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Reviewing the tear film's lipid layer

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Introduction

The stability and quality of the precorneal tear film (PCTF) is of primary concern when fitting a patient with contact lenses as these factors often determine patient success. However, the PCTF remains an obscure facet of optometry with a myriad of conflicting research with regard to its structure and thickness. Conventionally, the PCTF has been acknowledged to be an approximately 3-7 µm[1-4] thick film comprising three distinct layers, that is, an aqueous layer sandwiched between a mucous and lipid layer[1, 5, 6]. Conflicting research suggests that the PCTF is actually much thicker (34-45 µm)[6-8] and that the tear film may not be as compartmentalized as we believe it to be. The contrary belief suggests that the mucin and aqueous are not distinct layers but rather a mixture with the mucin forming the bulk of the mixture[7] and its concentration being highest close to the epithelial cells[6, 9]. This would insinuate that despite the years of research invested in numerous studies done on the PCTF, our understanding of this structure is still ambiguous. Reviewing the PCTF in its entirety is a formidable task thus by means of the following review we endeavor to enlighten the reader merely about the outer most layer of the PCTF, that is, the lipid layer (LL).

The lipid layer

The LL is a complicated structure that has been difficult to wholly understand. Even though there seems to be unanimous agreement regarding the fundamentals of this layer, that is, that the LL is the outmost layer of the tear film which is secreted primarily by the Meibomian glands and supplementary lipids secreted by the Glands of Moll and Glands of Zeiss[1, 5, 9-11], there still remains ambiguity regarding its thickness, structure and composition.

The LL's significance to the tear film is demonstrated by its functions[1, 10, 12-18]. The lipids: 1) coat the underlying aqueous thereby impeding evaporation, 2) create a hydrophobic barrier on the lid margin to avert the overflow of tears, 3) prevent the skin lipids from contaminating the tear film, 4) act as a lubricant to prevent friction between the eyelid and ocular surface and 5) facilitate in creating a smooth refractive surface of good optical quality.

Conclusive information regarding the thickness, structure and composition of the LL remains elusive. Various methods of measurement have led researchers to conclude that the normal LL can average between 100-370 nm in thickness[1, 10, 11, 19] and is likely to be even thicker in neonates[20]. The thickness of the LL is thought to be a key indicator of tear film stability[12, 21]. The thickness of this oily layer varies across the surface of the eye and forms a multilayer of lipids[10, 22] which have a melting point of approximately 32-35º C.[1, 23] It remains unclear whether the lipids form a bilayer or a trilayer[24] thus further discussion will be based on a lipid multilayer comprising two lipid phases, namely, a thick outer non-polar phase and a thin inner polar phase[1, 9, 24-26].

It is well known that oil and water simply do not mix. So how is it possible that the LL is able to combine with the aqueous-mucin layer to form a smooth coalesced tear film (TF)? To answer this question one has to delve a little into the biochemistry of the lipids

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that comprise the LL. Fundamentally, the main non-polar lipids include wax esters, cholesterol esters, triglycerides and hydrocarbons[9, 23, 26], and the main polar lipids include phospholipids, sphingolipids and free fatty acids[9, 24]. In order for the LL to perform its functions optimally, these lipids must be present in appropriate quantities and any variation in the lipid composition would result in a compromised tear film[5, 9]. Previous research demonstrated that all lipids present in the LL were derived from the meibomian gland secretions[9]. However, recent research[23, 25] established that polar lipids are not present in meibum and suggests that other sources of these lipids, such as the cornea, aqueous tears and conjunctiva, should be considered. The polar phase functions as a surfactant and provides a link between the aqueous-mucin layer and the non-polar phase thereby providing stability for the non-polar phase[9, 24]. To put it in perspective, phospholipids have a polar (hydrophilic) head (which interacts with the aqueous) and a non-polar (hydrophobic) tail (which interacts with the non-polar lipids)[9]. Having stable grounding upon the polar phase, the non-polar phase is able to conduct its primary function, that is, control the evaporation rate of the underlying aqueous[9]. Fundamentally, the hydrophobic and hydrophilic environments of the LL and aqueous-mucin layer respectively, are able to interact and form an intact TF due to the amphilic nature of the non-polar phase[27, 28].

