Submission to the American Optometric Association Contact Lens and Cornea Section Student Research Awards Committee

for

“The Evolution of Continuous Wear: How has our knowledge of corneal oxygen requirements, material oxygen transmission, tear exchange behind the lens and ocular pathogens, shaped our thinking about continuous wear contact lenses?”
Continuous Wear: The Long and Winding Road

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Living in an era with all types of advanced technology, one of the global mega-trends is convenience. A growing number of contact lens wearers want to safely sleep in their contact lenses longer.¹ As our understanding of continuous wear and the lenses available have advanced over the years, optometrists have become more able to meet this need without complications. Patient and practitioner interest in extended wear contact lenses was high in the late 1970’s and early 1980’s, and then declined over the next decade, predominantly as a result of many wearers experiencing complications and obtaining infections.²³ However, surveys continued to show that consumers were interested in wearing safe extended wear lenses, leading to the development of new lens designs and materials that allow for increased oxygen permeability and tear film movement, with less protein deposits. The relatively recent introduction of highly oxygen-transmissible silicone hydrogel and gas-permeable contact lenses represents a major breakthrough in satisfying corneal requirements for successful continuous wear. However, there are still many questions and challenges that remain regarding complications in continuous wear patients.

The Early Years

The question of how much oxygen the cornea requires to remain healthy has not been easy to answer. Although it is well-known that oxygen is essential in maintaining corneal health during contact lens wear, there is still much debate on how much oxygen is needed and how to best assess the oxygen needs of lens wearers.

The need for contact lenses that transmit high levels of oxygen to the cornea was first recognized almost 60 years ago.⁴ The first model of oxygen distribution across the cornea was proposed by Hill and Fatt in 1964; it predicted oxygen flow to the eye during
lens wear using equivalent oxygen percentage.\textsuperscript{5-7} This model is based on Fick’s Law of diffusion and states that the greater the difference in oxygen tension on either side of a lens, the greater the driving force across the lens, and that the greater the oxygen transmissibility, Dk/t, the more oxygen will flow.\textsuperscript{5-7}

Attempts to quantify the actual level of oxygen needed by the cornea were not published until the 1970’s. Using gas goggles in 1970, Polse and Mandell found that an atmospheric level of only 1.5% to 2.5% oxygen was needed to prevent corneal swelling.\textsuperscript{8} This estimate of the cornea’s oxygen requirement is only a tenth of the atmosphere’s 20.9% oxygen that an open non-lens wearing eye is exposed to. In the midst of this early research, John DeCarle was working to design contact lenses that were specifically for continuous wear. DeCarle’s approach was to develop a lens material with high-water content in order to provide better oxygen permeability.\textsuperscript{9} He succeeded in doing so in the early 1970’s and initial reports of continuous wear hydrogels were positive.\textsuperscript{10} Later in the 1970’s, however, it was found that even high-water content lenses could produce corneal edema and disruption,\textsuperscript{11} and significant corneal complication rates with hydrogel continuous wear were reported.\textsuperscript{12} Research done by Mandell and Farrell in 1980 using gas goggles found that between 3.5% and 5.5% equivalent oxygen percentage was necessary to avoid swelling, instead of the previously reported 1.5% to 2.5%.\textsuperscript{13} But several other studies raised this estimate and showed that actually between 10 and 15% oxygen is required for the majority of patients to prevent stromal swelling.\textsuperscript{14-15}

\textbf{Rise and Fall}

Nevertheless, the U.S. Food and Drug Administration (FDA) approved DeCarle’s Permalens 71% water content hydrogel lens for two weeks of continuous wear in January
The popularity of extended wear lenses grew rapidly in the United States. In 1983, Dow Corning Ophthalmics introduced the first silicone elastomer contact lens, Silsight, for extended wear and it was the first lens given FDA approval for up to 30 days of continuous wear between removals. Soon after that, hydrogel lenses were given approval to go from the previous 14 days of wear to 30 days of continuous wear. The silicone elastomer lenses had exceptional oxygen transmissibility because of the high solubility of oxygen in silicone. They displayed corneal adherence and poor lens movement, however, and were prone to poor wettability, discomfort, and lipid deposits. Since silicone elastomer lenses generally were not well-tolerated by patients, they failed to gain popularity. Hydrogel lenses did, though, and by 1985, about four million people were extended soft lens wearers, and there were more than 20 hydrogel lens products that were FDA approved.

