with the fluorescence of the tear film itself.

Korb and Hermann¹⁸ found a 20% increase in corneal staining observed, often showing damage that would not have been observed if a single instillation had been used. Again whether this has any significance is open to debate, sequential staining may merely show an increased cytotoxicity to fluorescein with repeat administration. In fact Josephson & Caffery²¹ found a remarkably high percentage of tear normal, non-contact lens wearers showed significant staining on sequential instillation

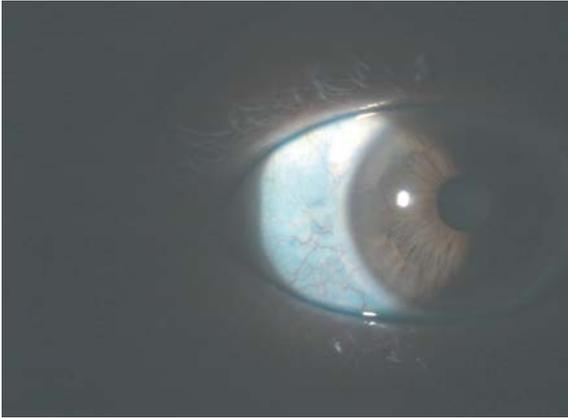
Ever since its use by Sjorgren in 1933 rose bengal has been widely used in the diagnosis of dry eye. Norn²³ proposed that rose bengal stains dead or degenerate epithelial cells and mucous. However, later work by Feenstra and Tseng¹⁹ showed that rose bengal stains healthy cells not protected by an intact mucous layer. It would seem that the presence of rose bengal staining indicates a deficiency of pre-ocular tear film protection. It still has to be shown if these cells are healthy, dead or damaged.

The conjunctiva generally shows more staining with rose bengal than the cornea. Norn²³, reported that as eyes age, rose bengal staining especially nasally and inferiorly becomes a normal finding.

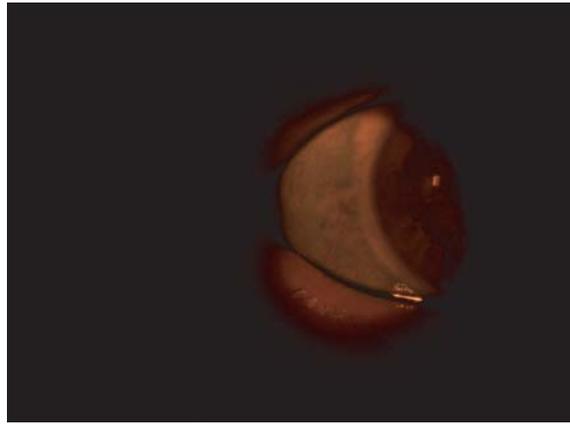
Lissamine green staining fades relatively quickly so should be assessed one eye at a time to prevent it being under-reported in the second eye.

When lissamine green is used it is important to instill an adequate volume (10-20ul) to allow adequate staining. At least a minute and no more than 4 minutes shows optimum staining. It is important not to view with too bright a light source or the staining is bleached out. The staining is enhanced if a red filter (Wratten no 25) is used as a barrier device on the slit lamp, in the same way that a no12 Wratten filter is used with fluorescein (see below). In these photos taken after wearing a silicone hydrogel bandage contact lens, the lissamine green staining of the exposed bulbar conjunctiva can be more clearly seen when the barrier filter is used in the right hand picture.

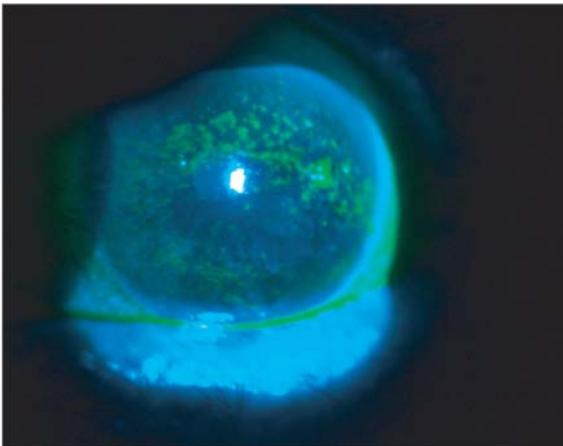
Without Wratten Filter
Photo A Matheson



With Wratten Filter
Photo A Matheson



Both fluorescein and Lissamine green stain mucous as seen in this case of adherent mucous in dry eye. This if untreated can lead to filamentary keratitis, which is extremely painful. Treatment is either by saturation dosing with hypotonic artificial tears such as Theratears Standard Drops , or a mucolytic such as acetylcysteine.



