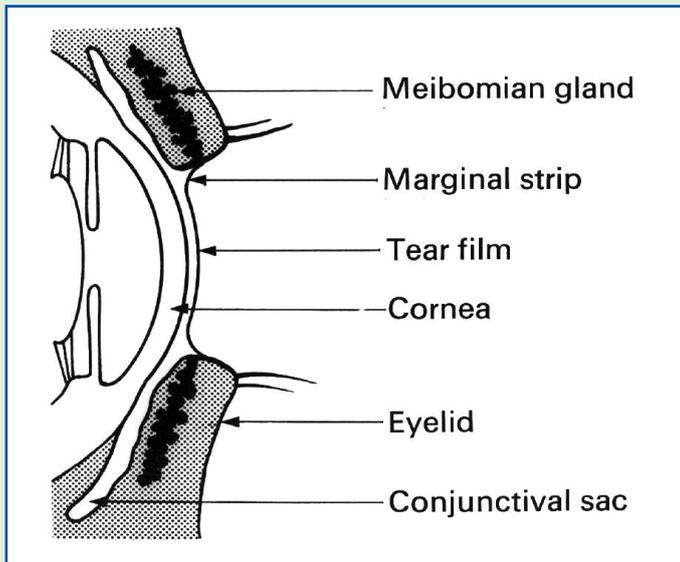


# Education

## The Tear Film and its assessment

by Andrew Matheson FCOptom, DipT<sub>p</sub>SP, FAAO



John Tiffany, 2004

The ocular surface is bathed in a moist film the structure of which is far more complicated than previously thought, and still not fully understood.

Of the total tear volume, approx 80% is found in the upper and lower tear menisci (Korb, 2002). Only a small amount lies beneath the open eyelids, the remainder covers the cornea and exposed bulbar conjunctiva.

It has been said that the average thickness of the tear film over the exposed ocular surface varies from approx 9 $\mu$ m immediately after a blink, to approx 4 $\mu$ m just before the start of the next blink (Mishima, 1965). The thinnest portion of the tear film is adjacent to the tear menisci, presumably due to forces exerted by the surface film.

The thickness of the pre-lens tear film can be assessed using the tearscope (Guillon, Guillon & Shah, 1995). The thickness of the pre-lens tear film is a function of the individual patients tear characteristics as well as the lens surface properties.

The tear film has the following functions:-

- It infills the irregularities in the epithelial shape, providing crisp optics
- It lubricates and hydrates the surface of the conjunctiva and cornea



The tearscope (photo Matheson, Alresford)

- It flushes cellular debris and foreign particles away towards the puncta for elimination
- It provides the cornea with gaseous exchange of oxygen and carbon dioxide and some nutrients, although most of the glucose requirement is said to come from the aqueous
- It provides the first line of defence against infection, notably lysosyme and lactoferrin

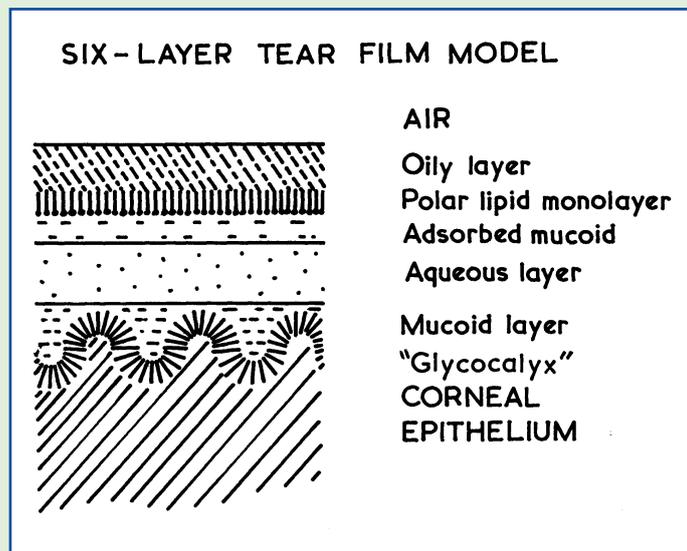
From the ocular health point of view the most relevant portion of the tear film is the pre-corneal tear film. It is damage to this part of the ocular surface that we are trying to modify in the course of dry eye management.

The structure of the tear film has been the subject of much heated debate, with estimates of its thickness varying from the original works of Wolff (1946), Holly and Lemp (1977) of approx 7 $\mu$ m, to the more extreme 40 $\mu$ m of Prydall et al (1993).

