CHAPTER 17

CONTACT LENS DEPOSITS

Deposits on contact lenses consist mainly of tear film proteins, mucins and lipids. Lenses are coated, mainly with protein, almost immediately on insertion. Other substances such as make up and skin lipids can also deposit on lenses. Lens deposits, especially proteins, have been associated with an increased risk of microbial cell attachment to the lens material (microbial biofilm), as well as inflammatory complications, such as CLPC or GPC [466]. In the past, before the advent of disposable contact lenses, great efforts were made to eradicate all forms of deposits from contact lens surfaces with surfactant cleaners and enzyme tablets. Patients frequently returned to the practice for intensive cleaning and protein removal from their lenses. The arrival of disposable lenses in 1995, seemed to spell the end of concerns about lens deposits, rubbing and rinsing in combination with frequent replacement of the lenses seemed to be sufficient to keep deposits in check. Recent research on lens deposits, differences in deposits with different materials and the interaction between the lens deposits and the eye, have led to a renewed interest in the subject. Although contact lens surface deposits were briefly discussed in chapter 5, this section will cover the latest information regarding deposits, their interaction with the eye and their role in bacterial biofilms.

The deposition of a specific tear component on a contact lens denudes the tear layer of that specific element, which may upset normal homeostasis, reduce the availability of essential tear components and disrupt normal tear functions [56]. Furthermore, protein deposits can denature (change its physical properties) or undergo conformational change, which can result in an autoimmune response [56]. Deposits may also be beneficial. The protein lysozyme in its native state, is a potent antibacterial, preventing infection by gram-positive bacteria. Lens deposits can also enhance contact lens biocompatibility with the eye [466].

PROTEINS

De Souza et al., 2006 identified 491 different proteins and mucins in the tear film, ranging in size from 10 kDa to 2360 kDa [467]. The most abundant proteins in the tear film are lysozyme, lipocalin, lactoferrin, albumin and secretory immunoglobulin A (IgA) [466]. The total protein content in the tear film ranges between 6.5–9.0 mg/L and its concentration can be influenced by factors, such as time of day, contact lens wear, tearing and eye disease. Protein deposits have an opaque, white filmy appearance and may have cracks when the films are thick. They are found primarily on the front surface of soft contact lenses and on both surfaces of RGP lenses.

Lysozyme

Lysozyme is a potent antibacterial enzyme that hydrolyses the bonds in the outer walls of bacteria, particularly those that are gram-positive, such as *Streptococcus* and *Staphylococcus*. Lysozyme may also directly permeate through bacterial cell membranes. It is positively charged and its molecular weight size 14.3 kDA. Lysozyme makes up an average of 36% of the total tear protein [468]. Lysozyme is secreted by the glands of Krause, Wolfring and the lacrimal gland, and is therefore part of the innate immune response [56].

Lipocalin

Lipocalin has a lipid-binding role within the tear film and has a strong affinity to fatty acids. This determines the surface tension and viscosity of the tears and it binds and removes long-chain fatty acids from the tears preventing them from deactivating lysozyme. Therefore, it indirectly enhances lysozymes antimicrobial function [469]. Lipocalin is ideally suited for scavenging lipophilic, potentially harmful substances, and it may act as a general protection factor of the corneal epithelium [470]. Lipocalin is positively charged and makes up 17% of the tear film proteins [468]. Its molecular weight is 18–40 kDa and it is secreted by the lacrimal gland. Lipocalin is a part of the innate immune response [469].

Lactoferrin

Lactoferrin can bind to both gram-positive, as well as gram-negative bacterial membranes. It inhibits the growth of various bacteria including, *Escherichia coli, Haemophilus influenza, Streptococcus and Pseudomonas aeruginosa.* Lysozyme and lactoferrin may also act synergistically and *Staphylococcus epidermidis* is only susceptible to lactoferrin in the presence of lysozyme. Lactoferrin provides antimicrobial efficacy by binding free iron, thus reducing the availability of iron necessary for microbial growth, survival, and pathogenesis. Lactoferrin has been shown to inhibit biofilm formation and may play a role in protecting contact lens surfaces from colonisation. Virus particles' entry into epithelial cells is also inhibited by lactoferrin [471]. Its molecular weight is 80 kDa, it is positively charged, makes up 21% of the tear protein and it is secreted by the lacrimal gland making it part of the innate immune response [56].

Albumin

Albumin is synthesised in the liver and is the most abundant protein in the serum. It enters the tear film by leakage from the conjunctival capillaries and is therefore associated with the blood-tear barrier. Albumin is part of the adaptive immune response [472]. Its molecular weight is 67 kDa and it is negatively charged [472]. The major role of albumin in serum is as a carrier of various insoluble components, such as free fatty acids and hormones, including thyroxine and corticosteroids. All of these functions can also apply to tear albumin, since the tear film contains many of the physiologically active components found in serum [473]. Generally, higher concentrations of albumin are found during sleep, in unstimulated tears, in patients with symptoms of dry eye and in contact lens wear [472].