Alongside the growing popularity of continuous wear lenses were an increasing number of published articles investigating their impact on corneal health. During open-eye lens wear, oxygen may reach the cornea by dissolving in the tear fluid layer between the lens and the cornea or by diffusion through the lens material itself. During hydrogel lens wear, however, most oxygen reaches the cornea by diffusion and not by tear pumping, because hydrogel lenses have little lens movement and poor tear exchange. Furthermore, Benjamin found that circulation of oxygen-rich tears behind a lens only occurs when the eye is open, and therefore, diffusion of oxygen through a contact lens is the major factor impacting oxygen supply during overnight wear. He concluded that oxygen deprivation is of particular concern in the closed-eye state of continuous wear, since the eye must obtain all its oxygen from under the lid without contribution from the
tears. In 1984, Holden and Mertz found that a lens that provides 18% equivalent oxygen percentage during open-eye wear limits overnight corneal edema to 4%, the level experienced when lenses are not worn during sleep. The Holden-Mertz criterion can be achieved with a lens that has an oxygen transmissibility, $Dk/T$, of $87 \times 10^{-9}$ (cm x mL oxygen)/(s x mL x mmHg). The high water content hydrogel lenses being used for continuous wear at the time fell well short of meeting this standard. Because the oxygen permeability, $Dk$, of water (80 barrers) limits the maximum $Dk$ that can be achieved with a conventional hydrogel lens material, even a 100% water content lens can not satisfy the Holden-Mertz criterion for overnight wear. It was becoming apparent that continuous wear corneas were not receiving the oxygen they needed.

In the 1985 Gothenburg study, chronic hypoxia from long-term extended wear of the low $Dk$ high-water content hydrogels was reported by Holden and Sweeney to cause reductions in epithelial thickness and oxygen uptake, increased incidence of epithelial microcysts, stromal thinning and chronic edema, and increased endothelial polymegathism. As noted by this study and many others, changes induced by chronic hypoxia can be observed in all layers of the cornea in long-term hydrogel continuous wear patients. This seemed to revive interest in developing new contact lens materials with oxygen permeability values that were higher than the 10 to 40 barrers of $Dk$ provided by the existing hydrogel lenses.

Soon there after, high $Dk$ rigid gas permeable (RGP) lens materials appeared on the market, with the promise of superior corneal physiology through higher $Dk$ values in the range of 50 to 110 barrers. By 1988, three RGP lens materials had received FDA approval for seven days of extended wear. As a result of their greater lens movement
and tear exchange, RGP lenses were shown to provide a greater amount of open-eye oxygen and less daytime edema and chronic hypoxic stress than hydrogel lenses, and in some reports, superior comfort and vision after the initial adaptation period. Lens movement and tear circulation also remove debris and contaminants from behind the lens; the lack of adequate tear circulation can cause the breakdown of trapped contaminants and a subsequent inflammation of the cornea. Despite their physiological and subjective advantages, the poor initial patient comfort and difficulty of fitting compared to hydrogel lenses prevented extended wear gas permeable lenses from gaining much popularity with patients or practitioners. Meanwhile, the reputation of extended wear as a whole was waning.