King-Smith et al (1999) using reflectance spectra have demonstrated values between 1.6 and 7.3 $\mu$ m, averaging approx 3 $\mu$ m, whereas Stuart Hodson using a microelectrode technique recently found a thickness of 5-7 $\mu$ m. There is some uncertainty as to whether this value is the thickness of the entire tear film or merely that of the aqueous phase. The future will hopefully hold the real answer. What is clear is that the original simple

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three layer model of mucous followed by a large aqueous layer, superimposed by a superficial lipid layer may need modifying. It has been shown that there are dissolved mucins throughout the aqueous phase, becoming less concentrated as you move anteriorly from the epithelial glycocalx to the lipid layer (Dilly, 1994). Recent studies may question this (quoted Tiffany, 2004).



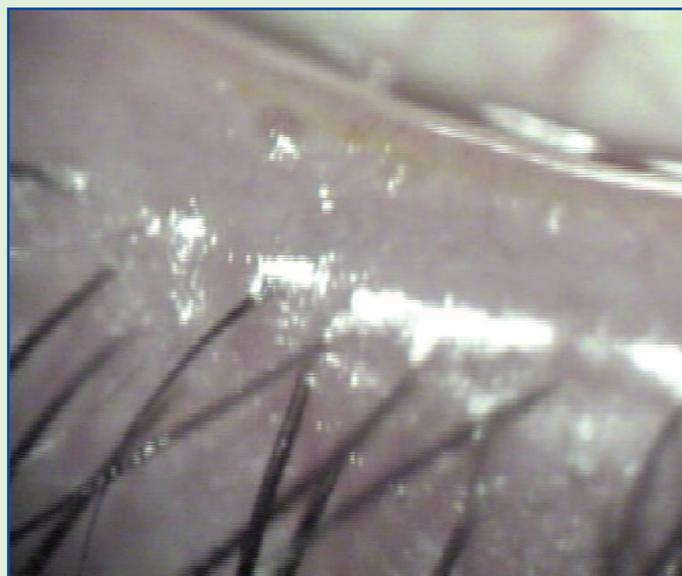
Tiffany (1988)

## The lipid layer

This layer is relatively thin, approx 0.1  $\mu\text{m}$ , and is derived mainly from the meibomian or tarsal glands, but also the accessory glands of Zeiss (sebaceous) and Moll (sweat) are thought to contribute slightly by some (Craig, 2002), but not by others (Gilbard & Chow, 1997). Its main role is to slow evaporation of the aqueous component of the tears to the atmosphere (Craig and Tomlinson, 1997). 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 film (McDonald, 1968)

Tiffany (1998) 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 vitro studies trying to replicate the retardation of evaporation of saline with meibomian lipids have failed, indicating that we do not fully understand the interactions of the lipid layer and the aqueous phase yet.



Blocked Meibomian Glands (photo Matheson Alresford)

In meibomian gland dysfunction and blepharitis the number of high melting point lipids increases, producing a poor quality tear film with increase evaporation characteristics. Patients with MGD often show irregularities of the lower lid margin, due to meibomian gland drop-out.



The Lipid layer as seen by the Tearscope (photo A Matheson, Alresford)

## The Aqueous Layer

This, mixed with the mucous layer is the major constituent of the tear film and mostly comes from the main lacrimal gland situated in the superior temporal angle of the orbit. It is divided into orbital and palpebral portions by the levator aponeurosis. The accessory glands of Krause lie mainly in the conjunctiva at the superior fornix, although some are found at the inferior fornix as well. The accessory glands of Wolfring, which are somewhat bigger, lie in the conjunctiva at the foveal ends of the tarsal plates.

Most of the lacrimal secretions arrive in the upper temporal fornix, passing then to the marginal strips (menisci). Blinking then distributes the fluid from the marginal strips to the pre-corneal tear film (Mishima 1965)

The construction of the lacrimal gland is similar to that of the salivary glands, in that it is a tubuloalveolar gland, similar to the salivary gland. Antibodies are secreted actively by plasma cells in the lacrimal gland, but also through serum leakage from dilated conjunctival vessels. The concentration of solutes secreted by the gland end-pieces and the overall volume of water secreted is modified as the fluid passes on its way down the ducts towards the eye. Water is either absorbed or secreted, depending on whether basal or reflex tears are needed. Also potassium ions are secreted into the fluid, along with proteins and other substances. Having finally left the lacrimal ducts the lacrimal fluid mixes with the secretions of the goblet cells, meibomian glands and accessory glands to form the final make-up of the tears (Dartt 1992).