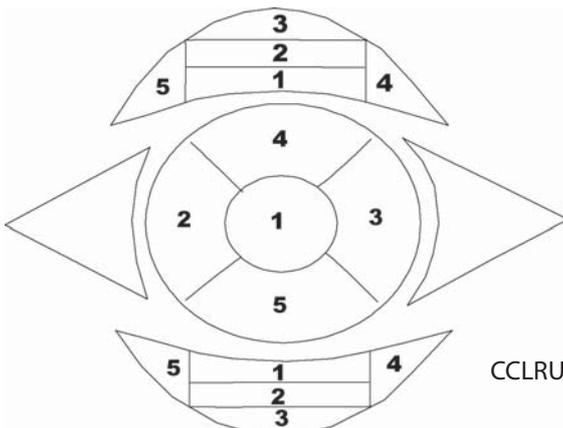
Mucous

Although the assessment of corneal staining with fluorescein is the conventional means of detecting and grading compromised corneal cells, it is always difficult to standardise the judgement of the exact amount of staining present, and whether or not progression or improvement has occurred.

Although digital imaging has helped with sequential comparisons, these are only valid if such things as the camera sensitivity settings, slit lamp illumination settings, use of barrier filters, absolute concentration of dye in tear film etc are kept constant between patients and repeat visits for the same patients.

If the conditions are variable between visits a comparison of the exact amount of staining present may not be valid.

If digital imaging is not available then grading each area of the cornea, conjunctiva and lids is the next best alternative:-



CCLRU Palpebral Conjunctiva and Cornea Grading Areas

Dry Eye Management

The aims of dry eye treatment can be broken down into improving corneal healing (ie reduce staining), and improving patient comfort. This is usually done by the following means:

- Improve tear volume by aqueous supplements
- Improve quality of mucous layer – Theratears/Ilube, gel suppl.
- Improve lipid layer – diet, lid hygiene, hot compresses, drugs (tetracyclines)
- Reduce tear drainage – punctal plugs, cautery
- Reduce tear evaporation – TCLs & improvements to lipid layer, Paraffin ointment
- Reduce inflammation – Omega-3, steroids, NSAIDs, Cyclosporin, anti-allergy products

Ocular lubricants/Artificial tears take many forms²³. The main active ingredients usually being CMC, PVA, HA, PEG and Poly vinyl-pyrrolidone. They come in preserved multi-dose and preservative free forms. Preservative free products are far superior as they do not suffer from the cytotoxic and allergy-causing problems suffered by their multi-dose counterparts. Personal clinical trials have shown much better patient comfort and reduced staining with preservative-free products.

The preservative free hypotonic artificial tears I use are a brand called “Theratears” developed by J.Gilbard at the Schepens Eye Institute. These are unit dose, preservative free, hypotonic, with the active ingredient CMC (0.25%). CMC is negatively charged and binds to the corneal epithelial surface well. It also has a cyto-protective function against the insult from the preservatives present in contact lens disinfecting solutions. The Theratears dropper has also been carefully designed to be easy to use by typically arthritic patients, with a very flexible diaphragm.



The Theratears Unit dose dropper and packaging

Theratears may have beneficial effects on conjunctival goblet cell populations, especially in patients fitted with punctal plugs, due to its hypotonicity. It also is a very “slippery” product which may help corneal healing by reducing the shear effects from the upper eyelid on blinking.

