

# Silicone hydrogels –

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## Adverse events, the epithelium in extended wear, and inflammation and infection in the closed eye

In part four of our series on extended wear, Professor Brien Holden, Padmaja Sankaridurg and Isabelle Jalbert examine the potential complications of silicone hydrogel lenses.

This series is based on the BCLA's 1999 CET day on extended wear

ADVERSE EVENTS with extended wear have been one of the major barriers to the more widespread use of contact lenses. The risk of developing the potentially blinding microbial keratitis has led to justifiable wariness among practitioners and the public regarding extended contact lens wear. Unfortunately, the advent of disposability in conventional hydrogel lens materials has not reduced the risk of microbial keratitis (MK). Moreover, although the incidence of some significant adverse events such as contact lens papillary conjunctivitis (CLPC) and contact lens-induced acute red eye (CLARE) has been reduced by more regular replacement, it has certainly not been eliminated. Though the impact of high oxygen permeability (Dk) on the rate of microbial keratitis is yet to be determined, it is already clear that practitioners using high-Dk lenses will have to manage the other adverse events.

The key to successful management of such conditions lies in prompt detection, correct diagnosis and use of appropriate management and treatment strategies. The symptoms, signs, diagnosis, management and treatment of the complications seen in a contact lens practice, especially with extended wear of hydrogels, are outlined in this article.

### ADVERSE REACTIONS AND EVENTS

A 'serious adverse reaction' is defined as one that 'produces a significant impairment of function or incapacitation, is a definite hazard to the patient's health and warrants counteractive treatment or alteration of therapy'. An 'adverse reaction' is an 'unwanted effect (ie physical and/or psychological symptoms and signs) resulting from treatment', or 'any undesirable effect or problem that is present during the period of treatment'.

Categorisation of adverse reaction(s) or event(s) into distinct classes is essential as it enables practitioners and researchers to define the clinical features, estimate the rates of incidence, identify the risk factors, investigate the pathogenesis of the condition and undertake a systematic

approach to management and treatment of the condition.

### Adverse reactions

#### *Microbial keratitis (MK)*

MK is the only serious adverse reaction seen during contact lens wear as it is potentially blinding. Risk factors such as hypoxia, trauma, ocular surface disease, certain systemic conditions and contact lens wear are known to be associated with the development of MK.

MK has been seen with all lens types and with all modes of lens wear. However, it was the increased incidence seen with extended wear of soft lenses in the late 1970s and the 1980s that has led to public awareness of this complication. Since then it has been clearly established that the risk of MK is significantly greater with extended wear of hydrogel lenses in comparison to other types and modes of lens wear.

The use of silicone hydrogel lenses virtually eliminates hypoxia for the vast majority of wearers, thereby eliminating one of the most important risk factors for developing MK. Whether this factor alone is enough to seriously impact the occurrence of MK is yet to be seen.

At the time of this publication, no events of MK have yet been reported with silicone hydrogel lenses. As our benchmark with six-night disposable hydrogel lens extended wear in prospective studies is an MK rate of five per 1,874 patient eye years, we have to await a similar sample size without an event to conjecture a statistically significant

reduction with high-Dk soft lenses. So although progress is promising, further experience in controlled studies is obviously needed.

Epithelial trauma and bacterial entrapment can cause infection even with extremely high-Dk materials such as silicone elastomer. Interestingly, though epithelial trauma has not yet been eliminated with early silicone hydrogel prototypes, and some prototypes have even caused increased rates of mechanical trauma related events such as superior epithelial arcuate lesions (SEALs) and erosions, no cases of MK have yet been reported. It is unlikely, however, that MK will ever be completely eliminated due to the tendency of some wearers to introduce significant self-contamination with very virulent micro-organisms when lenses are handled and stored.

Nevertheless it is hoped that the risk of MK will be significantly reduced with silicone hydrogel lenses due to the health of the epithelium. Only time and experience will determine whether this highly desirable outcome has been achieved.

### Adverse events

The following types of significant adverse events will be briefly reviewed: CLARE, contact lens-induced peripheral ulcer (CLPU), infiltrative keratitis (IK), CLPC, superior epithelial arcuate lesions (SEALs) and corneal erosion. Tables 1 and 2 give details of symptoms and clinical signs of these adverse events and MK.

