

# Continuous wear contact lenses: have we been here before?

Keith Edwards

***New developments in contact lens materials have led to the introduction of new lenses designed for up to 30 days of continuous wear. Will these lenses lead to safer and healthier overnight use of lenses?***

It has long been considered that wearing contact lenses overnight carried too many risk to outweigh any potential clinical benefits. These include:

1. No handling and therefore no contamination of lenses during insertion/removal
2. No exposure to chemical disinfection systems to which the patients may be sensitized
3. Patients with significant defects of sight can see to move about on waking without visual deficit.

However, experience with overnight use of lenses used lenses that were not specifically designed for the purpose and introduced without a genuine understanding of the physiological requirements of the cornea.

The first of a new generation of materials and lenses has been launched across Europe in recent months. These lenses represent a technical breakthrough in lens polymer design and recent clinical trials (Comstock et al, 2000) have shown them to be more successful than previous hydrogel lens types, as measured by incidence of adverse events or success rates over a predetermined period.

The development of this new generation of soft lens materials has been driven by the need to try and meet patient aspirations for contact lens wear. In trying to meet the physiological needs of the eye during prolonged wear of lenses, materials have been developed which could prove to be the best lenses for any wearing modality.

### **PATIENT ASPIRATIONS FOR VISUAL CORRECTION**

Ametropic individuals are looking for a permanent, non-intrusive reinstatement of normal vision. This requires the maximum period of uninterrupted wear, minimum episodes of lens handling and minimal lens care procedures. The wearers

also require good comfort and vision with safety and efficacy taken for granted. When viewed in these terms, it can be seen why refractive surgery is attractive since it promises a one-off permanent correction that will render the patient essentially emmetropic. It also explains why patient acceptance is good even if correction is not perfect.

### **THE QUEST FOR EXTENDED WEAR**

Patients' aspirations for contact lenses can best be met by prolonged periods of uninterrupted lens wear.

Since the first viable contact lenses were made available, they have been worn for prolonged periods. Dick (1957) reported a case of continuous wear (CW) with hard non-permeable lenses (made of polymethylmethacrylate; PMMA) in the 1950s and Sloan (1965) reported on a clinical trial that involved 50 patients wearing PMMA lenses over 7 years. While no one can argue that PMMA makes ideal lenses for this purpose the results highlight the great variation in oxygen requirements between patients. The fact that some people are able to wear a non-permeable lens overnight on a regular basis shows that they must have a very low oxygen requirement for their cornea. However, once soft lenses had been introduced, there was even greater enthusiasm for prolonged wear.

In Europe small diameter high water contact lenses were used for 'permanent' wear, pioneered by John de Carle. Lenses such as Permalens (71% water content) and Sauflon 85 (85% water content) were used and the initial clinical impression was favourable, with only occasional adverse responses reported.

However, subsequent reports of adverse reactions led to a decline in the use of any extended wear (EW) lenses in Europe, based on reports of

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infections (Poggio et al, 1989; Schein et al, 1994; Cheng et al, 1999), lens deposits, lid changes and variable vision. Research into ocular physiology showed that corneal oedema was apparent even with high water content soft lenses, especially in overnight wear, and that corneal endothelial cells responded adversely to prolonged wear.

In parallel, the Food and Drug Administration in America first offered guidelines to manufacturers to differentiate EW from CW. EW was defined as a period of wear up to 7 days and 6 nights of overnight wear. CW involved any period longer than 7 days and 6 nights of wear. In 1979 the first approval was given for EW in aphakia followed by approval for cosmetic use of up to 30 days in 1981. Approval was given for mid and high water content lenses. In 1983, ultra-thin hema, silicone elastomer and toric lenses all gained approval and by 1985 it was estimated that, with 20 contact lenses approved for overnight wear, over 25% of the 15 million soft contact lens wearers in the USA were using extended or CW.