Punctal Plugs and Cautery

There are 5 main ways of permanently occluding the lacrimal drainage system

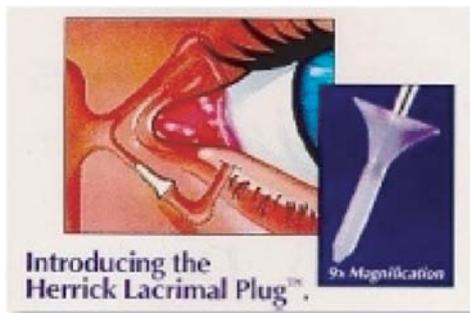
1. Cautery – this is the original method used. Although in the past many had problems with this technique, if performed cautiously in skilled hands, can be very successful, especially where the punctal opening/canaliculus is too large or lax to be plugged by other means. It is better to err on the side of under-treatment, than cause too much lid destruction and scar tissue. The punctum can always be retreated if complete closure is not achieved on the first attempt. It is uncomfortable if inadequate anaesthesia is used. Some advise fitting the patient's cornea with a protective contact lens for safety reasons. Treatment aims to produce a 0.7mm burn around the punctal opening (see below). If successful, 2 weeks later no evidence of the punctum can be seen (see below)



2. Conventional silicone plugs. These come now in many shapes and sizes. Choice is down to the individual practitioner. I like a plug to be fairly high modulus, have a small head and come in a variety of sizes and shapes. In the pictures below you can see the different profile of the standard Eagle vision punctal plug, compared to the ribbed profile of the Flex-plug. Having a small head improves patient comfort as there is less of the plug proud of the punctum to irritate the nasal bulbar conjunctiva.



3. Herrick intra-canalicular plugs, are fitted further down the canaliculus. They are more comfortable initially, but because of the stagnant column of tear fluid between them and the punctal opening, are theoretically more prone to infection. Once in place they cannot be seen, apart from by using X-ray photography, which shows them up as they are radio-opaque.



4. Smart Plug – a thin rod made from thermosensitive acrylic, is inserted into the punctum. Inside the punctum, the plug shrinks in length and expands in width, adjusting itself to fit the punctum. Once in place, SmartPLUG becomes a virtually undetectable, soft gel.

5. Oasis Form fit plug - again a one size fits all plug, this time made of a hydrogel material. Once inserted into the punctum, it hydrates over a 10 minute period. As it hydrates, it increases in size until it completely fills the vertical canalicular cavity to form a perfect fit. The Form Fit plug expands into a soft, pliable, gelatinous material when it contacts tear film. The Form Fit plug is easily removable by flushing saline solution through the punctal opening.

All plugs that are fitted deeper than the punctal opening are removed if necessary by syringing the plug through the lacrimal apparatus. It is therefore imperative that the canaliculi are irrigated prior to fitting to ensure this exit route is patent. If not then there is no point in fitting the plug.

Personally, I prefer to fit conventional silicone plugs wherever possible. They are trickier to fit, requiring the punctum to be measured first for size and elasticity. But because the right size of plug is fitted tightly into the punctum we know that tear flow is being stopped. A plug that is fitted initially tightly will function for longer. Also, the plug can be removed simply, if required. Opinions will differ between professionals on the choice of ideal implant, and no one type is suitable for everyone.



Hyaluronic Acid

Many recently developed products now contain 1 or 2% Hyaluronic Acid as the viscosity enhancer/lubricant. It is naturally found in the body in joints/umbilical chord and eyes (vitreous humour). It was sourced in past from chickens but the commercial pharmaceutical source is bacteria from the capsular component of Staphylococcus and Streptococci species.

Hyaluronic Acid has, like the natural tear film, Non-Newtonian properties. ie it has increased viscosity between blinks, becoming runnier with the shearing effect of the upper lid during the blink. Although this property is conceptually appealing, this is not always demonstrated clinically by improved comfort or reduced clinical signs²⁴. The older, constant viscosity product, CMC, often performs clinically better. This may be because of its negative charge which makes it adhere to the corneal surface better, or it may be due to other subtle differences in individual eyedrop formulations.