#### *Contact lens-induced acute red eye*

CLARE is always associated with overnight wear of lenses and is an acute inflammatory reaction to toxins such as lipopolysaccharide, enzymes and other by-products leaching from bacteria present on the contact lens.

Clearly, overnight wear of contact lenses colonised with significant levels of pathogenic bacteria, especially Gram-negative bacteria such as *H influenzae* and *S marcescens*, is the most important risk factor leading to a CLARE event. During asymptomatic lens wear there appear to be

◆ This is the fourth in a series of continuing education articles on the rebirth of extended wear contact lenses, edited by Professor Deborah Sweeney. Successful participation in each module of this College-approved series counts as one credit towards the College of Optometrists' CET scheme and towards the Association of British Dispensing Opticians' scheme. There are six multiple-choice questions and the pass mark is 70 per cent



no differences in the levels and type of micro-organisms colonising silicone hydrogel lenses in comparison to disposable hydrogels, suggesting that microbial adherence will continue to be seen with these new materials. A period of closely observing an adequate number of patients with the final marketed product over a significant period of time is clearly needed to determine the rate of CLARE.

#### *Contact lens-induced peripheral ulcer*

CLPU, like CLARE, is mostly observed with extended wear of contact lenses. The aetiology of CLPU remains somewhat unclear. However, since scrapings and biopsies show no micro-organisms, it is clear that it is not a corneal infection. Biopsies confirm CLPU to be an 'inflammatory' ulcer with the scarring being caused by post-inflammatory cicatrization. As CLPU events still occur with silicone hydrogel lenses, eliminating hypoxia is clearly not adequate to eliminate this adverse event. It would appear that epithelial trauma resulting from interaction of a lens surface with the corneal epithelium and bacterial contamination of the contact lenses are necessary to produce CLPUs.

#### *Infiltrative keratitis*

IK is a general category for sudden onset, symptomatic, infiltrative events observed during contact lens wear that are not categorised as events such as MK, CLARE and CLPU. Patients with IK typically report the onset of symptoms to be later in the day and not associated with sleep.

Given the multi-factorial nature of IK, it is difficult to predict whether silicone hydrogel lenses will have higher or lower levels of IK. However, it seems unlikely that such events will be eliminated.

#### *Contact lens-induced papillary conjunctivitis*

CLPC is a condition primarily affecting the upper tarsal conjunctiva and is the early stage of the condition commonly referred to in the literature as giant papillary conjunctivitis (GPC). The clinical signs of the various stages of this condition range from mild hyperaemia of the upper tarsus with a few, small papillae to severe hyperaemia with large, raised papillae, cobblestone in appearance.

Few data are available yet from long-term studies and therefore it is difficult to determine the rate of CLPC likely to be encountered with silicone hydrogel lenses.

The crucial factors will be type and level of deposits on the lens surface and the relationship of the edge to the lid surface. It is reasonable to speculate that, as these lenses are slightly more rigid, the lens edge shape and finish will be a critical issue.

#### *Superior epithelial arcuate lesions*

SEALs present as a thin arcuate, full thickness lesion of the superior corneal epithelium; usually within 1-3 mm of the superior limbus between 10 and 2 o'clock – the area normally covered by the superior eyelid. The lesion is typically up to 0.5 mm wide and from 1 to 5 mm in length. SEALs can be unilateral or bilateral and be asymptomatic or cause mild discomfort. Higher rates of SEALs may occur with silicone hydrogel lens wear in comparison to current extended wear products if the lens surface is not adequately wetting or if the lens design puts excessive pressure on the ocular surface – suggesting that mechanical interaction and not hypoxia is the major factor responsible for the development of SEALs. Practitioners should remain alert to the possibility of SEAL reactions in subjects fitted with the new products, particularly in view of their commonly asymptomatic nature.

#### *Corneal erosions*

Corneal erosions or epithelial abrasions can be observed in association with lens wear as a consequence of mechanical injury or physiological damage. Corneal damage from a contact lens is usually limited and anterior to Bowman's layer. Injury can also result from foreign objects trapped between the corneal surface and the contact lens. It is anticipated that corneal erosions will occur in association with silicone hydrogel contact lenses as they have with all other lens types. The lack of hypoxic effects may, however, ensure a healthier epithelial surface with tight junctions between cells that may be more resistant to mechanical injuries. Issues of management of corneal erosions will not differ from current practices.