However, research articles began to report changes in the ocular tissues with EW when compared to daily wear and these concerns received attention in the lay press. In particular, the definitive work of Holden and Mertz (1984) showed the

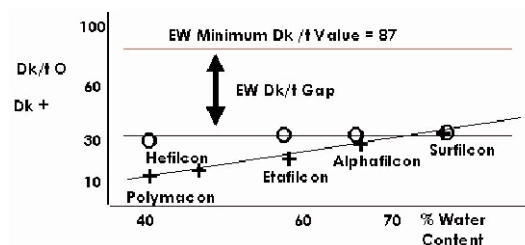


Figure 1. Oxygen permeability increases with water content. However, high water content soft lenses tend to be thicker than low water content lenses and so the central transmission values are similar. All lenses fall well below the 'ideal' transmission for extended wear (EW) (the EW-oxygen transmissibility (Dk/t) gap).

levels of oxygen required to limit overnight corneal swelling to that found with no lens wear ( $87 \times 10^{-9} \text{cm}^2/\text{secxmlO}_2/(\text{mlxmmHg})$ ). This level was (and still is) unattainable with any of the current soft hydrophilic lenses (Figure 1).

To investigate the increasing concerns about infections, the US contact lens industry supported a study of the relative risks of infectious keratitis in 1986–7. This showed an infection rate of 0.2% which was five times that of daily wear (20 per 10 000 vs 4 per 10 000) (Poggio et al, 1989). As a result, the contact lens industry in the USA voluntarily reverted from 30-day CW to 7-day EW. However, despite the obsession with infectious keratitis, the main clinical findings with the lenses were more to do with other ocular responses (Table 1).

Paradoxically, while the main concern of practitioners over EW has centred on the infection risk, the principal reasons for patients discontinuing EW continued to be discomfort, dryness and redness, all symptoms of chronic hypoxia.

## MATERIAL DEVELOPMENT

The quest for safer EW began as soon as the limitations of high water content soft lenses became apparent. Moves to super oxygen permeable rigid gas permeable (RGP) lenses led to the concept of RGP EW that eliminated many of the oxygen-related issues. However, chronic desiccation of the cornea at the 3 and 9 o'clock positions (3 and 9 o'clock staining) and lens adherence proved to be the major problems with this use of RGP lenses. Both effects may have been related to changes in the structure of the tear film, especially during sleep (Swarbrick and Holden, 1987).

One of the most permeable flexible lenses for EW proved to be silicone elastomers, lenses with no water content and dramatic oxygen permeability ( $Dk = 300 \times 10^{-11} \text{cm}^3/\text{secxmlO}_2/(\text{mlxmmHg})$ ). However, there were significant limitations to using these materials for contact lenses, including their high elastic memory and the hydrophobic lens surface. This led to the development of silicone hydrogels, in an attempt to combine the oxygen benefits of silicone elastomers with the best hydrophilic aspects of hydrogel lenses.

## THE NEW CHEMISTRIES

The primary properties required for the new generation of materials are shown in Table 2 and derive from the way the various elements of the polymer are balanced.

### Oxygen permeability

The limitation of high water content lenses for CW came from the method of oxygen transfer.

TABLE 1. Historical clinical findings with extended wear

Limbal injection
Contact lens induced papillary conjunctivitis
Inflammatory reactions (infiltrative keratitis)
Corneal oedema
Striae
Epithelial microcysts
Corneal thinning
Altered epithelial adherence
Neovascular changes
Endothelial polymegethism

Since water provides the route for oxygen transmission and since there are physical limitations to the water content of the lens, the Dk is also limited. Even if it were possible to make 100% water content lenses, the Dk would still only be around  $80 \times 10^{-9} \text{cm}^2/\text{sec}(\text{mlO}_2/(\text{mlxmmHg}))$ . Attempts to make high water content lenses hyperthin to increase oxygen transmission resulted in corneal epithelial staining as a result of pervaporation.

Silicone elastomers provided (and still provide) unrivalled oxygen availability under the lens but the advantages that this provides are lost because the other material properties are less than optimal. Silicone elastomers (Silflex, Silsoft) are still available and are mainly used in aphakic EW.

Silicone hydrogels use the silicone elements to provide oxygen transmission while employing the hydrogel components to provide the other desirable properties. Unlike conventional hydrogels, silicone hydrogel Dk drops as the water content increases until the Dk curve meets that of conventional hydrogels (Figure 2).