Carbomer Gel

Examples of these include Viscotears, Optrex Dry Eye Gel, Liposic and Gel Tears. They are too viscous for most people to use during the daytime in both eyes at the same time, but often are useful for overnight use. Contain Cetrimide as a preservative, apart from the unit dose product.



Ointments

Lacri-Lube ocular lubricant for dry eye conditions is an eye ointment containing medicinal liquid paraffin, white soft paraffin and wool alcohols. This formulation is particularly useful at night as it remains in the eye longer than drops. But should not be used where there is known allergy to lanolin alcohols.

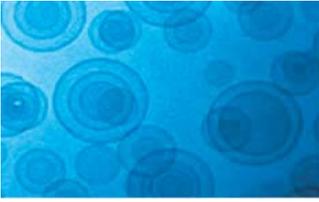
Because of the greasy nature of this product, most practitioners use lacrilube as a last resort, usually where a recurrent erosion problem may be developing.

Liposomal Lipid Spray

The “active ingredient” of Clarymist™ is Phosphatidylcholine phospholipid liposomes. They are prepared from natural soy lecithin of pharmaceutical grade. A phospholipid is a polar molecule consisting of a fatty acid component that is lipid-soluble, along with a charged phosphate group that is water-soluble. Phosphatidylcholine is the main lipid component of soy lecithin (94%), and also the most common phospholipid in natural tears.

Phospholipids as raw material are solid. The only possible way to get phospholipids in a form which is suited to applying to the eye is by producing liposomes. It was found that phospholipids combined with water under sonic vibration immediately forming a spherical structure, the liposome. Liposomes are used elsewhere in the pharmaceutical industry as “containers” to aid drug delivery to awkward sites in the body.

Clarymist is sprayed onto the closed eyelids from a distance of approximately 10 cm. After a few minutes the liposomes start to migrate from the lid margin into the tear film, where it is thought that they may improve the quality or quantity of the polar surfactant layer of the tears. This product needs more clinical trials, but anecdotal evidence does show improved relief from dry eye symptoms in many patients. The liposomes in Clarymist liposomal eye spray have a shelf life of at least 3 years.



Liposomes in solution



Lid Hygiene

It has been shown that a regimen of warm compresses and lid hygiene can make a significant improvement in tear film stability. They should apply a heat retaining gel pack or hot flannel to the affected area of the lower lid with pressure to melt the waxy lipid and then clean with a lid-care (Ciba vision). Personally I dislike the use of flannels due to hygiene considerations (Pseudomonas).

The “Eyes-Pack” hot gel pack in use (Photo A Matheson)



A new product called “Sterilid” has been released recently which is the first antibacterial lid hygiene product. This is a foam formulation that is massaged onto the lids and lashes then rinsed off one minute later. It is a great help in those dry eye cases that have an infective lid margin element, such as in blepharitis and meibomitis.