#### **Non-significant adverse events (asymptomatic)**

##### *Asymptomatic infiltrative keratitis (AIK)*

AIK is a mild corneal infiltrative event observed with both daily wear and extended wear of hydrogel lenses and also during non-lens wear. As the terminology indicates, the event is asymptomatic and is observed at routine aftercare visits.

##### *Asymptomatic infiltrates (AI)*

AI appear to be faint clusters of a few inflammatory cells in both lens and non-lens wear. As with AIK, the condition is observed at routine aftercare visits. The conjunctiva is normal and the corneal signs

TABLE 1

#### Symptoms of MK and adverse events

ADVERSE REACTION/EVENT	SYMPTOMS
MK	Moderate to severe pain of rapid onset Severe redness ('meaty' appearance) Blurred or hazy vision; decreased visual acuity if the lesion is on the visual axis Discharge (mucopurulent or purulent), tearing Photophobia Puffiness of lids
CLARE	No symptoms prior to eye closure Patient woken from sleep by symptoms or symptoms noticed soon after waking Irritation to moderate pain Redness, tearing, burning sensation and photophobia
CLPU	Redness Pain Watering Foreign-body sensation Asymptomatic
IK	Redness Mild to moderate irritation or pain Watering Foreign-body sensation
CLPC	Itchiness or irritation Mucous discharge ('stringy' or 'ropy') Excessive movement of lens on eye Blurred vision (due to lens mislocation, discharge, or coatings on lens) Foreign-body sensation Redness
SEALs	Commonly asymptomatic If symptomatic can present with edge awareness or irritation and/or foreign-body sensation

TABLE 2

## Clinical signs of MK and adverse events involving the cornea

Feature		MK	CLARE	CLPU	IK	SEAL
Corneal infiltrate	Location	Central	Peripheral to mid-peripheral	Peripheral or mid-peripheral	Peripheral to mid-peripheral	Peripheral
	Type	Usually large focal infiltrate which is dense	Diffuse infiltration with small focal infiltrates	Single, circular focal infiltrate	Diffuse infiltration or small focal infiltrates	Arc-like greyish white epithelial lesion
	Depth	Anterior to mid-stroma, may involve entire depth	Anterior stroma	Anterior stroma	Anterior stroma	Epithelium
	Overlying epithelium	Full thickness loss	No significant involvement	Full thickness loss (when active)	Slight to severe	Significant involvement
	Endothelium	Commonly dusting with cells	No involvement	No involvement	No involvement	No involvement
Corneal oedema		Common: striae/folds	Uncommon	Rare	None	None
Anterior chamber		Common: flare to hypopyon	Uncommon	Only if severe	None	None
Lid oedema		Usual: may be blepharospasm	Uncommon	Uncommon	None	None
Bulbar/limbal redness		Severe: may be conjunctival chemosis	Moderate to severe	Moderate	Slight to moderate, localised	Slight to none
Unilateral/bilateral		Unilateral	Unilateral	Unilateral	Unilateral	Unilateral

include the presence of small focal infiltrates less than 0.2 mm in size. Usually single, these infiltrates are commonly seen in the periphery but could be located anywhere on the cornea. The infiltrates are limited to the anterior stroma. The epithelium overlying the infiltrates is intact and the condition resolves rapidly with no sequelae.

### SUMMARY

For contact lenses to truly challenge spectacles they need to provide excellent vision, be extremely comfortable and cause no adverse events. Silicone hydrogel lenses that virtually eliminate hypoxia

have enabled us to test the feasibility of a truly convenient lens – the major unfulfilled challenge. It is hoped that because epithelial metabolism is virtually normal, the cells will function normally, synthesising the key elements that make the cornea resistant to infection.

Proper patient hygiene and careful instructions on lens handling are also critical to avoid contamination and adverse events. The two most important 'rules' are:

- ◆ If a lens is removed from the eye for any time it should be properly cleaned and disinfected
- ◆ If an eye becomes red or sore, the lens should be removed and

advice sought immediately.

The current generation of silicone hydrogel lenses is unlikely to eliminate adverse responses, thus patient selection, careful lens fitting, appropriate diagnosis. Proper patient management of adverse events will be key to this modality being as successful as possible.

