Ocular surface - tear film interface

Dr Christine Croker

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Understanding the morphology and function of the ocular surface and tear film interface is important in the context of ocular health and various eye conditions, such as dry eye disease and disorders affecting the cornea.

The ocular surface refers to the outermost layer of the eye, including the cornea, conjunctiva and tear film. The role of the ocular surface is to provide, protect and maintains a smooth refractive surface. This is achieved through the integration of the innervation, endocrine, vascular and immune systems for each anatomical unit. One should think "epithelium" when conceptualising the ocular surface. This is because a continuous sheet of epithelium lines the cornea, anterior glands, tarsi and terminating at the zone between the skin and conjunctiva, known as the mucocutaneous junction(1).

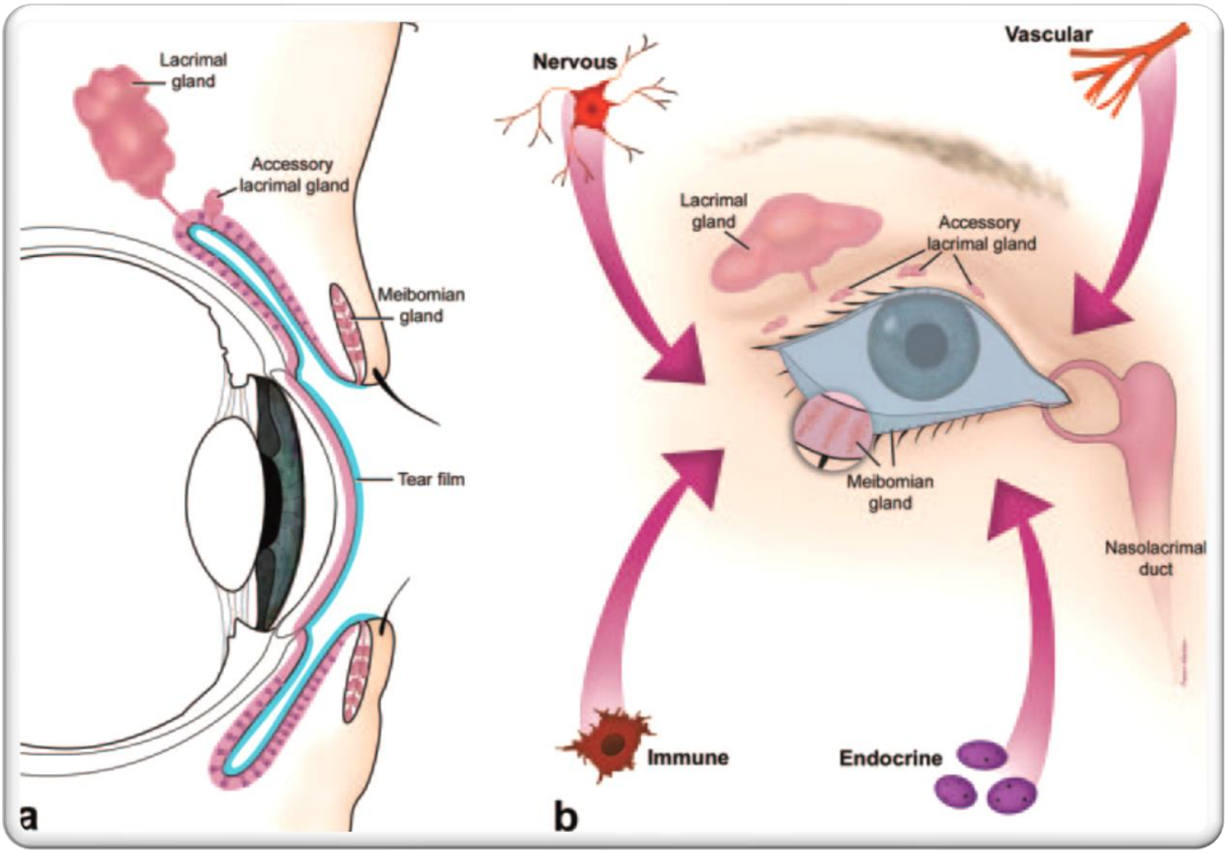


Figure: 1 The Ocular surface

a. The ocular surface

b. There is an integration of the innervation, endocrine, vascular and immune systems

From Gipson IK. The ocular surface: the challenge to enable and protect vision: the Friedenwald lecture. *Invest Ophthalmol Vis Sci*. 2007;48(10):4390-4398(1)

The Micro-projections of the Epithelium

The corneal epithelial micro-projections refer to specialised structures on the surface of corneal epithelial cells. The micro-projections collectively contribute to the overall health and function of the ocular surface. They aid in the maintenance of a stable tear film, essential for ocular comfort, clear vision and protection of the underlying structures(1, 2).