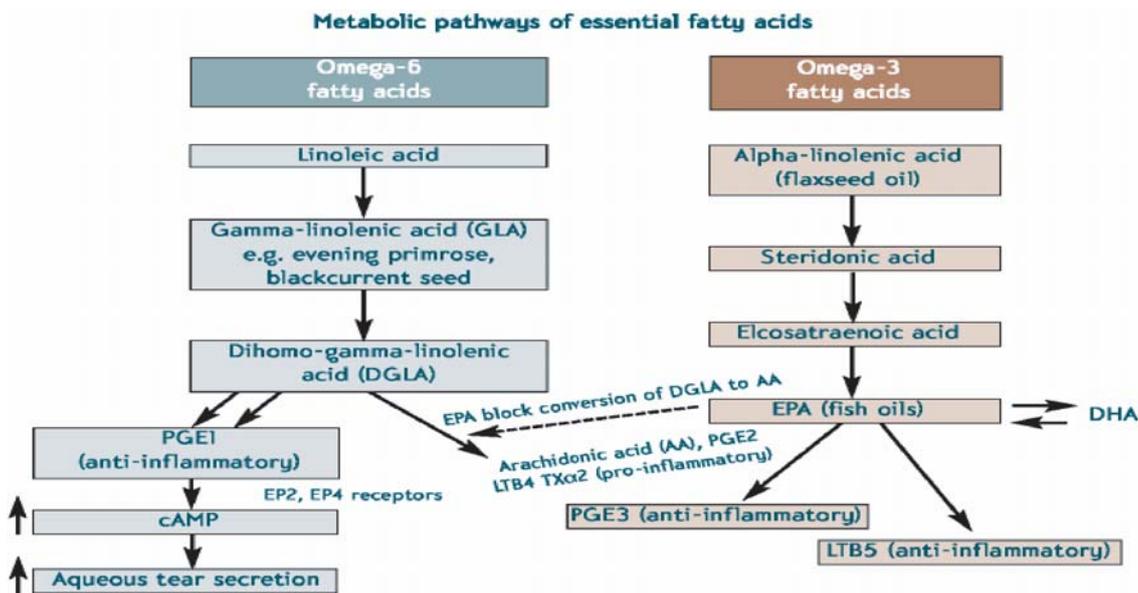
If the meibomian gland dysfunction is unresponsive to treatment a patient may need to be referred to their GP for systemic tetracyclines. Often a six-month course seems to help, with improvement waning after this time period. The mechanism of action is thought to be by inhibiting the Staphylococcal lipase and free fatty acids rather than a direct bactericidal effect.

Omega-3 and omega-6 fatty acid supplements may also help by reducing inflammation and improving meibomian gland secretions.

The Role of Omega-6 and Omega-3 fatty acids

Gilbard argues that we have enough omega-6 fatty acids in the typical western diet, so further supplementing this with such things as Evening primrose oil, serves no purpose and may further increase the imbalance between omega-6 and omega-3 fatty acids. He proposes that the simple flaxseed oil (Alpha-linolenic acid) and the fish oils (EPA) act synergistically, reducing inflammation through the production of LTB3 and PGE3 directly, and by blocking the production of Arachnodonic Acid from DGLA (see above diagram).

The use of antioxidant nutrition supplements has been shown to help improve the tear film quality and quantity - in particular, vitamins A, C and E, zinc and selenium²⁵. Vitamin A, for example, helps to improve corneal clarity and with the production of conjunctival goblet cells so will be beneficial with marginal dry eye attributed to mucous deficiencies, although patients should be reminded that too much vitamin A can be harmful in pregnancy. Vitamin A is also useful in severe cases of dry eye in ointment or oil drop form, although the usefulness of vitamin A in an aqueous solution (e.g. Vit-A drops/Viva drops) is questionable.



We will need to wait for further long term, multicentre studies, using large cohorts of patients before we can be certain as to the absolute contribution of dietary supplements in the clinical management of dry eye. A reduction in cholesterol intake to improve the quality of meibomian secretions in lipid disorders has also been suggested as a useful management option²⁶. This may also be a mechanism by which the omega-3 supplements help the meibomian secretions. Flaxseed oil ideally should be organically-grown, cold-pressed, and not contain the ligand portion because phytoestrogens have potential to make eyes drier.

Pharmaceutical-grade fish oils should be processed under nitrogen to maintain freshness. This avoids "rancid" fish odour. Also vitamin E in these preparations, prevents oxidation, maintaining the integrity of the oils. Molecularly distillation process removes mercury and any other heavy metals.

Unfortunately, long-term supplementation with omega 3s depletes serum levels of vitamin E, so the addition of vitamin E to Theratears Nutrition maintains serum levels of vitamin E.

Evaporation Reduction

Dry eye sufferers should optimise their environment to reduce tear film evaporation. They need to modify the local environment around the eye by, for example:

- Avoiding drafts
- Avoiding excessive air conditioning
- Using room humidifiers
- Avoiding lens wear in aeroplanes where there is generally low humidity
- Avoiding the use of air-borne pollutants that can break up the lipid layer and increase tear evaporation.

In extreme cases, the use of spectacles with tight fitting side shields or wearing swimming goggles can be beneficial to maintain high humidity levels around the eyes²⁶.