◆ *Brien Holden is professor of optometry at the University of New South Wales, Australia. Padmaja Sankaridurg is executive director clinical research and Isabelle Jalbert senior research optometrist at the Cooperative Research Centre for Eye Research and Technology*

# The epithelium in extended wear

Professor Graeme Wilson discusses the effect of extended wear on the anatomy and physiology of the ocular surface

WHEN THE EYE IS OPEN the central cornea is remote from blood vessels therefore ocular glands use tears to deliver their secretions to the corneal surface. During sleep the corneal epithelium is in intimate contact with the epithelium of the back of the lid and thus has access to the capillaries of the palpebral conjunctiva. Movements of the eye and lids assist transfer of substances. Part of the

challenge of extended wear is that the lens interferes with this transfer because it continuously isolates the cornea both from tears and from the palpebral conjunctiva.

### THE CORNEAL EPITHELIUM

#### *Cell migration and mitosis*

The basal cells of the corneal epithelium

arise from stem cells at the limbus and migrate slowly towards the centre of the cornea. The mitotic rate can be reduced by a contact lens, which renders the epithelium hypoxic. Following mitosis, the two daughter cells either remain in the basal layer or they both migrate to the surface. After the daughters have lost their attachment to the basement membrane they rarely divide and they are exfoliated

from the surface in a few days. At any position on the cornea, the most mature cells, known as the terminally differentiated cells, are on the surface. The most travelled (and probably oldest) epithelial cells will be located in the central cornea. This could be an important finding for extended wear, as the centre of the lens is that region where there is likely to be the least amount of pumping and least exchange of materials.

#### Surface cells

In extended wear, the size of corneal surface cells increases with the wearing time. An easy way of collecting cells is by using a soft contact lens in which cells are irrigated from the lens after it has been removed from the eye. Cells collected by this technique, known as contact lens cytology (CLC), have the same appearance as cells irrigated from the pre-corneal film with an irrigating chamber. A summary of cell size in normal, daily wear and dry eye is shown in Figure 1.

#### Barrier function

The corneal and conjunctival epithelia must maintain a barrier to protect the deeper and more vulnerable layers of cells. Tight junctions and the cell membranes provide this permeability barrier between the interior of the epithelium and the outside world. It can be disrupted easily by trauma, by preservatives, and by inadequate oxygen transmissibility.

#### The shedding rate

The rate at which cells detach from the surface of the corneal epithelium in relation to the rate at which they can be transported away could determine the success of extended wear. There are a number of factors in tears which are known to change and may alter the shedding rate. These include:

- ◆ Osmolality: When the osmolality is very high or very low, the shedding rate of the epithelium is increased. However, in near physiological conditions (260 to 350 mOsm/kg), osmolality changes do not cause increased shedding. Any osmolality changes occurring in extended wear will be well within this range.
- ◆ Hypoxia: There is a decrease in cell shedding in extended wear that suggests a slowdown in epithelial turnover. The idea of a slowdown is supported by the influence of hypoxia on mitotic rate.
- ◆ Toxic exposure: Preservatives such as benzalkonium chloride and surfactants increase the shedding rate, as does exposure to suprathreshold ultraviolet radiation.
- ◆ Small ions: Any contact lens is a barrier to the traffic of cells and large molecules between the epithelial surface and tears, but small molecules which can diffuse

through a lens will not be withheld from the ocular surface. Potassium and calcium have been shown to have a role in the maintenance of the epithelium and could affect shedding rates. Potassium has been included in irrigating solutions and tear supplements for this reason.

◆ Shearing forces: The shearing force exerted on the eye by the lids has a profound effect on the rate cells are removed from the surface. A major change that the epithelium experiences during extended wear is the prolonged reduction in the removal of cells from the surface by shearing force. It is likely that cell shedding and cell stagnation will become of increasing importance in extended wear.

◆ Tear replenishment: The rate at which cells are lost from the epithelium is affected by the presence of a contact lens. Although the loss of cells from the epithelium itself is reduced, cells accumulate beneath the lens, due to the relatively low rate of tear exchange. First, a reduction in the rate of cell shedding might be unhealthy for the epithelium. Second, the stagnation of cells on the surface facilitates invasion by foreign organisms.

#### THE PRE-CORNEAL TEAR FILM

The corneal surface is the interface between the eye and the outside world. The final optical interface between air and eye is the lipid layer of the tear film, which disperses over the aqueous component at each blink and is anchored

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at the orifices of the meibomian glands above and below. It does not take part in the flow of tears from lateral canthus to punctum. Debris and desquamated cells flow along the lacrimal river but beneath the lipid layer. At each blink the smooth surface of the squamous cells of the marginal conjunctiva and the secretions of the conjunctival glands are drawn over the surface of the corneal epithelium.