Secretory IgA (sIgA)

sIgA's role in the tear film is to prevent bacteria from gaining a foothold on the ocular surface and making them targets for phagocytosis. It is part of the adaptive immune response. sIgA makes up 7% of the total tear proteins [56]. sIgA is secreted by IgA-secreting plasma cells within the lacrimal gland itself. While the tear firm contains other immunoglobulins, secretory IgA is the predominant antibody and is the only immunoglobulin, whose concentration significantly increases during infection, suggesting its critical role in the defence of the ocular surface [474].

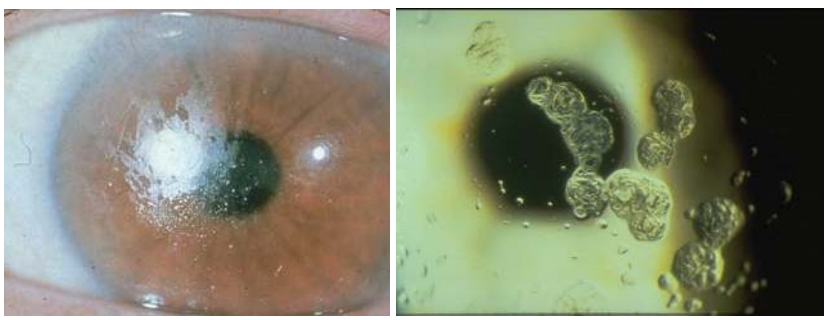

Figure 113: Protein deposits (left) and lens calculi (right)

LIPIDS

Tear film lipids include steroids such as cholesterol, saturated and unsaturated fatty acids, glycerides and polar lipids (see chapter 2). In the presence of excess oxygen, such as found in the atmosphere, and UV radiation, lipids change their function by oxidation and enzymatic degradation rather than denaturation [56]. This leads to the breakdown of the native fatty acids and the production of various intermediate and end products of lipid oxidation [56]. Different lens materials interact differently with lipids. Generally, conventional hydrogel group IV materials deposit less lipid than group II materials and uncoated silicone hydrogels more than coated silicone hydrogels (Figure 114) [56]. Tear lipids were traditionally regarded as relatively inert, but they are now seen as a potentially important family of compounds related to lens-induced discomfort [56]. Lipid deposits have a smeared, greasy whitish appearance. Patients more prone to lipid deposition, include those with tear film potassium deficiency, dry eye, high fat diets and high alcohol consumption.

LENS CALCULI

Lens calculi also known as jelly bumps or mulberry spots, are raised circular bumps that penetrate the front surface of the contact lens. They are composed of lipid, protein and calcium, and result from improper lens handling and care. Calculi are more common with high-water-content or extended wear lenses and in patients who have high fat, protein and alcohol intake, low tear potassium, dry eye, or incomplete blinking. The upper eyelid may be irritated by the deposit or grab onto it, causing the lens to decentre. Because removal would result in pits in the front lens surface, the contact lenses need to be replaced

MUCINS

Mucins adhering to contact lenses are altered forms of intracellular mucins. Different degrees of adherence of mucins to contact lenses may occur, either because of specific mucin characteristics, or after mucin interaction with other adherent materials [475]. Both membrane associated mucins (MUC1, MUC 2, MUC4, and MUC16), as well as secreted mucin (MUC5AC) have been detected on contact lens surfaces [56]. Mucins have an overall anionic charge and their polar nature may be associated with their affinity for contact lens surfaces, making them a component of contact lens deposition. This has potential implications in the wettability and tolerability of contact lenses, the presence of lid wiper epitheliopathy, and may be impacted by lens surface coatings, polymer characteristics or lens care products [476]. Due to the affinity of mucins for charged moieties, such as free radicals, their presence may offer some protection from toxins in the tear film [475].

