Infiltrates can be of an infectious or sterile nature. Infectious infiltrates are much rarer but can develop into sight-threatening keratitis, therefore, differentiating between the two is extremely important. However, this is not always straightforward, as there is significant overlap in both signs and symptoms, especially in the early stages. This article guides the practitioner through investigation, differential diagnosis and how each should be managed.

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**Learning objectives**
6.1.5 Know how to recognise corneal infiltrates and the differential diagnosis
5.2.1 Know the correct management of corneal infiltrates

**Learning objectives**
6.1.11 Understand the causes and disease process of corneal infiltrates
8.1.1 Know the likely symptoms, causes and signs of corneal infiltrates
5.2.2 Know how corneal infiltrates are managed

**Learning objectives**
5.4.1 Know how to recognise corneal infiltrates and the differential diagnosis.
Understand the causes and disease process of corneal infiltrates
5.4.2 Know the correct management of corneal infiltrates

**About the author**
Dr Caroline Burnett-Hodd is a fourth generation optometrist working with her father, Nigel, and Sophie Taylor-West at Mr Burnett-Hodd’s specialist contact lens practice in central London. She also works as a consultant to No7 Contact Lenses and until recently ran the contact lens service at Croydon University Hospital. Previously, she gained a master’s degree in neuroscience and a PhD in particle physics, plus taught secondary school science.
Corneal infiltrates
In order to remain transparent, the cornea has a tightly ordered structure which is completely avascular and hence devoid of white blood cells. However, in some circumstances, an immune or inflammatory response of the cornea recruits white blood cells (mainly neutrophils) to the affected area from the limbal vasculature or from the tears. These white blood cells can aggregate together, forming what is known as an infiltrate. Figure 1 shows a typical infiltrate. The presence of the white blood cells affects the transparency of the cornea and the infiltrate shows up as a white lesion. This is often referred to as an ulcer.

Infiltrates can be of an infectious or sterile nature. Sterile infiltrates are far more common and are usually relatively benign and self-limiting. Infectious infiltrates, on the other hand, are much rarer but can develop into sight-threatening keratitis. Therefore, differentiating between the two is extremely important. However, this is not always straightforward as there is significant overlap in both signs and symptoms, especially in the early stages.

Examining the eye
The slit lamp biomicroscope is an essential tool in assessing the corneal infiltrates as they may not be visible to the naked eye. Topical anaesthetic may be necessary to allow examination. Begin with low magnification and diffuse illumination and then focus in on the infiltrates using direct and indirect illumination, attempting to assess the depth of the lesion. Sodium fluorescein staining is essential to check for epithelial defects. The severity and pattern of redness should be noted and whether there is an anterior chamber reaction. Lids should be assessed for blepharitis and also for swelling. The presence of any discharge should be recorded.

Symptoms
The patient's symptoms are also important when assessing corneal infiltrates. The patient should be asked to grade the severity of the pain and also asked if they have photophobia, a watery eye or a sticky discharge. They should also be asked how rapidly the condition came on. A full history should be taken as the patient may be immuno-compromised, or may have suffered trauma to the eye. Finally, it is essential to measure the visual acuity of the patient.

Symptomatic sterile corneal infiltrates
The term sterile corneal infiltrate covers conditions such as contact lens peripheral ulcer (CLPU) and contact lens associated red eye (CLARE). These two conditions have a similar aetiology but differ in their signs and symptoms.

Sterile corneal infiltrates used to be associated with a reaction to old generation preservatives such as thiomersal but now most are thought to be caused by an inflammatory response, usually to substances released by bacteria. They are referred to as sterile because a scrape of the cornea does not usually culture microorganisms, however, analysis of the contact lens itself or the case may. It is thought that bacterial toxins adhere to the lens, or that the mechanical interaction of the lens disrupts the corneal epithelium, allowing the cornea to react to the toxin. They are associated with contact lens wear and risk factors include overnight wear, smoking and poor lens hygiene, specifically bacterial contamination of the lens case. They are more common in older patients over 60, possibly due to increased bacterial load from blepharitis, younger patients under 25, possibly due to poor compliance and in ammetropes greater than five dioptres, possibly due to over-wear of lenses.

Sterile infiltrates can occur in non contact lens wearers, usually concomitant with blepharitis.

The incidence of symptomatic corneal infiltrates is around five per 100 wearers, although study results vary hugely. The incidence is higher in daily wear and extended soft lens wear compared to rigid gas permeable lenses. There is some evidence for increased incidence in silicone hydrogel wear, but this might be due to the rigidity of early materials.

Contact lens peripheral ulcer/culture negative peripheral ulcer
Contact lens peripheral ulcer (CLPU), (Figure 2), now sometimes referred to as culture negative peripheral ulcer (CNPU), refers to a single focal infiltrate. In most cases, the infiltrate is caused by an immune response to toxins released by the bacterium Staphylococcus aureus.

Symptoms
The patient will most likely present complaining of a red and moderately sore, watery eye, which came on quite rapidly.