The corneal epithelial micro-projections include:

1. **Microvilli:** Microvilli are small, finger-like projections on the apical surface of corneal epithelial cells. These micro-projections increase the surface area of the cell facilitating absorption and secretion. Additionally, these microvilli aid in the adhesion of the tear film and contribute to the overall stability of the tear film on the ocular surface.
2. **Microplicae:** Microplicae are tiny, irregular folds or corrugations on the surface of corneal epithelial cells. These structures are thought to enhance the structural integrity of the corneal epithelium and also contribute to the overall stability of the tear film. Microplicae may play a role in cell adhesion and the integrity of the corneal surface.
3. **Tight Junctions:** While not projections in the traditional sense, tight junctions are specialised regions where adjacent corneal epithelial cells are tightly bound together. These junctions create a barrier that regulates the passage of ions, molecules and cells across the corneal epithelium. Tight junctions contribute to the maintenance of corneal transparency and play a crucial role in corneal homeostasis.

Therefore, where the cornea and conjunctiva are covered by stratified squamous epithelium, micro-projections play several important roles:

1. **Surface Area Increase:** Epithelial micro-projections increase the surface area of the cells, facilitating better absorption and secretion of substances. This increased surface area is particularly important improved water-binding.
2. **Mucin Secretion:** Goblet cells – specialised epithelial cells – found in the conjunctiva, produce mucin, a key component of the tear film. Micro-projections on the surface of goblet cells increase the area available for mucin secretion, contributing to the muco-aqueous layer of the tear film.

3. **Barrier and Protection:** Micro-projections can contribute to the formation of a physical barrier on the epithelial surface, providing protection against environmental factors, mechanical stress and preventing the entry of pathogens & foreign substances into the eye.
4. **Cellular Adhesion:** Some micro-projections may be involved in cellular adhesion, helping cells stick together and form a cohesive layer. This is essential to maintain the integrity of the epithelial barrier.
5. **Sensory Functions:** Micro-projections may have sensory functions, allowing cells to detect changes in their microenvironment and respond accordingly.