Side Shields



Radiator Humidifier

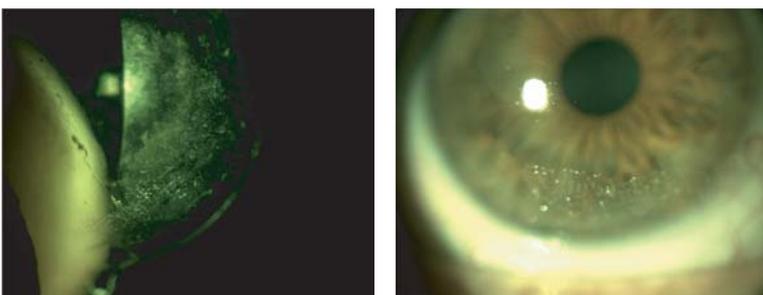
Bandage Silicon Hydrogel Contact Lenses

Bandage soft Silicon hydrogel contact lenses can be used to enhance corneal healing, prevent corneal dehydration and improve comfort. In cases of recurrent erosions, the patient may wear the contact lens on an extended wear basis, to reduce overnight adhesions forming between the cornea and the tarsal conjunctiva.

It has to be noted that a dry eye sufferer could be at higher risk of potential complications including bacterial conjunctivitis and inflammatory conditions such as sterile corneal infiltrates should be advised to seek advice if they develop any symptoms of pain or redness during lens wear.

Recently several studies have been published that show the benefit of Silicone Hydrogel contact lenses for therapeutic cases (Kanpolat et al 2003, Lim et al 2001). These studies were using the lenses on a continuous wear basis where the high oxygen transmission of these lenses was a real benefit over previously used hydrogel therapeutic extended wear lenses. In this setting, the indications for the fitting included things such as pain relief, enhancement of corneal healing, corneal protection, improvement of vision and corneal sealing/splinting. Lenses were changed monthly by hospital staff to reduce the trauma caused by more frequent lens removal, and also chair time per patient. These studies concluded that both Focus N&D and Purevision made good therapeutic lenses for such hospital cases.

Because of the silicone content of these lenses they attract lipid deposits badly. The use of alcohol based cleaners such as Miraflow reduces lipid deposition, although it might damage the surface coatings of the Purevision and N&D contact lenses. The newer SiHy lenses recently made available, having a lower silicone content seem to contaminate with lipids less. Also, not being surface coated, they can be more easily cleaned with alcohol based cleaners.



Examples of Lipid contamination on Silicone hydrogel Contact Lenses

Superior Epithelial Arcuate Lesions

Because SiHy contact lenses transmit so well, hypoxic effects are very rare. This by implication means that most induced mechanical changes are due to the stiffness of the material. The most significant of these is SEAL formation. These occur close to the superior limbus, are often irregular, raised above the nearby epithelial surface stain with fluorescein and may be associated with infiltrates.

They probably are caused by a mechanical shearing effect on the epithelial basement membrane by the contact lens. They tend to occur more often patients with steep corneas, tight eyelids, males and orientals. Sometimes this can be prevented by fitting with a different base curve or a less stiff material. Once resolved there is usually no residual corneal opacity.



SEAL

The stiffness and edge design of the currently available SiHy contact lenses poses a potential CLPC risk. Hyperaemia and large papillae similar to those found in SiHy wearers occur in patients with loose bulbar sutures and ocular prostheses. This can occur almost straight after commencement of lens wear or equally after two or more years of contact lens wear. According to Schovin (2004 & 2003), this is more indicative of a mechanical aetiology. He recommends fitting with a daily disposable or a less rigid SiHy contact lens.

The future of SiHy contact lenses probably is dependant on new materials with better surface qualities, better physical properties, and a greater range of parameters. The surface needs to be more wettable with less lipid deposition. It must be less stiff so that less pressure is placed on the mucous layer and corneal epithelium and and thus also will mechanically irritate the tarsal plates less. They also need to come in a wider range of parameters so that more corneal shapes can be accommodated without compromise.