#### Surface wettability

Having developed a silicone-containing polymer, it is important to ensure that the surface remains wettable and that there are no exposed hydrophobic silicone groups. This can most readily be achieved by surface modification after polymerization to change the surface chemistry. A highly wettable surface is required for good comfort, deposition resistance and good acuity.

#### Biocompatibility

The lens surface should be wettable, and should also resist deposition so that immune-based reactions to surface deposits are limited. Prevention of lipid deposits is also important since these will lead to reduced vision and comfort.

#### Fluid/ion transport

During development of the new generation lenses, it was found that good lens movement, particularly after overnight wear, was linked to fluid transport through the lens. Part of the problem with silicone elastomers was that significant negative pressure could be produced under the lens and there was no opportunity for fluid to move through the lens and counteract it over time. This led to lenses adhering to the cornea. To ensure that this is not a feature of the silicone hydrogels, fluid transport is essential.

#### Resistance to dehydration

While many of the symptoms of dryness with conventional EW lenses could be linked to hypoxic symptoms, it is, nevertheless, important to ensure that lenses will remain comfortable

during the wearing period with no dryness attributable to lens dehydration. This will be less of a challenge if water content is low and thickness is not reduced to very low levels.

#### Visco-elastic properties

While the lack of fluid transport is one aspect that contributes to the lens binding problem with silicone elastomer lenses, the high elastic memory of the material is another. These materials behave like elastic bands and, when deformed, rapidly return to their original shape. When this occurs with lenses on the eye and following a blink, there is significant potential for the lens to create substantial negative pressure under the lens that cannot then be released. The result is a lens that is bound or stuck to the cornea and does not move.

In contrast, low water content lenses made from materials such as hema have good shape memory but their elastic properties are lower so that they take longer to return to their original shape. This prevents the build-up of negative pressure under the lens and permits free lens movement. The ideal CW material would have visco-elastic properties similar to hema.

#### SILICONE HYDROGEL CHEMISTRY

While the objective of making silicone hydrogels is clear, namely to blend the hydrogel characteristics of wetting comfort and movement with the silicone characteristics of high Dk, there are sig-

**TABLE 2.**  
Required properties for silicone hydrogels

High oxygen transmissibility (Dk/t)
Surface wettability
Biocompatibility
Fluid/ion transport
Resistance to dehydration
Viscoelastic properties similar to hema

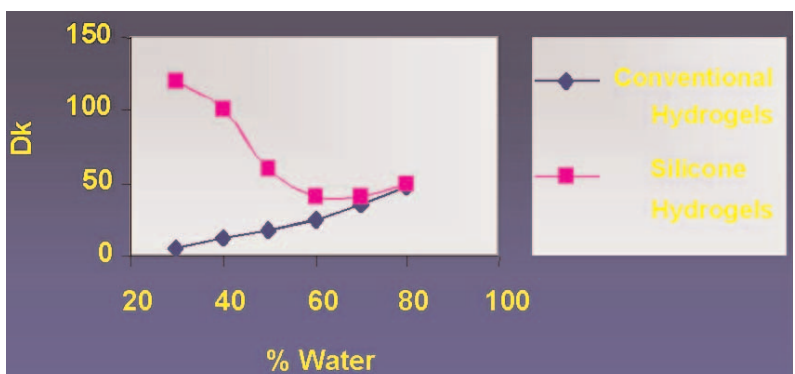


Figure 2. Relationship of water content and oxygen permeability (Dk) for hydrogel and silicone hydrogel lenses.

nificant challenges in developing an appropriate polymer. The two components are hydrophobic and hydrophilic, so do not mix readily. In many instances, silicone hydrogels will be opaque as the components interact with one another.

Figure 3 shows typical silicone hydrogel chemistry where polydimethylsiloxanes (the silicone element) are attached to N-vinyl pyrrolidone (NVP) (the hydrogel element) through a cross-linking polymer.