Blinking removes debris from the pre-corneal film and maintains the corneal surface in a condition that sustains acute vision. The upper lid accomplishes most of the lid activity of blinking. The rapid downward movement of the upper lid sweeps the surface clean and deposits debris in the marginal tear strip for transport to the puncta. The slow retraction of the lids might have some action in reconstituting the pre-corneal film.

#### THE CONJUNCTIVAL EPITHELIUM

Conjunctival cells migrate from the fornix stem cells by two routes. One route takes them from the fornix to the bulbar conjunctiva and towards the limbus, and the other to the palpebral conjunctiva and towards the margins of the lids.

The tears over the conjunctiva are derived not just from the lacrimal gland but also from the secretions of the goblet

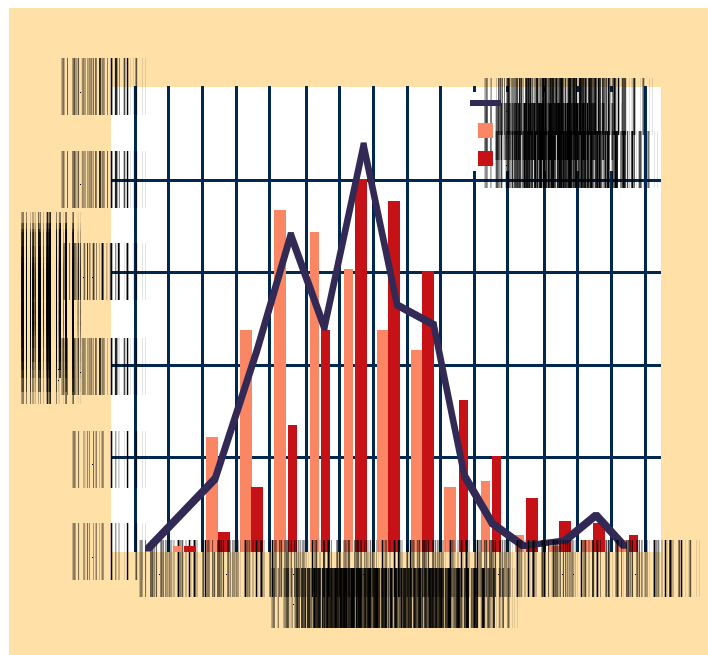


FIGURE 1. Shows the size of cells collected by contact lens cytology (CLC) from three different categories of patients: diagnosed dry eye, daily contact lens wearers and non-contact lens wearers (normals). Contact lens wearers tend to have larger cells than normal and dry-eye patients tend to have smaller cells than normal

cells and the epithelial cells. The conjunctiva expresses surface antigens, adhesion molecules and cytokines.

Goblet cells share the same progenitor as other cells of the conjunctiva. The secretions of goblet cells are mucin molecules, which in hydrated form become important structural and functional components of the pre-ocular tears.

Cells of the conjunctival epithelium are less squamous than cells of the cornea and probably do not shed as readily. The general belief is that epithelia with high shedding rates have squamous cells on their surfaces.

Changes in cells in contact lens wear occur in the bulbar conjunctiva including: increased keratinisation, snake-shaped nuclear material, increased inflammatory cells, and reduced nucleus to cytoplasm ratios. There are differences in goblet cell counts and nucleus to cytoplasm ratio between rigid-gas permeable lenses and hydrogel lenses. Thus contact lens wear places stress on the conjunctiva.

Dry eye also places stress on the conjunctiva and so it is not surprising that contact lens overwear can have similar symptoms.

### CONCLUSIONS

The ocular surface is a functional unit represented by the corneal and conjunctival epithelia, the tear film and other structures.

The privileged immune status of the cornea is due to the delegation of its needs to the conjunctiva, which contains an abundance of lymphoid tissue. Conjunctival inflammation can be tolerated because the optical requirements are less demanding than those of the cornea. Whenever one of the components changes its functional, physical or chemical characteristics, the equilibrium with the others can also change and the final result is symptoms of ocular discomfort and signs of sub-clinical inflammation or cytological changes. Any one of these can be a

precursor to more serious conditions.