Interferometry

During routine clinical slitlamp evaluation of the cornea, one would have at some point come across a patch of rainbow-like colours. This phenomenon occurs due to interference between the light reflected off the LL and the aqueous-mucin layer. When monochromatic light is incident on a thin film (such as the TF), there is reflection off the anterior surface (LL) and the posterior surface (aqueous-mucin layer)[22, 29]. The reflected light from the two surfaces will interfere either constructively (rays are in phase) or destructively (rays are out of phase) to generate bright and dark fringes respectively[8]. When white light is reflected, the wavelengths of all the colours in the spectrum interfere with each other resulting in colour fringes[30]. The colours that are visible are dependant on the thickness of the thin film; therefore, we are able to estimate the thickness of the LL with the aid of interference patterns. This is a rather simplistic explanation therefore for a more detailed summary of the physics involved with interferometry, the interested reader can refer to the paper by King-Smith *et al*[8].

Interferometry is a method of quantitatively and qualitatively evaluating the LL based on the interference patterns that are observed[8]. Evaluating the thickness of the LL provides insight on its structure and stability[12, 19] and can therefore be used as a diagnostic tool in determining the success of a new contact lens (CL) patient and may also aid in the diagnosis of dry eye[31, 32]. Interference patterns can be used to estimate the thickness of the LL[19, 22]. The thickness, confluence and intactness of the LL are factors that contribute to the stability of the LL and therefore the stability of the TF[19]. A simple and convenient method of viewing the interference patterns created by the LL is with the use of a tearscope. Jean-Pierre Guillon[19] invented the Keeler Tearscope Plus to facilitate the non-invasive evaluation of TF characteristics. This instrument allows the practitioner to visualize the LL and determine its stability based on the dominant colours and patterns of the interference fringes. The LL can be classified into six main categories[12, 14, 19-21, 32, 33], namely, Amorphous, Marmoreal Open Meshwork, Marmoreal Closed Meshwork, Flow/Wave, Normal Coloured Fringes and Abnormal Coloured Fringes. An Amorphous pattern is indicative of the ideal TF (with a well mixed LL) which in turn represents a potentially successful candidate for CL wear. Marmoreal Closed Meshwork, Flow/Wave and Normal Coloured Fringes represent average TF stability which is also indicative of a potentially successful candidate for CL wear. Marmoreal Open Meshwork represents a thin LL and Abnormal Coloured Fringes represents an unstable TF, thus the presence of either of these patterns renders the patient unsuitable for CL wear. Table 1 provides further details on classifying the interference patterns[12, 14, 19-21, 32, 33]. If a tearscope is not at hand in clinical practice, then a slitlamp serves as a useful alternative to gain a basic insight regarding the thickness of the LL. Using a parallelepiped at an angle of between 45-60˚ with high illumination and high magnification, one is able to view the LL interference patterns which lie adjacent to the patch of endothelium. Classification of the LL can be determined based on the dominant colour and pattern present. It is important to have at least an estimate of the LL thick ness when fitting CL's given that LL thickness is a useful indicator of TF stability[12, 21] and therefore CL success. ness when fitting CL's given that LL thickness is a useful indicator of TF stability[12, 21] and therefore CL success.

Contact lenses and the tear film

Placing anything foreign into the human body is probably going to provoke an adverse reaction therefore it comes as no surprise that inserting a CL onto the eye evokes havoc on the TF. Introduction of a CL onto the eye changes the structure of the perfectly designed TF which may affect the capacity of the TF to carry out its functions optimally. The altered structure of the TF is made up of a prelens tear film (PrTF) and a postlens tear film (PoTF)[18]. A sufficiently formed PoTF affects lens movement34 and is required for tear exchange under a lens (which is necessary to remove debris[35] such as decomposing epithelial cells, which, if remain trapped, could instigate corneal problems

Table 1: Classification of interference patterns[12, 14, 19-21, 32, 33].