It has become apparent that there is a corneal staining issue with SiHy contact lenses when used with multipurpose solutions. This seems to be greatest with solutions containing polyhexamethylene biguanide, although not all formulations seem to affect all patients to the same degree. Carboxymethylcellulose (CMC) found in products such as Theratears has been shown in peer-reviewed studies to be cytoprotective when used prior to wearing contact lenses treated with cationic disinfecting agents such as polyhexamethylene biguanide. It is therefore an ideal eye-drop to be used on contact lens prior to lens insertion.

Dry eye patients who wear SiHy bandage contact lenses are more prone to these staining issues due to their fragile corneal epithelium and the fact that the toxic elements in the disinfecting solutions are not diluted and eliminated as efficiently as in a tear-normal patient. In these dry eye bandage lens cases I use either Panasept, Regard or Synergi disinfecting solutions which do not contain polyquat disinfectants and can be considered preservative free. My personal preference is for the Panasept system as does not contain a cleaning agent in its make-up.

Summary – Clinical Pearls

It is important that we listen to the patients symptoms as well as any signs visible. For example are they worse on awakening, which may indicate a recurrent erosion problem or meibomitis, or do they get worse as the day progresses, which may indicate osmolarity rising as tear secretion reduces and the tears evaporate. Are symptoms purely in adverse conditions such in air conditioned environments, or while using a VDU. If so improving the lipid layer and hypotonic tear supplementation may be needed, if addressing any humidity issues does not alleviate symptoms. However, simply supplementing the lipid layer with a liposome spray may be sufficient to reduce evaporation enough to alleviate symptoms

Is there evidence of a poor tear break up time? If an adequate tear meniscus is present, this can indicate a tear quality, rather than quantity issue. Is there corneal fluorescein staining present? Depending on its location it might point to a meibomitis/lid margin component, or a more generalized desiccation problem. Is Lissamine Green staining of the bulbar conjunctiva present? This in the presence of a poor TBUT is suggestive of goblet cell loss due to increased osmolarity. What is the lipid layer like? If poor this may suggest that flaxseed/fish oil supplementation may be appropriate, lid hygiene, hot compresses and possibly systemic tetracycline therapy may help.

An electrolyte balanced, preservative free, hypotonic tear supplement will help in all cases of dry eye syndrome, as tear osmolarity increases independently both in reduced secretion and evaporative dry eye. If after trying to normalise the lipid, aqueous and mucous secretions as much as possible, there is still an obvious low tear volume or excessive tear drainage problem, or if the patient just wants to put their eye-drops in less often, then punctal occlusion either with silicone plugs or cautery may be indicated. Cautery should be used with caution as it is irreversible and carries significantly greater risks to the patient.

Do we have a predominately infective lid margin component? In this case we would probably veer towards using an antibacterial lid hygiene product such as Sterilid with our hot and cold compress treatment. We might prescribe a course of Fucidic Acid Gel antibiotic, which has both excellent anti-staphylococcal properties, and also has some anti-inflammatory capability. If we have a predominantly inflammatory element to the problem then flaxseed/fish-oil supplementation would be a good idea, possibly adding a preservative free NSAID eye-drop such as diclofenac.

An Optometrist not on the therapeutics specialist register is not able to supply diclofenac. This and other anti-inflammatory medicines such as Acular, or a low risk/ ocular penetration steroid such as Fluoromethalone (FML), can be prescribed by a supplementary prescriber by agreement with an independent prescriber (usually the patient's GP). Alternatively, the patient could be referred back to their GP with a recommendation for this treatment. Obviously, when primary care optometrists achieve independent prescriber status for such products this will no longer be necessary. .

Optometrists might choose to refer back to an ophthalmologist as independent prescriber when more advanced medication is required or when surgery is indicated. For example, patients being managed with silicone punctal plugs could be referred to an ophthalmologist if it was decided that cautery might be a more appropriate solution. It is important for supplementary prescribers to put in place relationships and protocols with their independent prescriber(s) to be able to manage such situations smoothly.

By attacking dry eye in a systematic way, much of the mystery is removed. If the patient and practitioner understand the mechanisms involved they can work in unison towards a common goal.

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