The Fatal Blow

In addition to the findings of corneal morphing as a result of extended wear, there were numerous reports that suggested a substantial risk of corneal infection and ulceration among extended wear lens patients. Further studies were conducted to better understand the extent and cause of these complications. Particularly, in 1986, the Contact Lens Institute sponsored a study by Schein and Poggio of Harvard Medical School to investigate the relative incidence and causative factors of microbial keratitis. The study, published in 1989, found that the risk of ulcerative keratitis was 10 to 15 times greater with extended soft lens wear than with daily soft lens wear, that the risk increased with each consecutive day of wear before removal, and that proper lens cleaning and disinfection of the lens could reduce the risk. Overnight lens use, whether regularly with extended wear lenses or occasionally with daily wear lenses, emerged as the preeminent risk factor for ulcerative keratitis. It was also shown that mucoprotein
deposits commonly found on soft lenses serve as a vehicle for the transport of the most common sight-threatening pathogen, *Pseudomonas aeruginosa*, to the cornea. These findings, particularly the data of Schein and Poggio, led to attention from the media and the FDA about the concerns over infections in extended wear. Along with the hypoxic corneal effects of low Dk extended wear soft lenses, the increasing number of articles making media headlines caused extended wear lens use and wear time to decline in the late 1980’s. In May 1989, the FDA mandated a one-week maximum for overnight wear of soft lenses, and changed continuous wear product labels to indicate a recommended wear time of one to seven days, and to stress the importance of proper lens care and the risk of microbial keratitis.

**Now What?**

Since patient compliance was considered to be one of the main problems contributing to the occurrence of microbial keratitis, momentum was provided for the expansion of simplified lens care systems, and more notably, the advent of the disposable extended wear hydrogel lens. While the use of blister packaging and 7 to 14 day disposability were new, the lens material itself was, unfortunately, not. Contrary to some people’s expectations that regularly replacing hydrogel lenses would make overnight wear more safe, disposable lenses did not minimize the chronic corneal changes that occur during extended wear, nor did they decrease the risk of ulcerative keratitis associated with sleeping in lenses. Additional research showed that *P. aeruginosa* adherence to corneal epithelial cells was enhanced in those who used extended wear low Dk soft contact lenses, perhaps due to the decreased metabolic activity and protective secretions of the hypoxic corneal epithelium. What is more, it was shown that *P.*
**aeruginosa** can rapidly create a protective biofilm on contact lenses that have sluggish tear circulation, therefore increasing the number of pathogens on hand to march into the hypoxically compromised cornea. The concern over hypoxic and infectious corneal complications continued to decline the extended wear market, and it was quickly realized that an entirely new lens material and design would be necessary in order for continuous wear to get back on its feet.

**Back to the Drawing Board**

Scientists certainly had their work cut out for them, and the industry worked to design a lens that would exceed the necessary oxygen requirements established at that time (Holden and Mertz criterion of Dk/T of at least 87). Though some rigid gas permeable and silicone elastomer lenses did just that, there remained the challenges of improving comfort and maintaining good lens movement. On the other hand, hydrogel materials needed more oxygen permeability and tear circulation. Researchers worked feverishly to develop this ideal lens, experimenting with both wettable silicone-based materials and higher-strength hydrogel materials. They were not able to attain the material they needed until the development of silicone hydrogels.

**The Rebirth of Continuous Wear**

For over a decade, patients and practitioners were limited to seven days of extended wear; this ended with the arrival of silicone hydrogels. Silicone hydrogel was and still is a ground-breaking lens material that combines the high Dk levels of silicone with the fluid diffusion characteristics of hydrogel lens materials that facilitate lens movement. The Dk of silicone hydrogels is controlled by the level of silicone incorporated into the base material and they provide an oxygen transmissibility, Dk/T, of
at least 86 to 175 (cm x mL oxygen)/(s x mL x mmHg), while also giving initial comfort and adequate lens movement. One weakness of the new generation of silicone hydrogels is that they are hydrophobic and require a surface treatment or an internal wetting agent to be more hydrophilic and biocompatible.