CLASSIFICATION	DESCRIPTION OF PATTERN	COLOUR	ESTIMATED THICKNESS (nm)	CL SUITABILTY
Marmoreal Open Meshwork	Vague marble-like pattern	Grey	10-20	Patient should be cautioned on dryness problems that are likely to ensue with lens wear. Patient may have existing dryness symptoms that could be exacerbated with CL wear.
Marmoreal Closed Meshwork	Distinct marble-like pattern	Grey	20-50	Average TF stability. Patient should be advised on potential dryness symptoms.
Flow/Wave	Dynamic wave-like pattern	Grey/grey-white/ grey-yellow	30-90	Average TF stability. Suitable for CL wear.
Amorphous	No distinguishable pattern	Blue-whitish	80-90	Ideal candidate Good TF stability
Normal Coloured Fringes	Multicoloured fringe pattern with colours changing gradually across the surface.	Yellow-brown/ brown/blue	> 90	Average TF stability. Suitable for CL wear.
Abnormal Coloured Fringes	Swift changes in colour with a globular appearance.	Variable coloured fringes.	Variable thickness	Unstable TF. Usually associated with conditions such as blepharitis therefore treatment recommended before CLwear.

such as infiltrative keratitis[18]). An adequately formed PrTF is considered to fundamentally facilitate comfort. An inadequate PrTF is associated with increased evaporation (which in turn causes dryness symptoms) and lens deposition, both of which elicit uncomfortable lens wear[36]. Non-invasive methods such as Optical Pachometry and Optical Coherence Tomograpy have been used in an attempt to quantify the thickness of the PrTF and PoTF. Lin *et al* utilized Optical Pachometry to conclude that the PoTF is approximately 11-12 µm[35]. With the use of Optical Coherence Tomography, Wang *et al* concluded that the PrTF is between 3.6-3.9 µm and the PoTF is between 4.5-4.7 µm[4]. Wang *et al* claim that the large discrepancy in the values for PoTF between the two studies can be attributed to the method of measurement employed by Lin *et al*. Wang *et al* believe that optical pachometry may give exaggerated values because the measurement taken may include the mucin layer as well.

Regardless of an adequately formed PrTF and PoTF, the presence of a CL on the eye has been found to change ocular physiology[37], destabilize the TF[18, 21, 36, 38, 39] and compromise the integrity of the cornea thus making it vulnerable to infection[18]. Even though corneal compromise is inevitable, the prudent CL practitioner should ensure a CL fit that minimizes these detrimental effects. Patients using CL's are more susceptible to dry eye than spectacle users or emmetropes. Approximately 50% of CL wearers complain of dryness symptoms and this is one of the major reasons for cessation of lens wear[33]. The reason for this high incidence of dryness symptoms among the CL population is attributed to an unstable TF[30] as mentioned above. Tear meniscus height, non invasive tear break up time, tear surface quality and prelens thinning time are a few key indicators of tear stability and have all been adversely affected by the presence of a CL according to the research done with soft CL's[17, 18, 33, 39, 40]. It is therefore important that TF stability and quality is assessed before as well as after CL fitting.

Conclusion

As discussed earlier, the LL plays a crucial role in maintaining a stable TF therefore evaluation thereof is important in determining the integrity of the TF. Clinically, TF stability can be assessed with the use of a slitlamp. In clinical practice, it may not be essential to have exact measurements for the key indicators of TF stability; therefore perhaps a more qualitative assessment of the tears would suffice. A quick, basic qualitative evaluation of the tears with a slitlamp may include assessing: 1) the amount of debris in the tears, 2) tear meniscus height, 3) meibomian glands and secretions and 4) interference patterns of the LL. The tear break up time can be measured non-invasively with the aid of the mires in a keratometer.

Every individual's LL is unique and does not always abide by the expectations outlined in literature (in terms of thickness, structure and composition). It is probably because of this uniqueness that researchers find difficulty in establishing unanimous facts about the LL. With all the discrepancies found in literature regarding the TF, it is difficult to convince one self that we actually understand what happens under a CL. Even though literature provides conflicting evidence of the true nature of the LL, the prudent CL practitioner should be aware of how the introduction of a CL affects each patient individually and provide the best fit CL that would achieve optimal vision without compromising ocular health. CL practitioners should equip themselves with the skills and knowledge required to assess the TF so that decisions can be made for patient suitability for CL wear and patient management after fitting CL's.

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