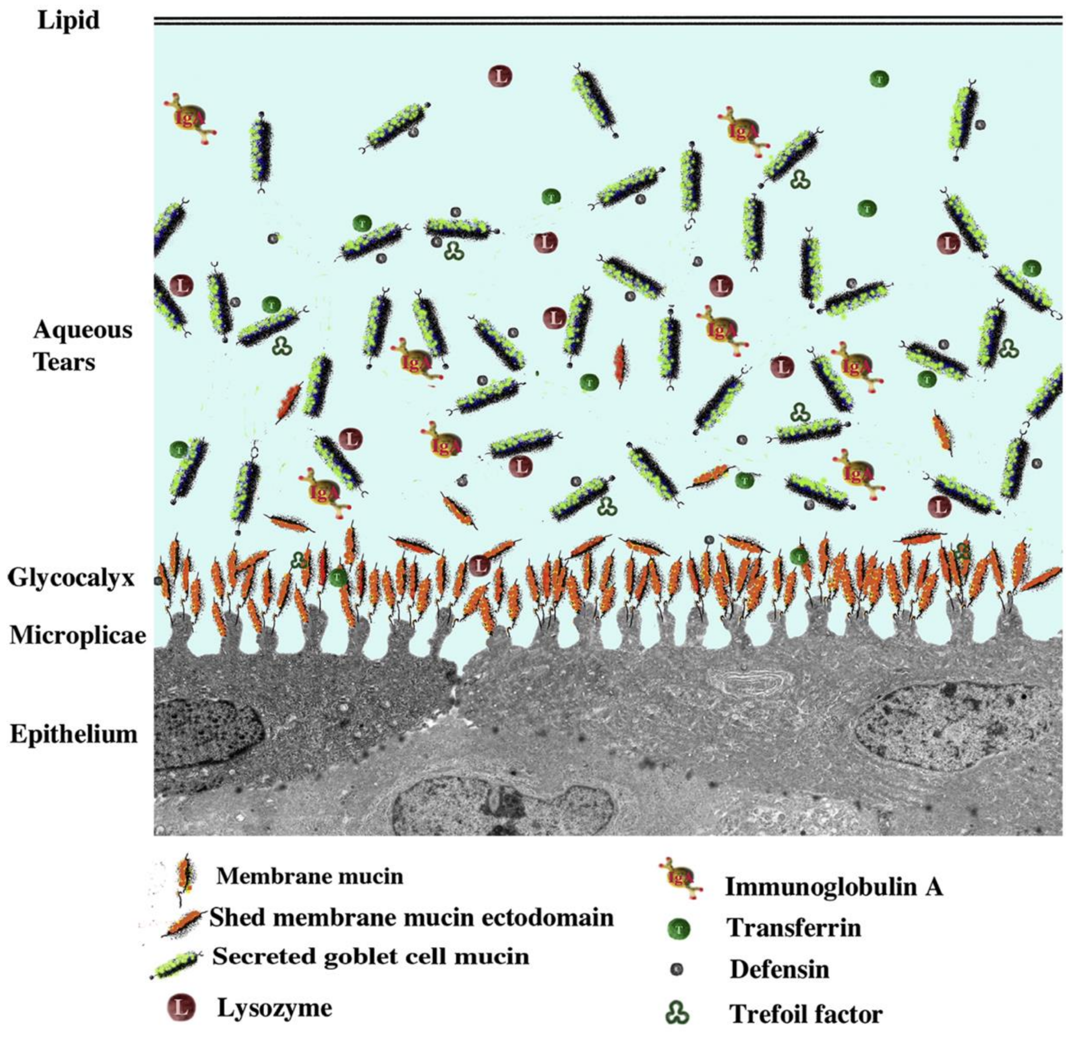


Figure2. Components of the ocular surface

From Gipson IK. The ocular surface: the challenge to enable and protect vision: the Friedenwald lecture. *Invest Ophthalmol Vis Sci*. 2007;48(10):4390-4398. doi:10.1167/iovs.07-0770 (1)

The Glycocalyx

The corneal glycocalyx is a 'fuzzy' coating covering the micro-projections apical surface of corneal epithelial cells. The glycocalyces which are hydrophilic protein-sugar compounds, which enhance mucin and water adhesion, also create a barrier to microbes and chemicals, and reduce friction. This layer is primarily composed of membrane-bound glycoproteins-polysaccharide with proteoglycans which create a central protein backbone. In conditions where the glycocalyx is compromised, the cornea may be more susceptible to damage, inflammation and other pathological changes.

Key features and functions of the corneal glycocalyx include:

1. **Protection:** The glycocalyx acts as a protective barrier for the corneal epithelium, shielding it from environmental factors, microbes and, mechanical and chemical damage.
2. **Lubrication:** This gel-like layer provides lubrication to the cornea, helping to reduce friction during blinking and maintaining a smooth ocular surface. Proper lubrication is essential for the comfort and health of the eyes.
3. **Adhesion:** The corneal glycocalyx contributes to the adhesion of the tear film to the corneal surface. This helps in the even distribution of tears and ensures that the ocular surface remains properly lubricated.
4. **Cell signalling:** Glycoproteins within the glycocalyx play a role in cell recognition, signalling and communication. They can be involved in various physiological processes, including cell adhesion, immune response and tissue repair.
5. **Maintenance of Homeostasis:** The glycocalyx is involved in maintaining the homeostasis of the corneal microenvironment. It helps regulate the exchange of nutrients, ions, and other molecules between the tear film and the corneal epithelial cells.

The Glands of the Ocular Surface

Several glands contribute to the health and function of the ocular surface. These glands play crucial roles in producing and maintaining the tear film, which is essential for lubrication, protection, and nourishment of the ocular surface. The main glands involved in ocular surface health include:

1. **Meibomian Glands:**
   - **Location:** Meibomian glands are located within the upper and lower eyelids, particularly in the tarsal plates.
   - **Function:** These glands secrete meibum, an oily substance that contributes to the lipid layer of the tear film. The lipid layer helps prevent excessive evaporation of tears, maintaining tear film stability and preventing dry eyes. Dysfunction of Meibomian glands can lead to conditions such as meibomian gland dysfunction (MGD) and evaporative dry eye(3).
2. **Lacrimal Glands:**
   - **Location:** The main lacrimal gland is located above the outer corner of each eye, beneath the upper eyelid.
   - **Function:** Lacrimal glands produce the aqueous (watery) component of the tear film. Tears produced by the lacrimal gland help keep the ocular surface moist, wash away debris, and provide essential nutrients to the cornea.
3. **Accessory Lacrimal Glands:**
   - **Location:** These smaller glands are scattered throughout the conjunctiva.
     1. **Glands of Krause** are found in the fornices
     2. **Glands of Wolfring** are found in the palpebral conjunctiva
   - **Function:** Accessory lacrimal glands contribute additional secretions to the tear film, including mucins. Mucins help stabilise the tear film and enhance its adherence to the ocular surface.