The hypoxic era for the cornea is drawing to an end but a new round of challenges might come from several directions:

- ◆ Is the epithelium compromised in some way by a slowing down in shedding and mitosis?
- ◆ Is stagnation beneath the lens a problem? Does stasis beneath the lens make the epithelium more vulnerable to infection?
- ◆ Should tear exchange beneath a lens be decreased?
- ◆ Should tear exchange beneath a lens be increased? If mucus from goblet cells is an important part of the protective mechanism of the pre-corneal tears, will the susceptibility to infections be increased by the prolonged functional isolation of the corneal epithelium in extended wear?

◆ *Graeme Wilson is professor of optometry at Indiana University*

# Inflammation and infection and the effects of the closed eye

Dr Mark Wilcox et al discuss the microbiology and the effects of bacteria on safe extended wear

THE MAJOR PROTEINS found in tears are lysozyme, lactoferrin, immunoglobulins, lipocalin (tear-specific prealbumin) and mucin. Lysozyme and lactoferrin each constitute approximately 30 per cent of the total protein in open-eye tears and are both bactericidal and bacteriostatic.

Immunoglobulins are highly specific proteins that are synthesised by specialised white blood cells to be specific for particular antigens. Secretory immunoglobulin A (sIgA) is the major immunoglobulin in tears and is present in open-eye tears at a concentration of approximately 1 mg/mL in non-lens wearers.

The function of sIgA is thought to be predominantly anti-adhesive. Once sIgA is bound to the surface of micro-organisms (bacteria, fungi or viruses) it prevents their adhesion to surfaces and also acts as an opsonin (coats substances for engulfment by cells) facilitating the removal of micro-organisms by specialised phagocytic white blood cells such as polymorphonuclear leukocytes (PMNs).

TABLE 1

The frequency of microbial contamination of either the lid margin or conjunctiva for subjects wearing hydrogel or silicone hydrogel lenses on two different wear schedules

	Hydrogel lens (n=53)		Silicone hydrogel lens (n=171)	
	Lid microbiota	Conjunctival microbiota	Lid microbiota	Conjunctival microbiota
<i>Corynebacterium sp</i>	9*	6	27*	10
<i>Micrococcus sp</i>	11	4	8	4
<i>Propionibacterium sp</i>	83	42	79	46
<i>Staphylococcus epidermidis</i>	94	36	87	46
<i>Staphylococcus hyicus</i>	11	4	14	8
<i>Staphylococcus saprophyticus</i>	26	15	30	18

NOTE: The hydrogel lenses were worn for six nights' extended wear and the silicone hydrogels for 30 nights' extended wear.

\*Differences between the frequency of isolation were statistically significant ( $p < 0.02$ ). No other statistically significant differences were found. Other micro-organisms, eg Gram-negatives, *S Aureus* or fungi were found very infrequently and there was no difference in isolation rates between the lens types.

*S Epidermidis*, *S Hyicus* and *S Saprophyticus* are coagulase negative staphylococci

TABLE 2

Frequency of microbial colonisation of hydrogel and silicone hydrogel lenses worn on two different extended wear schedules

Bacteria	Hydrogel lens (n=213)	Silicone hydrogel lens (n=183)
	Frequency (%)	Frequency (%)
Coagulase negative staphylococci	47	54
<i>Propionibacterium sp</i>	48	43
Gram-negative bacteria	3	2
<i>Staphylococcus aureus</i>	0	2

NOTE: The hydrogel lenses were worn for six nights extended wear and the silicone hydrogels for 30 nights' extended wear.

No significant differences were seen between the bacterial types above and any other bacterial or fungal types isolated from the different lens types

During sleep, active tear flow is stopped and the antimicrobial factors in tears change. Lysozyme and lactoferrin are present in similar concentrations in closed-eye tears as in open-eye conditions. However, their percentage concentration actually decreases to approximately 10 per cent of total proteins as these proteins are regulated by the production of the fluid component of tears. During sleep, the fluid component of tears is reduced causing an increase in total protein content of tears. Mucin concentration, on the other hand, increases five-fold during sleep. The concentration of sIgA also increases dramatically at this time reaching up to 60 per cent of the total tear protein.<sup>1</sup> There is also increased leakage of serum into the tears in the closed-eye state overnight. Serum contains several antimicrobial proteins/ glycoproteins including the complement cascade.