MATERIAL PROPERTIES AND CONTACT LENS DEPOSITS

The amount of protein deposits that accumulate on a contact lens is closely related to the water content, ionicity or charge, modulus of elasticity, surface properties of the lens material, as well as the tear film characteristics of the individual patient [56]. Ionic lenses that contain methacrylic acid (MAA) attract much higher levels of protein compared to non-ionic lenses that contain N-vinylpyrollidone (NVP) [466]. Contact lenses that consist mainly of polyHEMA (pHEMA) are categorised as group I non-ionic (<50% water) materials. These lenses deposit less protein than pHEMA materials combined with other monomers, such as MAA and NVP [466]. MAA is the most commonly used hydrophilic monomer used in combination with pHEMA materials. It is found in some group III ionic (<50% water) materials and in most group IV ionic (>50% water) materials. It increases the water content of pHEMA, resulting in higher oxygen permeability [466]. The downside is that the negatively charged MAA attracts positively charged protein, such as lysozyme, therefore the higher the concentration of MAA, the higher the deposition of lysozyme and the lower the deposition of positively charged albumin [466, 472]. N-vinylpyrollidone

(NVP) is another hydrophilic monomer that is used to increase the water content of either pHEMA or polymethyl methacrylate (pMMA) lens materials. NVP can either be incorporated into the bulk material or grafted onto the surface of the material. It is present in most group II non-ionic (>50% water) materials and in combination with MAA in some group IV materials [466]. NVP impacts the overall charge of the material, increasing NVP content, less positively charged lysozyme and more negatively charged albumin deposits on HEMA-based lenses [466]. Table 16 in chapter 5, lists the different groups of materials and their characteristics. Figure 114 illustrates the concentration of lipid and protein deposits on available conventional hydrogel and silicone hydrogel materials.

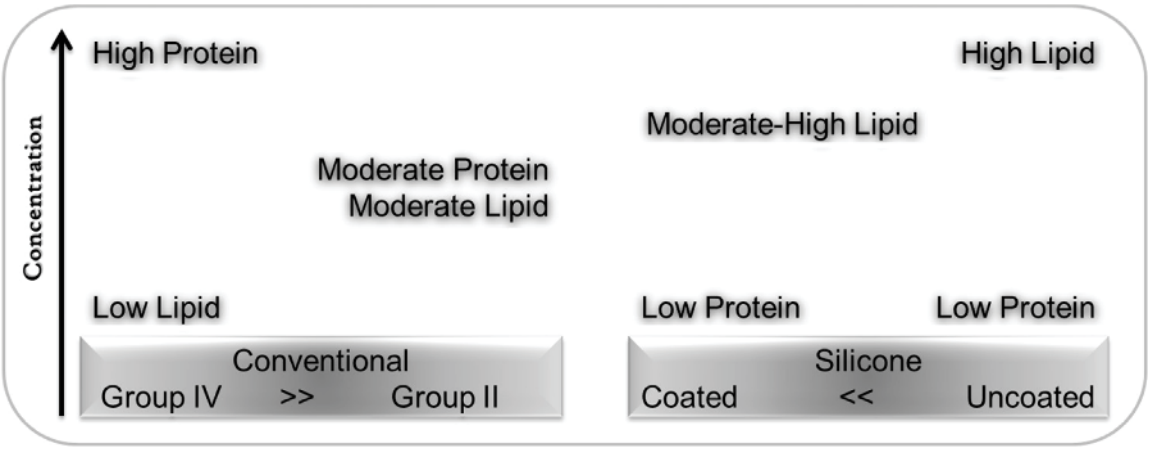

Figure 114: Protein and lipid deposits on conventional and silicone hydrogel lenses [56]

Pure silicone is a highly gas permeable, hydrophobic contact lens material that wets poorly [477]. Silicone hydrogel lenses show higher rates of lipid deposition and lower levels of protein deposits than ionic hydrogel lenses [62]. Most silicone hydrogel lenses require surface modifications to overcome the hydrophobic nature of the silicone components, which impacts the distribution of the protein on the surface and within the lens matrix [466, 478]. Binding of lipids on contact lenses are of concern as they might contribute to the thinning of the lipid layer and increased evaporation of the aqueous phase of the tear film [478]. Lipid deposits may also impact clarity of vision, wettability and comfort, but they have not been associated with ocular surface inflammation [466].

Protein penetration into lens materials depends on the pore size and density of the polymer chains in the material, as well as the structure and size of the protein under evaluation. The pore size of pHEMA contact lens materials vary between 2–7 nm (<10 nm). Silicone hydrogel materials pore sizes are < 5.5 nm [472]. Most folded up proteins are around 2 nm in diameter. However, proteins are flexible and can change their original structure and size by binding to other molecules, such as fatty acids or the surface of contact lens materials. The average diameter of albumin is 5.5 nm and lysozyme 4 nm, but this can vary significantly affecting its penetration and absorption into contact lens materials.