Figure 1 Typical infiltrate
Figure 2 CLPU (image courtesy of B+L)
1 CET POINT

Infected infiltrates and microbial keratitis
Infected infiltrates are caused by microbial keratitis (MK), (Figure 4), a sight-threatening condition which is, unfortunately, associated with contact lens wear. In this case, the infiltrate is the immune response to an infection of the cornea, usually by bacteria such as Pseudomonas aeruginosa or by Acanthamoeba or fungus (very rare in the UK). Without early treatment, the condition can progress rapidly and permanent corneal damage is done. It is associated with over-night contact lens wear, poor hygiene and some kind of compromise to the cornea, either traumatic or immunological.8

In MK, the pain is usually moderate to severe, there is photophobia and often a decrease in vision. The eye will be very red, especially at the limbus and there may be an anterior chamber reaction. Usually there is one infiltrate which can be larger than 2mm, it may also have irregular edges and a ring infiltrate around it. It is more likely to be located centrally than a CLPU, but if the lesion is mid-peripheral or even peripheral, this does not totally discount MK. There is often a purulent discharge and swollen lids (Figure 5).

Fortunately, the incidence of MK is very low, which indicates how good the eye is at protecting itself from infection. It occurs in around four per 10,000 wearers in daily wear and 20 per 10,000 in extended wear. MK is less common in RGP lenses than in soft lenses.4

Differentiating between sterile infiltrates and MK
Unfortunately, in the early stages MK can look very similar to a sterile infiltrate. MK can progress to vision loss very quickly, so it is important to identify sufferers at as early a stage as possible. As a cell culture of a corneal scrape takes a significant time to yield results (if it does at all) it is up to the eye care specialist to use the presenting symptoms and signs to make a diagnosis.

In terms of symptoms, a patient presenting with any of the following should be considered highly suspicious:
• Moderate to severe pain of rapid onset
• Photophobia
• Any vision loss
• Mucopurulent discharge or swollen lids.

In terms of signs, a very red eye, with a meaty appearance and/or redness in two or more quadrants would be highly suspicious. A suspicious lesion would be greater than 2mm in diameter or irregular in shape and run deeper into the stroma. A central lesion would be more indicative of keratitis, but a peripheral lesion does not exclude keratitis. However, the presence of flare or hypopyon is a strong indication of MK.

If there is any suspicion that the lesion might
Management of sterile corneal infiltrates

If the lesion is not suspicious of MK and instead appears to be a sterile infiltrate, then as long as the practitioner feels confident that they have the skills and experience required, they can manage the condition themselves. It should be noted that a sterile infiltrate will not progress to MK, it is only through misidentification in the first place that MK occurs.

Even though the infiltrate is considered sterile, it should be monitored closely over the following 24 hours to ensure that it is not early MK. If it is not possible to monitor the infiltrate then it is advisable to refer.

If the practitioner has access to broad spectrum topical antibiotics then these may be considered as a prophylactic against MK. However, this would apply only to independent prescribers. It should be borne in mind that chloramphenicol is not effective against Pseudomonas aeruginosa. In addition, use of an antibiotic or bacteriostatic substance would make cell culture less sensitive if MK did occur.

The patient should be told to cease contact lens wear until the condition is resolved, which should take a few days. If the patient wears the lens on an extended wear basis then it may be worth considering daily wear or daily disposable wear if possible. Any blepharitis should be treated, as this will reduce the amount of bacterial toxins present.

The lesion will usually heal to a non-staining scar, which should be noted on the patient’s record to prevent misidentification in the future.

Other causes of infiltrates

Adenoviral conjunctivitis

Corneal infiltrates may also occur with adenoviral conjunctivitis (Figure 6). In this case, the patient will have the classic signs and symptoms of viral conjunctivitis but will also have multiple sub-epithelial infiltrates, which are probably immune responses to the viral antigen. These infiltrates may persist for many months and there can be some mild reduction in vision until they resolve.

Atopic/vernal conjunctivitis

Corneal infiltrates can also occur in vernal conjunctivitis, especially superiorly, presumably because the swollen lid mechanically rubs this area. The patient should have other accompanying signs of allergic eye disease such as papillae and chemosis. Without treatment, vision loss can occur.

Asymptomatic infiltrates

These are small infiltrates which are completely asymptomatic. They can occur in both contact lens and non-lens wearers and are believed to be due to environmental antigens. There is no accompanying epithelial defect and no treatment is necessary.

Auto immune disorders

Infiltrates may also occur in certain autoimmune disorders such as rheumatoid arthritis, Crohn’s disease and Wegener’s granulomatosis.

Conclusion

Any practitioner managing contact lens patients will come across corneal infiltrates from time to time. In almost all cases, the condition is self-limiting and can be managed simply by ceasing lens wear for a short period, treating blepharitis and switching from extended wear. Unfortunately, we may see MK in practice, although it is rare, therefore, it is important to manage corneal infiltrates conservatively and if there is any doubt, then an urgent referral should be made.