4. **Goblet Cells:**
   - **Location:** Goblet cells are found in the conjunctiva, particularly in the fornices (the recesses of conjunctiva).
   - **Function:** Goblet cells secrete mucins, which contribute to the muco-aqueous layer of the tear film. Mucin helps trap particles and microorganisms, preventing them from reaching the cornea.
5. **Glands of eyelashes:**
   - **Glands of Zeis:**
     1. **Location:** Glands of Zeis are sebaceous glands located near the base of the eyelashes (eyelash follicles).
     2. **Function:** These glands secrete sebum, an oily substance that helps to lubricate the eyelashes and the skin of the eyelids. The sebum from the Glands of Zeis contributes to the tear film's lipid layer and helps to prevent the eyelashes from sticking together.
   - **Glands of Moll(4):**
     1. **Location:** The glands of Moll are apocrine, sweat-type glands found exclusively at the margin of the eyelids and their ducts empty into the lash follicle.
     2. **Function:** An important function of the gland of Moll in immune defence. protecting the conjunctiva, cornea and the eyelid shaft from harmful pathogens.
   - **Sweat Glands:**
     1. **Location:** These eccrine glands, are found in the skin of the eyelids.
     2. **Function:** Sweat glands produce a watery fluid that, when combined with other secretions, contributes to the aqueous component of the tear film. While not the primary source of tears, sweat glands may play a minor role in tear production(5, 6).

The coordinated function of these glands ensures the proper composition and stability of the tear film, which is crucial for maintaining the health and clarity of the ocular surface. Dysfunction of these glands can lead to conditions such as dry eye disease, inflammation, or other ocular surface disorders. where the eyes may experience discomfort, redness, and visual disturbances due to inadequate tear production or instability. Proper eyelid hygiene and management of conditions affecting these glands are essential for maintaining ocular health.

The Tear Film

The tear film is a complex and dynamic liquid structure that covers the surface epithelium of the eye. It is crucial for maintaining the health and function of the ocular surface. Tear components are produced by the main lacrimal gland, accessory glands, the meibomian glands and the goblet cells. The proper balance and interaction – often referred to as homeostasis - between component of the tear film are essential for maintaining a healthy and stable tear film. In a healthy tear film, the all of the components of the entire tear film, will reduce evaporation and improve stability.

A initial model of the tear film referred to a triphasic structure of lipid, aqueous and mucin layers. However, a better interpretation proposed by The DEWS II and other important works refer to a biphasic model:

Muco-aqueous layer: The aqueous component and mucin component form a gel, although the muco-aqueous gel is denser towards the cornea