Complement, a series of up to 30 proteins, is bactericidal and opsonic. Complement is normally in an inactive state, however, during complement activation the proteins designated C5 to C9 form pores in the membranes of micro-organisms and thus facilitate their lysis. In addition, the complement protein designated C3 is an opsonin for PMNs, ie once bound to the surface of micro-organisms it facilitates their ingestion by PMNs.

Several studies have been conducted into the effect of wearing hydrogel lenses on tear proteins and inflammatory mediators. It is generally accepted that hydrogel lens wear does not affect the concentrations of lysozyme, lactoferrin or lipocalin in tears, even when Group IV hydrogel lenses, known to absorb large amounts of lysozyme, are worn. Presumably, lysozyme taken up by the Group IV lenses is rapidly replenished during tear turnover/flow. It is less certain whether contact lens wear affects the level of immunoglobulins in tears. The concentration of sIgA in tears has been shown to decrease during daily wear and extended

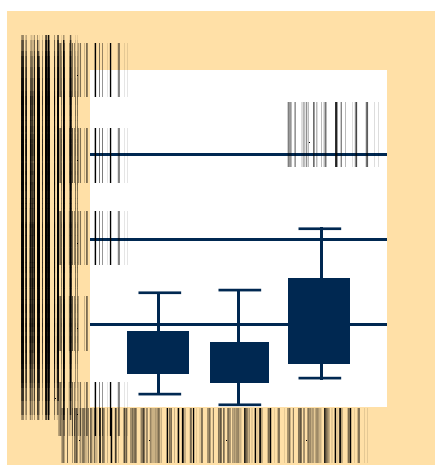


FIGURE 1 The effect of contact lens wear on the concentration of sIgA in tears. Box-Plot of levels of IgA alpha chain immunoreactivity in open-eye tears of soft contact lens wearers and non-wearers. Heavy bars represent median values. Box represents the interquartile range, with error bars representing extreme values with outliers (shown) excluded.

wear of hydrogel Group IV lenses. A decrease in the concentration of specific sIgA, with specificity for *Pseudomonas aeruginosa*, has also been reported. The consequence of less sIgA in tears may mean that the eye is more prone to infection.

Contact lens wear does not affect the concentration of complement C3 in tears; however, wearing lenses during sleep does alter the concentrations of interleukin 8 (IL-8), a small protein that attracts PMNs. Tears of adapted daily wearers who slept in their lenses for one night had significantly higher levels of IL-8 compared to either neophytes who wore lenses for the first time for one night or non-lens wearers. This demonstrates that contact lens wear has the potential to disrupt the normal homeostatic mechanisms that occur in tears during sleep. Production of the lipid inflammatory mediator 12-HETE is induced by wearing contact lenses and

this is thought to be due to either hypoxia or mechanical trauma.

Currently there are few studies examining the effect of new silicone hydrogel materials on tear proteins/ glycoproteins and inflammatory mediators. It is unlikely that the concentrations of lysozyme or lactoferrin would change during wear of silicone hydrogel materials given that there is no change of these proteins during wear of conventional hydrogels. The silicone hydrogel lenses are not as negatively charged as Group IV lenses and therefore are unlikely to bind lysozyme as avidly. In subjects who have worn lenses for at least 12 months, wearing silicone hydrogel lenses on a 30-night extended wear schedule still resulted in decreases in sIgA concentrations in tears compared to no lens wear. However, there was no statistical difference between subjects wearing commercially available Group IV lenses on a six-night extended wear schedule compared to the 30-night wear of silicone hydrogel lenses (Figure 1). This reduction in sIgA may mean that eyes wearing lenses are predisposed to colonisation by micro-organisms.

In a short-term study, the recruitment of PMNs into the tears during sleep was similar for a group of five neophytes wearing a silicone hydrogel lens, a Group IV hydrogel lens, or no lens, on successive nights. However, it remains to be seen whether wearing silicone hydrogels over a longer period results in the decrease in PMN numbers seen with hydrogel lens wear.

Wearing silicone hydrogel lenses on a 30-night extended wear schedule does not greatly alter the types of bacteria that colonise the lids or conjunctiva (Table 1). Similar colonisation rates were found for hydrogel (Group IV) lenses worn on a six-night schedule and silicone hydrogel lenses worn on a 30-night schedule (Table 2). However, there was a slightly greater frequency of colonisation by *Corynebacterium sp* on the lids of silicone hydrogel lens wearers than on the lids of Group IV hydrogel lens wearers. As *Corynebacterium sp* are considered part of the normal ocular microbiota and the number of colonies on each lens type was not different, this finding is unlikely to be clinically important.

