Corneal Infiltrates With Silicone Hydrogel Contact Lens Wear and the Role of Compliance

By Kathryn Dumbleton, PhD, MCOptom, FAAO, and Doerte Luensmann, PhD, Dipl Ing (AO), FAAO

Corneal infiltrates occur as a result of corneal inflammation and can range from very mild, self-limiting focal infiltrates to sight-threatening microbial keratitis. The primary focus of this issue of Optometry Rounds is on non-sight-threatening infiltrates, which are seen frequently in contact lens wearers and represent an inconvenience for the both the patient and the eye-care practitioner due to additional chair time, therapeutic management and counseling.

Corneal infiltrates are discrete accumulations of inflammatory cells that have migrated into the usually transparent corneal tissue in response to a variety of stimuli. They can be indicative of both inflammatory and infectious corneal disease. Eye care practitioners (ECPs) have been observing corneal infiltrates in their soft contact lens wearers since the introduction of these lenses in the 1970s.1-3 Corneal infiltrates have historically been reported to be associated with hypoxia, contamination of contact lenses or storage cases with microorganisms, and sensitivity to cleaning solutions.3,5

Since the 1970s there have been many changes in the types of soft lens materials available, the recommendations for replacement frequency, wearing modality, and the care systems used for cleaning and disinfecting lenses. Arguably the most significant change has been the introduction of highly oxygen permeable silicone hydrogel materials, which now account for the majority of contact lenses prescribed in Canada, the United States (US), and many other countries.6 Despite these significant improvements in contact lenses and their care products, infiltrates continue to occur in some wearers.7,8

Classification

The first detailed analysis of corneal infiltrates in contact lens wearers was made more than 30 years ago. Josephson and Caffery7 categorized infiltrates primarily according to their presumed etiology – many of which are not as relevant in contemporary contact lens wear – but also with reference to the associated signs and symptoms. Another approach is to classify infiltrates according to their severity.9,10 Despite its inherent difficulties, the most frequent method of classifying infiltrative events is to consider them as being either “sterile” or “microbial”.11,14 Further classification of infiltrates has also been suggested according to clinical subtype.15 Three broad categories have been proposed using this classification:

- Serious and symptomatic
- Clinically significant and symptomatic
- Clinically insignificant and asymptomatic

“Serious and symptomatic” infiltrates are limited to those associated with microbial keratitis. The more common cases of corneal inflammation fall under the latter 2 categories; this review will concentrate principally on these infiltrates, while still recognizing that it is not always possible to be certain about the underlying etiology. The clinical presentation, epidemiology, and incidence of microbial keratitis with silicone hydrogel lenses have been reported elsewhere,16-18 and will not specifically be discussed in this review.
Clinical Appearance

When observed with the slit lamp biomicroscope, “sterile” corneal infiltrates have the appearance of small round hazy greyish-white opacities, which may be focal (Figure 1) or diffuse. They may be located just beneath the epithelium or in the anterior stroma. These areas of opacity are composed of inflammatory cells, in particular polymorphonuclear leukocytes. The size of the infiltrates can vary from <0.5 mm to 1.5 mm in diameter. Infiltrates may be graded according to number, severity, size, and area affected.

Commonly Used Terminology

Infiltrative keratitis (IK) is a general term used to describe the presence of infiltrates in the cornea. Many cases of IK are thought to be due to the presence of gram-positive exotoxins found on or near the lid margin. Symptoms associated with IK include mild to moderate irritation (often described as a foreign body discomfort), mild redness, lacrimation, photophobia and occasionally mild discharge. In many cases, however, patients report no associated symptoms. In most cases, discontinuation of contact lens wear for a few days results in full resolution of any signs and symptoms. While no specific treatment is required in these cases, ocular lubricants may alleviate symptoms and topical corticosteroid therapy may expedite resolution.

The term contact lens peripheral ulcer (CLPU) is frequently used to describe the inflammatory response that presents as a single small, circular, peripherally or mid-peripherally located infiltrate in the anterior stroma, with associated fluorescein staining of the overlying epithelium (Figure 2). This condition has been described as being a hypersensitivity reaction to the (usually gram-positive) exotoxins released by pathogenic bacteria. CLPU may cause mild to moderate pain (foreign body sensation), mild lacrimation, and mild photophobia. Following acute presentation with associated symptoms, the corneal epithelium regenerates within a few days. During this time, diffuse infiltration surrounding the lesion may also develop. In some cases, there is no acute presentation and the only telltale sign is a well-defined circular “scar” that fades with time. Because of the similarities in appearance to microbial keratitis, particularly in the early stages of development, differential diagnosis between the 2 conditions is extremely important. Since CLPUs are self-limiting, no specific treatment is required for their resolution; however, antimicrobial treatment may be instigated as a precautionary measure in cases of suspected microbial keratitis. Similar to IK, ocular lubricants may be dispensed to alleviate symptoms and topical corticosteroid therapy may also expedite the recovery process.