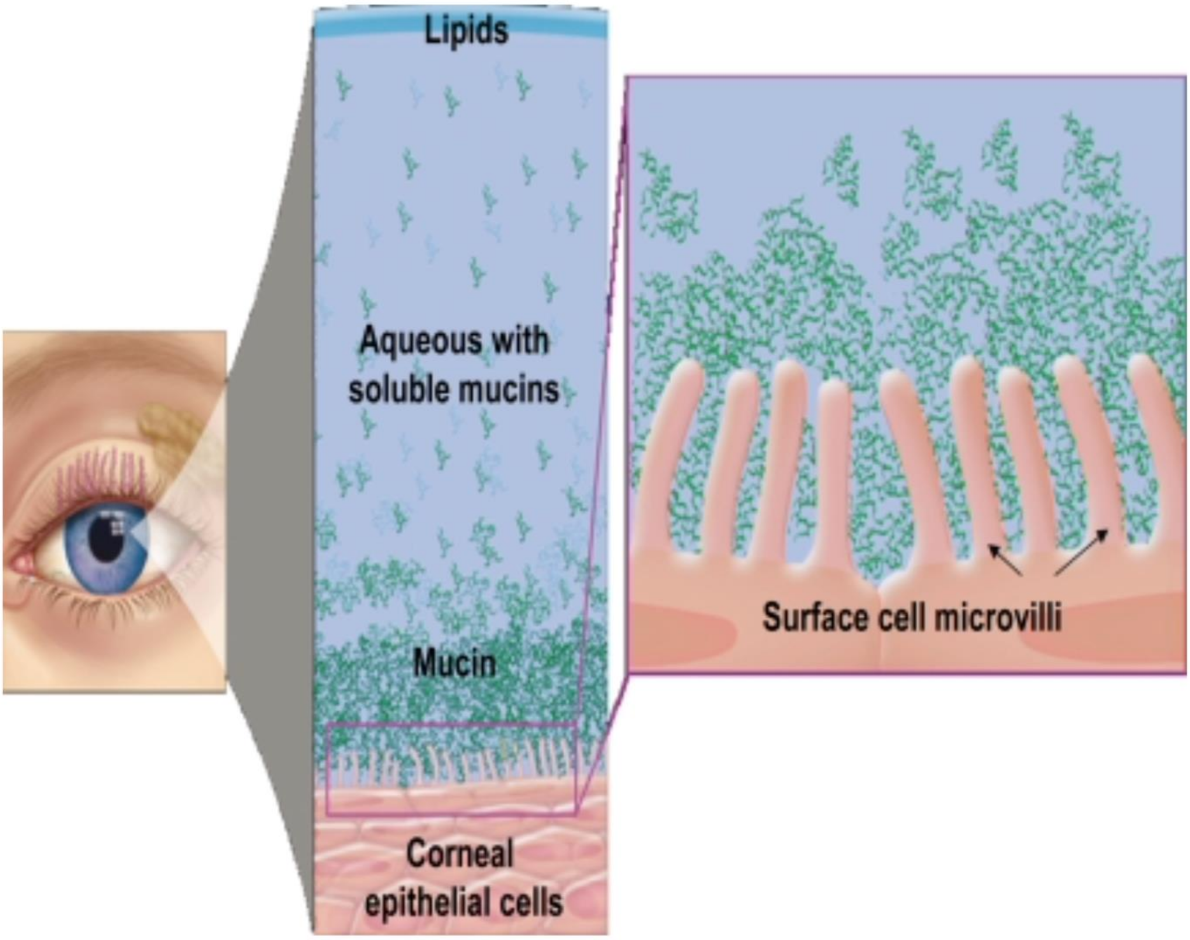
Tear film lipid layer: The lipid layer has a polar- and a non-polar lipid sublayers or phases(7).

The Muco-aqueous Layer

1. **Location:**
   - This inner tear film layer – the muco-aqueous – sits between the glycocalyx on the surface of the cornea and the outer lipid layer.
2. **Composition:**
   - The muco-aqueous layer consists mainly of water and mucins.
   - Mucins produced by goblet cells of the conjunctiva and other cells in the cornea, are large molecules with sugar residues that contribute to the layer's viscosity and ability to adhere to the underlying corneal and conjunctival epithelium.
   - This layer also contains thousands of proteins or peptides, e.g., glycoproteins, electrolytes (salts), proteins enzymes, and other substances that contribute to its composition.
   - The muco-aqueous layer has a thickness of about 8 microns.
3. **Source:**
   - The primary source of the muco-aqueous layer is the lacrimal gland, a gland located above the outer corner of each eye. The lacrimal gland secretes watery fluid into the conjunctival sac.
   - Goblet cells, specialised cells found in the conjunctiva, are the primary source of mucins. These cells release mucins into the tear film.
4. **Function:**
   - **Lubrication:** The muco-aqueous layer provides lubrication to the ocular surface, preventing friction between the eyelid and the cornea during blinking.
   - **Nutrient Supply:** The muco-aqueous layer supplies essential nutrients to the cornea and other tissues on the ocular surface.
   - **Oxygenation:** It facilitates the transfer of oxygen from the air to the avascular cornea.

- **Protection:** The muco-aqueous layer acts as a protective barrier, flushing away debris and pathogens and preventing them from adhering to the ocular surface. The muco-aqueous layer also promotes a reduction in inflammation.
- **Maintenance of Ocular Surface Integrity:** The muco-aqueous layer plays a role in maintaining the integrity and health of the corneal and conjunctival epithelium by providing a protective coating and preventing damage.
- **Stabilisation:** Mucins help stabilise the tear film by improving the adherence of the aqueous component to the ocular surface.
- **Facilitation of Spreading:** Mucins contribute to the even spreading of the tear film during blinking, ensuring uniform coverage and preventing dry spots on the cornea.
- **Regulation of Osmolarity:** The composition of the muco-aqueous layer is crucial for maintaining the osmotic balance of the tear film. Osmolarity refers to the concentration of solutes in a solution. Proper osmolarity is necessary for the health of ocular surface cells.
- **Dynamic Production:** The production of the aqueous layer is dynamic and increases in response to various stimuli, such as irritation, dryness, or the presence of foreign bodies. This mechanism helps restore the tear film's stability and comfort.