Table 59: Protein deposits on commonly used silicone hydrogel lenses in South Africa. Adapted from Luensmann et al., 2012 [466]

Material	Trade name	Dk/Water content	Surface and Material treatment	Lysozyme µg	Lactoferrin µg	Albumin µg
Balafilcon A	Pure Vision Pure vision 2HD	110/36 & 130/36	Reactive gas plasma surface treatment – no barrier to penetration of lysozyme and albumin into lens matrix	10–50	6–17	2
Lotrafilcon A	Air Optix Night and Day	175/24	Gas plasma treatment permanently modifies lens surface and wettability. Minimises penetration of lysozyme and albumin into lens matrix	2–4	1–2	X

Material	Trade name	Dk/Water content	Surface and Material treatment	Lysozyme µg	Lactoferrin µg	Albumin µg
Lotrafilcon B	Air Optix Aqua	138/33	Gas plasma treatment permanently modifies lens surface and wettability. Minimises penetration of lysozyme and albumin into lens matrix	4–10	2–3	1.8
Senofilcon A	Acuvue Oasys	147/38	High molecular weight chains of PVP are incorporated into the material to enhance surface wettability	1–13	3–5	1.8
Comfilcon A	Biofinity	160/48	Material incorporates silicone based siloxy-macromers, no specific surface treatment or internal wetting agents are used	<2	X	X

Protein Denaturation

Proteins can adopt multiple conformations *in vivo* which are different to the proteins native conformation [56]. Denaturation occurs when its secondary and tertiary structures are disrupted or destroyed. This usually occurs as a result of temperature changes, pH changes, UV radiation, surface hydrophobicity and peroxidising lipids. Denatured proteins lose their biological function, which in the case of lysozyme is its innate antibacterial properties. Denaturation of deposited protein may be partly responsible for autoimmune reactions, such as CLPC or GPC [56, 479]. Denaturation may be reversible [56]. The preservation of deposited proteins in their native state should therefore have considerable benefits for contact lens wearers, including maintaining the anti-infective functions of the tear film proteins, as well as preventing adverse inflammatory response to non-native protein structures present on lenses [479].

DEPOSITS ON RGP LENSES

The hydrophobic, lipophilic nature of RGP contact lenses makes them more prone to lipid than protein deposition. Among the different materials (Chapter 6) the Siloxanyl alkyl acrylate RGP-type lenses accumulate 2–3x as much total lipid as any of the other lenses [480]. Lipid deposition on rigid gas-permeable contact lenses is dependent on lens matrix hydrophobicity, while protein deposition is minimal and not material-dependent [481]. The hydrophobic sites of the lipid molecules are attracted to the lens matrix while the more hydrophilic sites are repelled by the matrix and therefore exposed to the aqueous surroundings [480]. The presence of protein decreases lipid deposition on siloxanyl alkyl acrylate RGP lenses, while lipid binding to rigid gas-permeable contact lenses reduces the hydrophobicity of the lens surface allowing protein to bind [481, 482]. The bound deposited hydrophilic protein then alters subsequent binding of both protein and lipid [481, 482].

CONCLUSION

Historically, the accumulation of contact lens deposits, including tear film proteins, lipids and mucins, have been regarded as a negative development leading to inflammation and comfort problems. Consequently, great efforts were made to remove these deposits from lens surfaces. However, in light of the beneficial antimicrobial characteristics of tear film proteins, as well as the lubricating characteristics of mucins, their accumulation on contact lenses may be beneficial. This hypothesis is supported by the literature [56, 466, 483]. In the study by Williams et al., 2003 they found greater numbers of viable gram-negative bacteria on new lenses compared to worn lenses, suggesting that protein deposits in their native state maintain their antibacterial function [483]. However, denaturation of the protein deposits can cause a reduction in their protective benefits [484] and the presence of these denatured proteins

themselves may be related to the development of CLPC or GPC [485]. Finally, the presence of denatured proteins can also lead to a loss of lens clarity and comfort.

The development of lens care products and lens materials that limit or reverse the denaturation of protein deposits may help to promote ocular health and comfort, while still providing the patient with optimal vision correction. One multipurpose solution (Biotrue, Bausch & Lomb Inc., Rochester, NY) proclaims to prevent denaturation of protein deposits and others are sure to follow soon. Dobson et al., 2011 found that deposited proteins antimicrobial activity is maintained after exposure to Biotrue MPS, but inhibited after exposure to hydrogen peroxide (Oxysept 1-Step) [486]. In a later study by Wright et al., 2012 Biotrue MPS's efficacy was evaluated. They concluded that the protein stabilising agents; hyaluronic acid, poloxamine, and sulfobetaine contained in Biotrue MPS prevented the denaturation of lactoferrin and lysozyme and that the stabilised proteins retained their innate functions [479]. Additional studies should be conducted to further elucidate the relationship between the antimicrobial properties of tear film proteins, contact lens solutions and lens materials.

To achieve optimal biocompatibility with contact lens materials, the material needs to be accepted by the ocular environment. This may require the deposition of selected tear film components, such as proteins, which should be bound loosely allowing easy removal by lens care products designed to maintain their native state. [466]