Phlyctenulosis is an inflammatory response that presents with white nodules and associated hyperemia in the limbal region. This condition is typically self-limiting; however, in more severe cases it progresses to the peripheral cornea and may require treatment with topical steroids.

Contact lens acute red eye (CLARE) is a generally unilateral, acute inflammatory condition that occurs with overnight lens wear and is thought to occur in response to gram-negative organisms (e.g., Pseudomonas species) colonizing the lens surfaces and releasing endotoxins. CLARE has been reported to be associated with upper respiratory infections, which may be due to the presence of other gram-negative organisms including Haemophilus influenzae. Cases of CLARE generally occur in the early hours of the morning, following sleeping while wearing contact lenses, and are accompanied by a moderately painful (foreign body sensation) red eye, with associated epiphora and photophobia (Figure 3). The inflammation manifests as either focal or diffuse subepithelial infiltrates, which are usually observed in the mid-periphery of the cornea, close to the limbus. The infiltrates rarely stain with fluorescein and rapidly resolve. Since CLARE is self-limiting on removal of contact lenses, management involves simply temporary discontinuation of lens wear and ocular lubricants during the acute stage.
Smoking

Smoking is associated with a doubling of risk of developing corneal infiltrates in hydrogel lens wearers,\(^\text{19}\) and a similar increase in risk (1.4–4 times greater) has been reported for silicone hydrogel lens wear,\(^\text{41,42}\) but not in younger wearers.\(^\text{37}\)

Previous inflammatory events

A history of previous inflammatory events has been shown to be associated with a 4–7-fold increase in risk for developing corneal infiltrates in silicone hydrogel wearers.\(^\text{34}\) Dumbleton et al\(^\text{43}\) reported that 25% of overnight wearers of silicone hydrogel lenses with infiltrates or CLPU experienced repeated episodes. Conversely, Morgan et al\(^\text{41}\) found that patients who experienced previous ocular complications were 1.8 times less likely to develop corneal infiltrates. The reason for this is not clear but may be related to the fact that these individuals are more likely to take greater care when wearing their lenses.

Daily wear versus overnight lens wear

Most clinical trials investigating the incidence of inflammatory events with silicone hydrogel lenses have been reported for overnight wear.\(^\text{8,35,41,44-49}\) These studies describe incidence rates for sterile keratitis of 1.3–5.5 per 100 patient-years for conventional hydrogel lenses and 2.9–6.7 per 100 patient-years for silicone hydrogel lenses.\(^\text{50}\) A meta-analysis by Szczotka-Flynn and Diaz\(^\text{51}\) determined nearly twice the corneal inflammatory event (CIE) rate with extended wear (≤30 days) of silicone hydrogel lenses as with 7 days of conventional hydrogels (14.4 versus 7.7 per 100 eye-years). A prospective study evaluating corneal infiltrative events with continuous wear of silicone hydrogel lenses reported a cumulative 1-year incidence of 26.7%\(^\text{42}\). A multicentre case-control risk analysis for the development of symptomatic infiltrative events by Chalmers et al,\(^\text{52}\) including >50 different contact lens types and >10 different care regimens, found that the risk associated with extended wear was 4.6 times higher than daily lens wear.

Incidence rates for corneal infiltrates in patients using daily-wear silicone hydrogel lenses are not as well defined as they are for overnight wear, which have been investigated in large post-marketing surveillance studies.\(^\text{45,46}\) A 1-year incidence rate of 19.6% identified by Carnt et al\(^\text{53}\) with daily-wear silicone hydrogel lenses conflicts with reports of few or no adverse events in other daily wear studies.\(^\text{48,54,55}\) This disparity is most likely due to differences in study design, particularly the more frequent subject follow-up in the Carnt study.