5. **Drainage and Clearance:** Excess tears drain into the lacrimal puncta, small openings at the inner corner of each eyelid. From there, tears travel through the lacrimal canaliculi and into the lacrimal sac before ultimately draining into the nasal cavity.
6. **Dynamic Secretion:** Goblet cells release mucins in response to various stimuli, including irritation or dryness. This dynamic secretion helps adapt the tear film to changing conditions and maintain ocular surface health(7-10).



Healthy tear film with lipid, aqueous, and mucin layers and healthy ocular surface with intact microvilli.

Figure 3. Tear film and the Epithelium

From Gayton, Johnny. (2009). Etiology, prevalence, and treatment of dry eye disease. Clinical ophthalmology (Auckland, N.Z.). 3. 405-12. 10.2147/OPTH.S5555.(11)

Key characteristics and functions of the tear film lipid layer include:

1. **Position:** The lipid layer is the outermost layer of the tear film, at the air interface and rests on the muco-aqueous layer.
2. **Composition:** The lipid layer is a thin film, primarily composed of lipids, including meibum, which is an oily secretion produced by the meibomian glands. Meibum is rich in lipids such as triglycerides, wax

esters, and polar lipids. This important layer only makes up 1% of the thickness of the tear film.

3. **Surface Tension Reduction:** The primary function of the tear film lipid layer is to reduce the surface tension of the underlying aqueous-mucin layer. This reduction in surface tension helps to prevent the rapid evaporation of tears from the ocular surface. Without the lipid layer, tears would evaporate quickly, leading to dryness and discomfort.
4. **Prevention of Tear Film Breakup:** The tear film lipid layer contributes to the stability of the tear film by preventing its breakup. A stable tear film is essential for maintaining a smooth and optically clear surface for vision.
5. **Spreadability:** The lipids in the tear film lipid layer provide a smooth and even distribution of tears across the ocular surface during blinking. This ensures that the tear film covers the cornea and conjunctiva uniformly.
6. **Protection of Ocular Surface:** The lipid layer helps protect the ocular surface from environmental factors, such as wind and dust, by forming a hydrophobic barrier.
7. **Nutrient Transport:** The tear film lipid layer facilitates the transport of essential nutrients to the cornea and other ocular tissues. This is important for the nourishment and maintenance of a healthy ocular surface.

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The tear film lipid layer

The above-mentioned characteristics of the tear film lipid layer are achieved through the two parts:

- **Non-Polar lipid phase** – outer, air interface layer
- **Polar lipid phase** – the inner layer(8, 12, 13)