The main and accessory lacrimal glands work simultaneously. The main lacrimal gland is regulated both centrally (e.g. in response to emotion) and peripherally (e.g. due to trigeminal nerve stimulation such as nasal or ocular irritation), both sympathetically and parasympathetically. Parasympathetic fibres are in intimate contact with the acinar cells, duct cells, myoepithelial cells and blood vessels. Sympathetic innervation (noradrenaline) also affects the blood vessels and possibly with the myoepithelial cells. The parasympathetic nerves (acetylcholine) primarily control production of water and electrolytes and protein production. Stimulation by cholinergic agonists, e.g. adrenaline, causes vasodilation with increased secretion resulting. The exact role of this input to the gland is not fully understood. Both parasympathetic blockers and  $\beta_1$ -adrenergic blockers can diminish lacrimal gland secretion clinically. (Craig 2002).

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 (Yamanda, 1997). 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 mechanism (Milder, 1987).

The total protein content of the tears is on ave. 0.7g/100ml (Japelson & Lockwood, 1964). The tear proteins serve many uses, such as lowering the surface tension to increase wettability, control of infectious agents, metal transport, buffering pH and osmotic regulation (Records, 1979).

Although there are many protein components to the tears the main ones secreted by the lacrimal gland are Lysozyme, Lactoferrin, Tear Lipocalin and secretory IgA. Lysozyme makes up approx 30% of the total tear protein. It is the most alkaline protein in the tears and occurs at higher levels in the tear fluid than anywhere else in the body. It dissolves bacterial cell walls by dissolving the mucopolysaccharide component (Craig 2002).

Lactoferrin is also antibacterial; it is an iron-binding agent that removes the iron that the bacteria require for replication. The serum protein, transferrin is also present in small quantities, and acts in a similar manner.

Lysozyme and Lactoferrin levels decrease in dry eye and with age (Seal, 1986).

It is thought that Tear Lipocalin may bind fatty acid ligands to the surface of the tear film, helping to reduce tear evaporation (Craig 2002).

In the unchallenged eye the only tear immunoglobulin that is significantly present is Secretory IgA, derived from the lacrimal secretion. Under challenge, the serum proteins are released especially IgG and IgM, and under such stress they can rise to up to 20% of the total tear protein (Heremans, 1968).

Osmolality 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 eye (Gilbard, 1978). It can also occur in aqueous deficient dry eye. An osmolality of less than 312 mOsm/kg is physiological, rising to 323 mOsm/kg in moderate to severe dry eye (Craig, 1995).

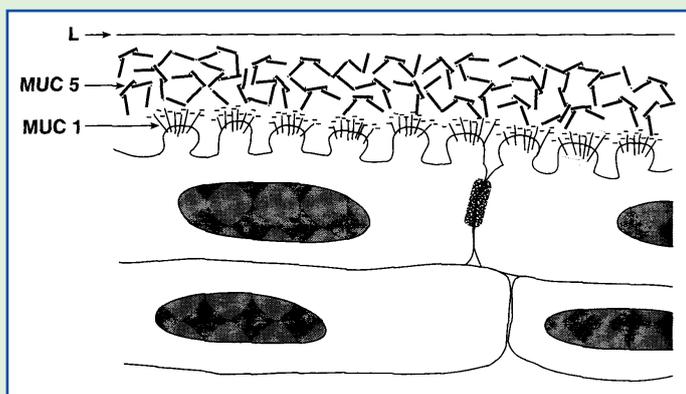
Some artificial tear supplements, e.g. Theratears, have a low osmolality, in an attempt to reverse that found in dry eye (Gilbard & Keynon, 1985).

## 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 conjunctiva (Kessing 1968).

As previously mentioned, the exact thickness of the mucous layer of the tear film is open to debate. It does represent the layer closest to the anterior surface of the corneal epithelium, where it is adherent to the glycocalyx covering the microvilli and their microplicae. The exact point where the epithelially secreted glycocalyx becomes the mucous layer of the tear film is also a bit indistinct.



Model of the mucin distribution on the cornea  
(Gipson & Inatomi. 1997)

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.

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 Bka preservative.

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 (Dilly 1985, Rolando & Zeirhut 2001). Lipocalin and tear lipids are now known to contribute to this property, although the precise mechanism is not fully understood as yet.

The glycocalyx is composed of epithelially secreted protein anchored mucins (MUC1).

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

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.

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