Replacement frequency

The majority of contemporary soft contact lenses are replaced after 1 day, 2 weeks, or 1 month. More frequent
replacement has been associated with fewer complications in patients wearing hydrogel lenses. A recent retrospective study by Chalmers et al found that wearers of reusable lenses are at an 8-fold greater risk of developing corneal infiltrates than daily disposable lens wearers. Counterintuitively, Dart et al found that the use of daily disposable conventional hydrogel lenses increase the risk of developing microbial keratitis 1.6-fold. They further reported on differences between daily disposable lens types and concluded that the interaction between the lens and the ocular surface may play a more important role in the development of microbial keratitis than oxygen permeability of the lens material and lens case contamination. The relative risks for daily disposable silicone hydrogel lenses are unknown as these lenses were not available commercially when the previous studies were conducted.

**Care regimens**

Multipurpose solutions have been reported to confer a significantly higher risk of infiltrates than hydrogen peroxide disinfection solutions. Recent speculation and discussion among ECPs that specific combinations of multipurpose solution and silicone hydrogel contact lens material may be more likely to cause corneal infiltrates has largely been based on the reports of case series. This has been supported by results of a recent study by Carnt et al, who investigated the incidence rates of CIEs in 20 combinations of silicone hydrogel contact lenses and lens solutions. They reported substantial differences between the combinations, and found significantly lower incidence rates of CIEs with hydrogen peroxide systems than with combination solutions. However, to date, there has been no prospective, controlled study in which the incidence of infiltrates has been compared between users of various combinations of silicone hydrogel lenses and multipurpose solutions. A recent retrospective analysis of 166 cases of corneal infiltrates in younger (<34 years) contact lens wearers found no association between the presentation of infiltrates and a specific lens material and solution combination.

**Compliance**

Noncompliance among contact lens wearers remains a significant problem despite many recent improvements in lens materials and care regimens. A recent study in the US reported that only 32% of patients are compliant in their lens wear and care behaviours.

**Hygiene and disinfection**

Failure to wash hands prior to handling lenses confers a 1.5-fold increased risk for developing microbial keratitis and 2-fold higher risk for developing sterile keratitis. Many contact lens wearers also fail to use their care systems as recommended. It has been reported that 40%-75% of wearers regularly fail to rub and rinse lenses despite evidence that these steps reduce the risk of microbial keratitis when using multipurpose care systems, and may be beneficial in avoiding corneal infiltrates. Incomplete contact lens disinfection can occur when patients “top up” their solution rather than completely replacing it with fresh solution. This practice was implicated in both of the recent outbreaks of Fusarium keratitis and Acanthamoeba keratitis.

**Lens replacement**

The most commonly reported aspect of noncompliance by contact lens wearers is lens replacement. Two recent studies have shown that failure to replace lenses appear to be associated with a higher overall risk of lens-related complications.

**Contact lens case cleaning and replacement**

Proper lens case cleaning includes daily rubbing and rinsing of the case with the multipurpose solution, tissue wiping, and air-drying the case. Poor case hygiene confers a 6.4-fold greater risk of developing microbial keratitis, and an association has also been reported between inadequate case cleaning and “sterile” infiltrates. Infrequent case replacement is another common problem, and was found by Stapleton et al to increase the risk of microbial keratitis by 5.4 times. The recommended replacement interval ranges from monthly to every 6 months. It is unknown whether patients with older cases are also at greater risk of developing corneal infiltrates, particularly since studies have confirmed that biofilm builds up in lens cases over time. Patients who experienced previous lens complications were subsequently 3.4 times more compliant with case replacement than those who had never experienced ocular problems.

**Conclusion**

Despite the fact that corneal infiltrates are not sight threatening as they are for microbial keratitis, they affect the patient’s ocular health and well-being as well as the ECP’s time in evaluation, management, and counseling. ECPs should be aware of the various
patient-related factors associated with corneal infiltrates for proper fitting of prospective wearers with contact lenses. Factors over which the ECP has more control include the wearing schedule, replacement frequency, and care system recommended for each of their contact lens wearers. Despite careful product selection and patient instructions, compliance remains a significant factor in the risk of developing infiltrates. Therefore careful counseling and education with respect to all aspects of contact lens wear and care are essential in the reduction of risk of all contact lens-related complications.

Dr. Dumbleton is the Head of Clinical Research, Centre for Contact Lens Research, University of Waterloo, Waterloo, Ontario, and President of the American Optometric Foundation. Dr. Luensmann is a Clinical Scientist in the Centre for Contact Lens Research, University of Waterloo, Waterloo, Ontario.

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