The silicone hydrogel lenses give vastly superior performance in terms of preventing hypoxic stress of the cornea but may still give rise to microbial keratitis and non-infectious keratitis such as CLARE, CLPU and IK. Therefore, although there is likely to be infection and inflammation, the severity or frequency may be reduced with silicone hydrogel lenses. However, a healthier epithelium should mean there is less compromise of the surface integrity and ocular surface defence mechanisms and therefore less chance of infection.

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## SUMMARY

Several changes occur during lens wear that disrupt the normal corneal homeostasis. These include reductions in the concentration of sIgA in tears, perturbations in the amounts of cytokines in tears, and changes in the number of PMNs in tears as well as location of Langerhans cells in the cornea. These changes may allow bacteria to proliferate, especially during sleep, to levels that are potentially pathogenic.

Lens wear does alter the types or numbers of bacteria that can be isolated from the ocular surfaces but the lenses themselves may provide a niche for colonisation of the eye by unusual bacteria, especially Gram-negatives. The Gram-negatives cause the majority of the inflammatory adverse responses seen during hydrogel lens wear.

Whether the highly oxygen permeable silicone hydrogel lenses will produce the same frequency or types of adverse responses remains to be seen. Controlled prospective clinical trials will clearly identify risk factors associated with silicone hydrogel lens wear and determine whether these lenses provide a safer alternative to hydrogel lenses for use on an extended wear schedule.

◆ *Dr Mark Wilcox is director of biological sciences at the Cooperative Research Centre for Eye Research and Technology. Padmaja Sankaridurg, Jenny Lan, Damon Pearce, Archana Thakur, Hua Zhu, Lisa Keay and Fiona Stapleton contributed to this article*

◆ *Silicone Hydrogels- the Rebirth of Extended Wear Contact Lenses*, edited by Professor Deborah Sweeney, will be published by Butterworth-Heinemann and the British Contact Lens Association early in 2000.

## MULTIPLE-CHOICE QUESTIONS

There is one correct answer for each question



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1 The following is a list of risk factors for microbial keratitis. Which one will be eliminated by the use of silicone hydrogel lenses?

- A Trauma
- B Hypoxia
- C Ocular surface disease
- D Bacterial entrapment
- E Inadequate care and improper storage

2 Which of the following constituents of tears increases five-fold during sleep?

- A Lactoferrin
- B Lysozyme
- C Mucin
- D Immunoglobulins
- E Complement

3 The shedding rate of corneal epithelial cells is affected by many factors. Which of the following is not true?

- A Shedding increases when osmolarity is very low or very high (<260mOsm/kg and >350mOsm/kg)
- B Preservatives and surfactants decrease the shedding rate of epithelial cells from the corneal surface
- C The shear force exerted on the eye by the lids increases the rate cells are removed from the surface
- D Shedding of epithelial cells is reduced initially with hypoxia
- E Shedding rate is affected by small ions

4 The ability to differentially diagnose microbial keratitis from contact lens peripheral ulcers is critical to the success of extended wear contact lens practice.

Which of the following is a point of differential diagnosis?

- A Pain
- B Redness
- C Excess tearing
- D Location of lesion
- E Unilateral

5 Contact lens wear alters the normal corneal homeostasis, which of the following tear proteins and inflammatory mediators have been shown to alter with contact lens wear?

- A Immunoglobulins
- B Lipocalin
- C Lysozyme
- D Complement
- E Lactoferrin

6 Which of the following is FALSE?

- A Mucus is secreted by goblet cells in the conjunctiva
- B Conjunctival cells are more squamous than corneal epithelial cells
- C There is increased keratinisation of the bulbar conjunctival cells during contact lens wear
- D The conjunctiva secretes surface antigens
- E Corneal epithelial cells are shed faster than conjunctival cells

The deadline for response is February 11

**Answers – Module EW4** Insert your answers to the multiple-choice questions on the answer sheet inserted in this week's issue and return it to OPTICIAN. Successful participation in each module of this College-approved series counts as one credit towards the College of Optometrists' CET scheme and towards the Association of British Dispensing Opticians' scheme. Participants will be sent an analysis of their response. The names of successful participants will be forwarded to the College and ABDO for entry onto their databases.



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