### SURFACE MODIFICATION

Following polymerization into the lens form, usually by cast moulding, the surface is then treated to render it wettable and biocompatible. There are a number of alternative processes but plasma treatment is, perhaps, most common. The surface is bombarded by a gas, which is excited in a vacuum. This precipitates a chemical change in the first few nanometers of the surface. This change is permanent, integral to the lens matrix and cannot be separated without damaging the lens itself. Other methods that rely on 'coatings' are less desirable because of the propensity for them to separate from the surface to which they are applied.

Having modified the surface, it is important to be able to quantify the surface chemistry and morphology in order to be sure that the surface has been modified in the desired way and in a repeatable fashion. Complex procedures such as X-ray photoelectron spectroscopy and atomic force microscopy can be used to analyse finished lenses.

In addition to providing a wettable surface to the lens, surface modification also provides biocompatibility, making the surface resistant to deposition and spoilage from tears and the environment.

### LENS DESIGN

One of the challenges in the design of successful CW lenses is to maintain an ocular environment that is as normal as possible, despite the presence of a contact lens for a prolonged period and especially overnight.

It is extremely important that there is adequate flushing of debris (physical and metabolic) that accumulates behind the lens, particularly overnight. Without this flushing effect the potential for inflammatory responses and the risk of infection both increase.

Several factors influence lens movement including back surface geometry, lens edge profile, edge stand-off and material rigidity (modulus). Most silicone hydrogels are among the stiffer contact lens materials and so may give rise to more negative pressure under the lens during blinks than more flexible materials such as hema or etafilcon. The design of the back surface and the edge profile and stand off are therefore critical in ensuring lens movement, especially in the period immediately after waking.

A lot of effort has gone into understanding the effects of various aspects of lens design in order to control this feature of lens fitting.

It is the blending of the key material properties with the surface modification and lens design that will all contribute to the success of CW contact lenses.

### CLINICAL PERFORMANCE OF SILICONE HYDROGELS

Silicone hydrogels have been in development for more than 10 years and prototype lenses have been in testing and clinical trial from a number of companies over many years. Results have been reported on many aspects of lens performance.

#### Overnight corneal swelling

With the transmissibilities found with these lenses, incremental overnight corneal swelling with lens wear should be eliminated or significantly reduced. That was the primary design goal. Reports confirm this to be the case and a typical response to overnight wear compared to no lens wear and a conventional EW hydrogel are shown in Figures 4 and 5. There is no significant swelling with these lenses beyond that seen with no lens wear, while the response with a conventional hydrogel is clinically and statistically significant.

The oxygen performance of these lenses means that overnight corneal swelling should not exceed levels seen without lens wear. For most patients, corneal striae and microcysts should be a thing of the past. In addition there are usually fewer complaints of hypoxic symptoms and there is generally less perilimbal redness with these lens types (MacDonald et al, 1995).

Oxygen is also thought to have some link to infection risk since the cascade may involve hypoxia, epithelial defect, microbial overload and an immune-based reaction. Indeed, in laboratory conditions, it is impossible to precipitate a corneal infection without the presence of surface epithelial damage. Sterile peripheral infiltrates or contact lens peripheral ulcers may be related to hypoxia, but are likely to have a complex aetiology involving microbial toxin release, hypersensitivity and



Figure 3. Typical silicone hydrogel chemistry. DMA = dimethylacrylamide; NVP = N-vinyl pyrrolidone.

toxic reactions. It is not safe to assume that the resolution of hypoxic stress will eliminate all inflammatory reactions and these have been seen to a limited degree in clinical studies (unpublished data, Bausch & Lomb Inc, 1998, 1999). However, similar inflammatory reactions can also be seen in non-lens wearers (Holden, 1999).

In an attempt to relate hypoxic stress to infections some researchers have looked at binding of *Pseudomonas* spp. to exfoliated epithelial cells. It has been found that when conventional EW lenses are worn overnight, there is a significant increase in binding between *Pseudomonas* and the epithelial cells (Cavanagh et al, 1998). When modern silicone hydrogels are worn overnight, this binding does not increase beyond the level seen with normal epithelial cells. While this does not automatically mean that there will be fewer infections with new materials, it suggests that hypoxic changes can make the corneal epithelial cells more susceptible to bacterial invasion.