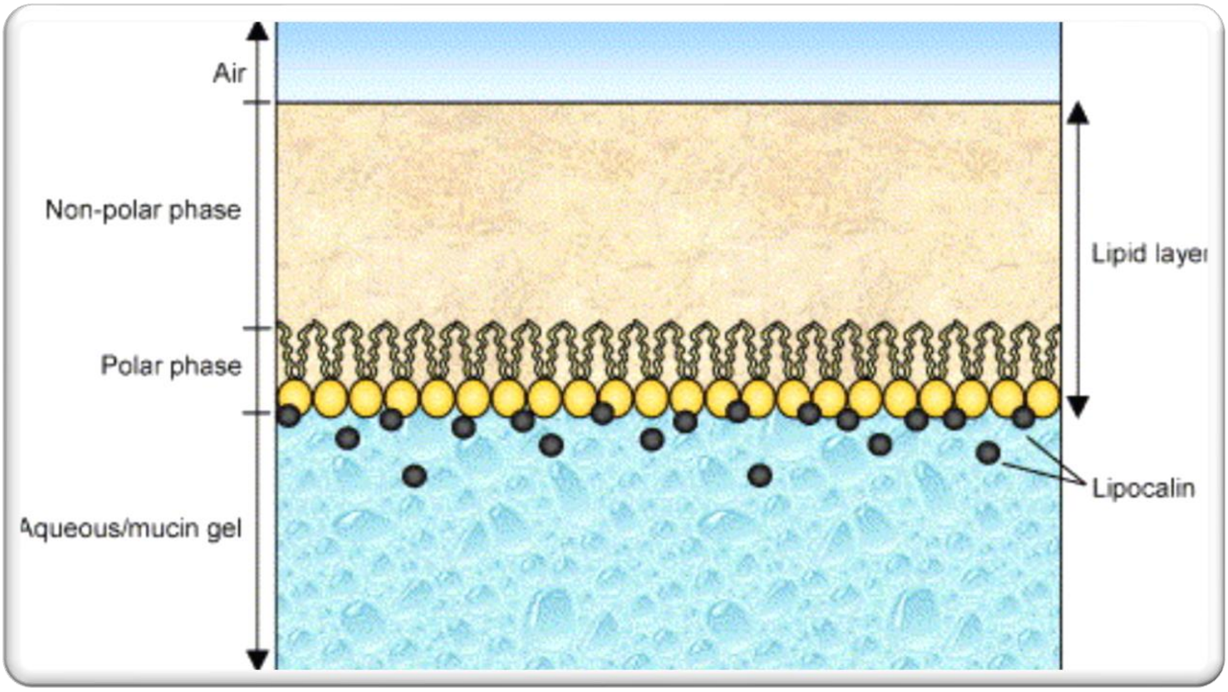

Figure 4. The lipid layer of the tear film has a biphasic structure. The relatively thick outer layer consists of nonpolar lipids and the inner layer contains polar phospholipids. The nonpolar lipids are generally thought to retard aqueous evaporation, whilst the underlying phospholipids facilitate interaction with aqueous.

From Johnson ME, Murphy PJ. Changes in the tear film and ocular surface from dry eye syndrome. Progress in Retinal and Eye Research. 2004;23(4):449-74(13).

The Polar Lipid Phase

Key features and functions of the polar lipid phase in the tear film include:

1. **Position:** The polar lipid phase connects the aqueous layer and the non-polar lipid phase.
2. **Composition:**
   - **Phospholipids:** The polar lipid phase is rich in phospholipids, which are molecules with both hydrophilic (water-attracting) and hydrophobic (water-repelling) regions. Phospholipids contribute to the amphiphilic nature of the polar lipid phase, making this layer a great sandwich layer which behaves as a surfactant, because normally water and oil do not mix.

- **Glycolipids:** These are lipids that have a carbohydrate chain attached. Glycolipids also contribute to the amphiphilic properties of the polar lipid phase.
- **Lipocalin:** Lipocalin acts as an extracellular transport protein
- **Thickness:** This layer is impressively thin at only 1-3 molecules thick which equates to about 2-9nm.

3. **Amphiphilic Properties:**
   - The amphiphilic nature of the phospholipids and glycolipids molecules allows them to align at the interface between the muco-aqueous layer and the non-polar lipid phase. This alignment helps to stabilise the tear film and facilitates the smooth spreading of the tear film during blinking. Therefore this layer is a surfactant.
4. **Stabilisation of Tear Film Layers:**
   - The polar lipid phase plays a role in preventing the mixing of the aqueous and non-polar lipid phase. This separation is crucial for maintaining the distinct functions of each layer and ensuring the stability of the tear film as a whole.
5. **Interactions with Mucin Layer:**
   - The polar lipid phase interacts with the mucin layer, which is the innermost layer of the tear film. This interaction helps anchor the tear film to the corneal and conjunctival surfaces and ensures that the tear film adheres to the ocular surface.
6. **Enhanced Spreading and Lubrication:**
   - The presence of the polar lipid phase enhances the spreading of tears across the ocular surface, promoting even coverage and lubrication. This is crucial for maintaining ocular comfort and preventing dry spots on the cornea.

Imbalances or disruptions in the composition of the polar lipid phase can contribute to tear film instability and ocular surface disorders. Understanding the role of each layer, including the polar lipid phase, is essential for diagnosing and managing conditions such as dry eye syndrome. Treatments may involve strategies to improve the quality and composition of the tear film, addressing underlying factors that contribute to tear film dysfunction.

The Non-polar Lipid Phase

The non-polar lipid phase is a crucial component of the tear film, providing stability and preventing rapid evaporation of tears from the ocular surface. This layer is primarily composed of non-polar lipids, including wax esters and triglycerides, and is produced by the meibomian glands located in the upper and lower eyelids. The non-polar lipid phase, along with the polar lipid and protein components, constitutes the lipid layer of the tear film.

Here are key aspects of the non-polar lipid phase and its functions:

1. **Composition:**
    - **Wax Esters:** These are esters of fatty acids and fatty alcohols. Wax esters contribute to the non-polar nature of the lipid layer, making it hydrophobic and helping to prevent water loss from the underlying muco-aqueous layer.
    - **Triglycerides:** Triglycerides are another type of lipid that adds to the overall non-polar character of the lipid layer. They contribute to the lubricating properties of the tear film.
    - **Thickness:** This layer is only about 33-40nm thick.
2. **Hydrophobic Barrier:**
    - The non-polar lipid phase forms a hydrophobic barrier on the surface of the tear film. This barrier is essential for reducing the

surface tension of tears, preventing them from breaking up and evaporating quickly.