In 1999, CIBA’s Focus Night and Day (lotrafilcon A material) and Bausch and Lomb’s Purevision (balafilcon A material) were brought to the market. With respective oxygen transmissibility values of 175 Dk/T and 110 Dk/T at -3.00D, both received FDA approval for up to 30 nights of continuous wear in 2001. No hypoxia-related effects were observed with these lenses, and overnight edema levels were similar to the levels seen with no lens wear. The high oxygen transmissibility of these stiffer, lower water content silicone hydrogels had eliminated the physiological corneal changes from hypoxia seen with hydrogel lenses, while providing similar comfort and fitting performance. In 2002, the FDA approved the gas permeable Menicon Z material for up to 30 days of continuous wear, the first time ever for a GP. This 163 Dk material provides better tear flow than silicone hydrogels, and has great potential for safe continuous wear. In 2004, CIBA Vision’s O2Optix (lotrafilcon B) and Vistakon’s Acuvue Advance (galyfilcon A) lenses were introduced to provide more options to practitioners wishing to fit silicone hydrogels, particularly on daily wear patients. Claiming to have better wettability, Vistakon’s Acuvue Oasys (senofilcon A) was introduced in 2005. There are also toric, multifocal and custom silicone hydrogel designs that are now available. With sales and the number of wearers increasing considerably each year, silicone hydrogels have captured a substantial portion of the soft lens market and are expected to continue doing so.
Not so Fast…

High Dk silicone hydrogel lenses have overcome many of the hypoxic problems associated with traditional continuous wear and the popularity of continuous wear with these lens types is increasing. However, there are still many questions that remain to be answered with regards to corneal oxygen requirements, material oxygen transmissibility, and ocular pathogens. Holden and Mertz established the foundations for the new generation of silicone hydrogel contact lenses for daily and extended wear in 1984. It now appears, however, that the Holden and Mertz criteria for extended wear critical Dk/t should be revised upwards to at least 125, or even higher. More than this, it has recently been suggested that there are many flaws in using Dk/T as a measurement for high Dk materials. The problem is that Dk/T loses its linear relationship to the amount of oxygen reaching the eye when lens Dk/T levels are 40 or above. Dk/T displays this limited ability to measure lens performance because it does not account for oxygen concentration at the interface of the contact lens and cornea. Despite vast increases in Dk/T, after a certain point there is little change in the actual quantity of oxygen reaching the cornea. Increasing the Dk and amount of silicone in a lens also increases modulus and stiffness, resulting in less comfort and increased complications secondary to mechanical trauma during continuous wear, like superior epithelial arcuate lesions (SEALs) and giant papillary conjunctivitis (GPC).

Though the incidence of loss of visual acuity due to microbial keratitis among users of the silicone hydrogel contact lens is low, the overall rate of presumed microbial keratitis with the wearing schedule of as many as 30 nights is similar to that previously reported for conventional continuous-wear soft lenses worn for fewer consecutive
nights. This means that corneal hypoxia cannot be the sole mechanism that causes infectious keratitis and that other possible mechanisms need to continue to be researched.

**The Future Looks Bright**

Practitioners and researchers are gradually realizing that the lens with the highest Dk/T is not automatically the lens that will provide superior ocular health and comfort, and that other lens characteristics are just as significant. CooperVision’s new silicone hydrogel, Biofinity (comfilcon A), combines a high Dk (128 barrers) with relatively low modulus, which appears to offer a better balance of Dk to modulus. In a clinical trial of Biofinity versus the Focus Night & Day and PureVision, Biofinity’s continuous wear performance was superior in terms of comfort, vision and overall preference. Biofinity is due on the market very soon and many practitioners are eager for its arrival.

From the Permalens 71% introduced by DeCarle in the early 1970’s to CooperVision’s Biofinity set to be released this year, continuous wear has steadily advanced. Thanks to years of dedicated efforts of clinical and institutional researchers like the ones mentioned here, practitioners and patients alike now benefit from healthier, safer, and more convenient options in contact lens wear. Despite the amazing progress that has been made, there are a number of potential areas of research that need to be explored for continuous wear to maintain its progress. It is our duty, as students and practitioners, to investigate these issues and to sustain the exceptional efforts that have been put forth over the last 40 years. With a continued worldwide collaboration in continuous wear research and development, there is no limit to what can be accomplished.
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