In clinical trials, results have shown overwhelming patient preference for the new lens types and especially for comfort, handling and lack of dryness compared to control hydrogel lenses.

### APPLICATION OF CONTINUOUS WEAR MATERIALS

Inevitably there will be a race for manufacturers to produce lenses with ever higher oxygen permeabilities and transmissibilities, while the profession has to try and decide which lenses will provide the optimum balance between Dk and the other material characteristics. Recent research on the optimum oxygen transmission has centred on fluorophotometry. However, when assessing all data relating to corneal physiology, it is important to consider the normal distribution of individual results that are compiled to give mean values.

Figure 6 shows the distribution curves for overnight swelling in groups of adapted daily wear contact lens users. From the no lens wear curve it can be seen that there are significant variations in response to eye closure even without a lens. A vertical line marks the 7% swelling level since swelling of this magnitude is visible to the practitioner without specialist equipment.

While the mean overnight swelling is approximately 2% (compared to 4% for non-adapted subjects) there is a significant range with swelling more than 7%. These will be subjects with high corneal oxygen demands and who will probably not make good daily wear contact lens users.

With conventional hydrogel lens wear the swelling response is much more marked, with the mean swelling being approximately 10%. However, some patients have a lower response,

with 17% swelling less than 7% with overnight wear. It is patients in this group that would make successful EW users with existing materials.

With an experimental silicone hydrogel lens of Dk/t=110, the average swelling is about 3% which is not statistically different to the no lens wear mean. Seven per cent of patients show overnight corneal swelling of more than 7% since the curve is slightly displaced from the no lens wear curve.

From this it can be deduced that if additional oxygen was supplied in attempt to superimpose the silicone hydrogel and no lens wear curves, only an additional 5% of patients would show any clinical benefit. If the trend to higher Dk was matched by compromises on other lens/material properties such as fluid transport or surface quality, there may not be an adequate trade-off.

### THE FUTURE OF SILICONE HYDROGELS

The first iterations of silicone hydrogel lenses are just coming to market as they gain regulatory approval both in Europe and the USA. There is no doubt that subsequent materials will build on the technological breakthroughs that have resulted in this new generation of materials.

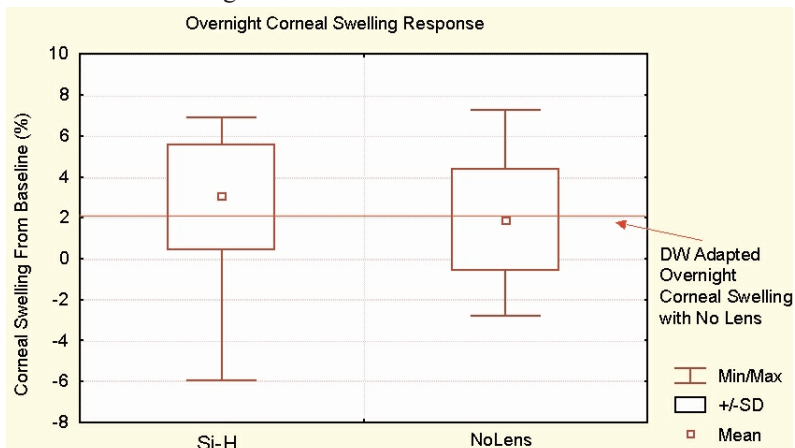


Figure 4. Typical swelling response of silicone hydrogel compared to no lens wear in adapted contact lens wearers. DW = daily wear; SD = standard deviation; Si-H = silicone hydrogel.

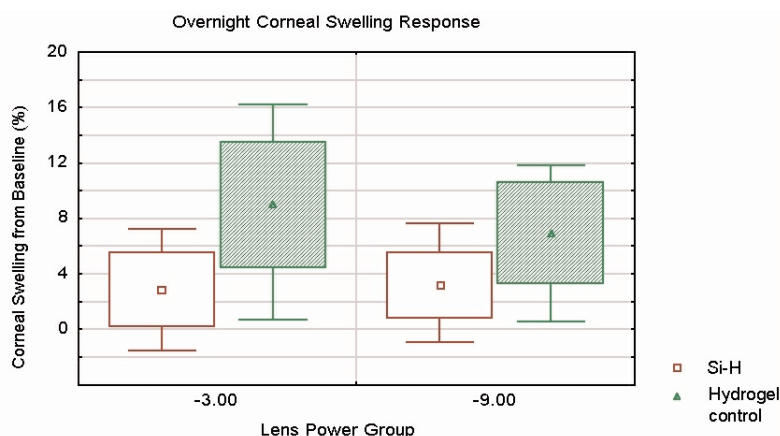


Figure 5. Comparative overnight swelling of a silicone hydrogel (Si-H) compared to a hydrogel control.