3. **Prevention of Tear Film Evaporation:**
   - One of the primary functions of the non-polar lipid phase is to inhibit the evaporation of tears from the ocular surface. Without this lipid layer, tears would evaporate rapidly, leading to dryness and discomfort.
4. **Stabilisation of the Tear Film:**
   - The non-polar lipids contribute to the overall stability of the tear film. They help maintain a uniform spread of tears across the ocular surface during blinking, preventing dry spots and ensuring optical clarity.
5. **Contribution to Ocular Comfort:**
   - The presence of the non-polar lipid phase contributes to ocular comfort by preventing irritation and dryness. It helps maintain a continuous and protective layer over the cornea and conjunctiva.

Conditions like meibomian gland dysfunction (MGD) can disrupt the production or quality of the non-polar lipid phase which can contribute to evaporative dry eye. MGD is characterised by abnormalities in the meibomian glands, leading to changes in the composition of the lipid layer and subsequent instability of the tear film(12, 14).

To make matters more interesting, the components of the tear film are not static but, continually disrupted by blinking and environmental stressors, and continually need to reform. However, blinking helps distribute the tear film evenly, and the integrity of the corneal and conjunctival epithelial cells. To maintain functional stability, the tear film should be continually replenished by both tear secretion and blinking. Disorders affecting any of these components can result in discomfort, blurred vision, and increased susceptibility to infections(15).

Abnormalities in any of the components, composition or function of the tear film lipid layer can lead to conditions like dry eye disease. Where there is an imbalance in tear film dynamics, symptoms such as dryness, irritation, and blurred vision can result.

As the ocular surface is an interconnected system, one condition can contribute to- or result in another. Some examples of this are: the loss of the tear film integrity increases the risk of ocular allergy, as allergens penetrating the cornea and conjunctival epithelium more easily, which creates additional ocular surface inflammation. Chronic allergic conjunctivitis and its associated inflammation can affect the epithelial lining of the meibomian glands, leading to meibomian gland dysfunction (MGD). Because the epithelium of the meibomian glands is a continuum of the epithelium of the conjunctiva and cornea, inflammation of dysfunctional meibomian glands may cause posterior blepharitis and further perpetuating the underlying inflammatory response. Tear film instability can cause the epithelia to lose their protective tear film, which may result in irregularities and discomfort(8).

In summary, understanding the ocular surface is crucial for diagnosing and managing conditions related to tear film dysfunction, such as dry eye disease. Treatments may include interventions to improve meibomian gland function, enhance lipid quality, and alleviate symptoms associated with tear film instability.

When the components of the ocular surface and tear film achieve homeostasis – the natural equilibrium of function, structure and chemical composition of fluids and tissue – optimum function and protection can be achieved.

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Questions

Please click here to answer

1. What is the primary role of the corneal epithelial micro-projections?

a. Aid in absorption of tears

b. Contribute to the stability of the tear film

c. Produce meibum for the tear film

2. What is the primary function of the corneal glycocalyx?

a. Lubrication

b. Protection

c. Production of tears

3. Where are Meibomian glands located?

a. In the cornea

b. In the conjunctiva

c. In the upper and lower eyelids

4. What is the composition of the muco-aqueous layer?

a. Mainly lipids

b. Mainly water and mucins

c. Proteins and electrolytes only

5. What is the primary function of the tear film lipid layer?

a. Lubrication

b. Surface tension reduction

c. Nutrient transport

6. Which layer prevents the rapid evaporation of tears from the ocular surface?

a. Muco-aqueous layer

b. Polar lipid phase

c. Non-polar lipid phase

7. What is the role of the polar lipid phase in the tear film?

a. Lubrication

b. Stabilization of tear film layers

c. Prevention of tear film breakup

8. What contributes to the non-polar nature of the tear film lipid layer?

a. Wax esters and triglycerides

b. Phospholipids

c. Glycoproteins

9. Where are Glands of Zeis located?

a. In the cornea

b. Near the base of the eyelashes

c. In the conjunctiva

10. What is the primary source of the muco-aqueous layer?

a. Goblet cells

b. Lacrimal gland

c. Meibomian glands

11. What is the primary role of tight junctions in the ocular surface?

a. Enhance structural integrity

b. Increase tear film stability

c. Regulate nutrient exchange

12. How do sweat glands contribute to tear film production?

a. Produce watery fluid for the aqueous component

b. Contribute to the lipid layer

c. Secrete mucins for the muco-aqueous layer

synapse
optometry