While these lenses have been designed specifically with the needs of cosmetic CW in mind other applications are obvious. The therapeutic use of overnight and prolonged wear has continued over the years since the risk–benefit ratio rests heavily in favour of lens wear. The use of silicone hydrogel lenses in therapeutic cases such as recurrent erosions, post-keratoplasty and even pathological dry eye can be envisaged. The potential to promote faster corneal healing through the delivery of ‘physiological’ levels of oxygen during CW is very real.

Silicone hydrogels may also provide a more balanced alternative to silicone elastomers in cases of aphakia unsuited to intraocular lenses.

Other high powered prescriptions will benefit from the increased levels of oxygen through the thickest parts of the lens even in daily wear. Indeed it could be argued that the minimum oxygen transmission through the thickest part of a contact lens should be at least  $30 \times 10^{-9} \text{cm}^2/\text{sec} \text{mlO}_2/(\text{mlxmmHg})$  if 95% of the population are to benefit from oedema-free daily wear. This is based on Holden and Mertz data. If this argument is accepted, then most patients would benefit from silicone hydrogel lenses for daily wear. The challenge will then be to produce the lenses at a price that is conducive to use with solutions on a daily wear basis.

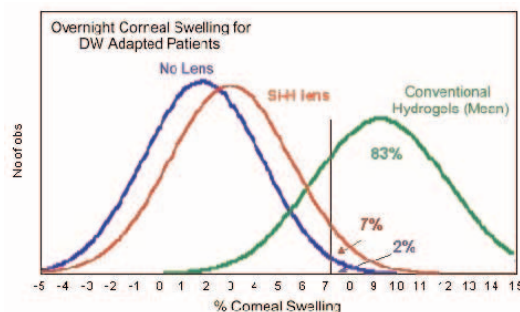


Figure 6. Overnight corneal swelling responses. DW = daily wear; Si-H = silicone hydrogel.

### KEY POINTS

- Soft hydrogel contact lenses have been relatively unsuccessful for overnight wear.
- Patient symptoms and an increased risk of infection have limited their popularity.
- In the last year, new lenses made from novel polymers have been introduced for overnight wear.
- These lenses resolve the problems of overnight wear related to a lack of oxygen reaching the cornea.
- Minor inflammatory reactions have been seen with these lenses but there is reason to believe that they may cause fewer infections than conventional extended wear lenses.
- Only with long-term use in the population, will the incidence of significant side effects be established.

### CONCLUSIONS

Silicone hydrogel lenses have been developed to address the needs of CW. Each lens in the genre has a different balance of the properties essential for prolonged overnight wear, which include:

- Oxygen transmission unparalleled in conventional hydrogels
- A wettable biocompatible surface
- Resistance to in-vivo dehydration
- Fluid transport through the lens to help maintain lens mobility
- Viscoelastic properties that avoid lens binding and promote movement
- A lens design that permits flushing of debris from beneath the lens reducing the likelihood of inflammatory responses.

The issue of the relative risk of infection in prolonged wear cannot be addressed until many thousands of patients have used the lenses for several years. The incidence of infections is so low that it will not be detected in any reasonable clinical trial.

The properties of the silicone hydrogel lenses means that they are likely to be equally suitable for other clinical uses including therapeutic applications and daily wear. It is likely that more complex forms such as torics and bifocals will follow. **HM**

*Conflict of interest: Mr Edwards is an employee of Bausch & Lomb Inc, a manufacturer of a silicone hydrogel contact lens. This article is based on an article published in Optician (Edwards, 1999).*

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