# Getting started in therapeutics

## Part 7 – How does therapeutics fit into contact lens practice?

**Chris Steele** and **Afroditi Sideropoulou** describe how to approach the management and treatment of contact lens-related conditions. C7543, two CET points, suitable for optometrists, supplementary prescribers and additional supply optometrists

It is estimated that approximately 6 per cent of contact lens wearers per year will develop contact lens-related complications.[1] These problems range from self-limiting conditions that resolve without intervention to sight-threatening diseases requiring rapid diagnosis and appropriate treatment to prevent vision loss. Contact lens complications are as varied as they are common, involving the lids, conjunctiva, and all layers of the cornea. Many contact lens-related problems will resolve on discontinuation of lens wear, albeit on a temporary basis. In many cases, speed of recovery may be enhanced by the appropriate use of a range of therapeutic agents now available to optometrists.

This monthly series is designed to provide optometrists with a practical, step-by-step guide to getting started in therapeutic practice and will seek to answer the following questions:

- How should I plan my strategy?
- What training will I need?
- What equipment will I need?
- What conditions should I manage and treat initially?
- What conditions can I manage and treat with training?
- How do therapeutics fit in to contact lens practice?
- What drugs will I prescribe and treat?
- What are the legal and ethical considerations?
- How should I market my therapeutics business?

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### Medicines legislation in optometric practice

The introduction of Additional Supply legislation in June 2005[2] enables suitably qualified and accredited optometrists to sell or supply an expanded range of therapeutic agents, allowing them to manage a variety of non-sight threatening ocular conditions including infective and allergic conjunctivitis, blepharitis, dry eye and superficial injury.[3] This has increased the number of contact lens-related complications that an optometrist may be able to manage without referral in every case. The recent Department of Health announcement, which gives the official go-ahead for the introduction of independent prescribing, will allow optometrists to prescribe independently. This will enable them to maximise their existing diagnostic skills and further develop their role in the management of eye disease. Independent prescribing has the potential to make a significant impact on contact lens practice in the future.

With the introduction of independent optometric prescribing, however, it is essential that contact lens practitioners are able to recognise sight-threatening conditions requiring referral. If a contact lens practitioner is going to self-manage a patient it is also vitally important that they are competent to monitor the response to treatment and to modify the management accordingly.

The College of Optometrists and City University are currently working on clinical management guidelines which will act as the framework on which independent optometric prescribing will develop. These will be for a range of specified conditions where individual optometrists will work within their own level of expertise.

Chloramphenicol has been available to optometrists for many years in the course of their professional practice. The inclusion of fusidic acid (Fucithalmic) in the entry-level list for use by all optometrists is useful in contact lens practice. This may be used in managing certain cases of bacterial conjunctivitis in contact lens patients, as prophylaxis following contact lens-related superficial trauma or even for managing infective blepharitis prior to contact lens wear (see Part 1).

Pre-disposing factors that commonly contribute to problems with wearing contact lenses include dry eye, blepharitis and allergic conjunctivitis. Before being fitted with contact lenses, all patients should be fully assessed. Any significant signs of these conditions should first be addressed to minimise their effects and improve the chances of achieving successful contact lens wear.

### Blepharitis

Blepharitis is a blanket term for inflammation of the lid margin (Figure 1). It is common in the general population where it is a frequent presenting complaint at ophthalmic casualties across the UK.[4] It is also a common cause of contact lens intolerance. Blepharitis can be exacerbated by contact lens wear which may also unveil previously asymptomatic blepharitis. Although blepharitis is not a contraindication to wearing contact lenses, it should be as fully controlled as possible before lens wear is commenced.

The main symptoms include itchy, burning eyes with a foreign-body sensation and sometimes mild photophobia. Often patients will report their eyes being stuck together in the mornings. In contact lens wearers this condition may reduce lens tolerance due to discomfort and produce unstable visual acuity. This is exacerbated by increased lens deposition due to the effects on the tear film.

Chronic blepharitis may be subdivided into anterior (affecting lash-bearing skin) and posterior lid margin disease (affecting the mucocutaneous junction and meibomian glands).

For anterior blepharitis, this requires regular lid hygiene to remove debris and flaky skin (often forming collarettes) from the lash bases. Staphylococcal colonisation may be treated with antibiotics available to optometrists such as chloramphenicol 1 per cent ointment and fusidic acid 1 per cent twice daily for up to three months. Traditional methods of treatment involving bathing and scrubbing the lid margins, boiled salt water, 10 per cent baby shampoo solution and cotton wool balls or tissues, are still commonly used. Hot compresses are recommended for treatment of meibomianitis. There are, however, a couple of relatively new over-the-counter (OTC) products designed specifically for the treatment of anterior and posterior blepharitis.

Lid-Care (Novartis) has been specifically developed as a complete system for daily eyelid and lid margin hygiene – an essential step in the management of blepharitis in non-contact lens and

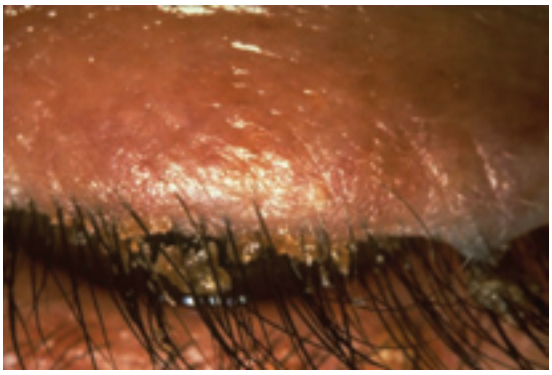

**Figure 1** Blepharitis

contact lens wearers. It removes accumulated oily debris, crusted matter and cosmetics from the eyelids and lashes. It is a sterile, pH adjusted, hypoallergenic detergent solution containing three gentle surfactants (Miranol, polysorbate and propylene glycol), a borate buffer and a preservative (domiphen bromide and disodium edentate), and purified water. Lid-Care is available in ready-to-use pre-moistened towelettes or a 120ml bottle with gauze pads, containing no potentially irritating perfumes or dyes.

Alternatively, there are Supranettes (Alcon) available. Supranettes were developed specifically for external eye hygiene. These are individually packed, sterile, soft viscose eye pads moistened and soaked with plant extracts (such as witch hazel) to provide soothing effects. In the authors' experience, both these products can cause some mild irritation and so are not suitable for all patients.

## Dry eye

Dry eye is a condition of complex and diverse aetiology encompassing ocular adnexal and surface disorders as well as tear film lipid, aqueous and mucin deficiencies. Dry eye may be categorised into two groups, which may occur together or separately. Tear-deficient dry eye relates to an abnormality of the lacrimal gland, with resulting decreased tear fluid production. Conversely, tear-sufficient dry eye relates to the evaporative form in the presence of adequate tear fluid production. Causes of dry eye include abnormal lipid production, ocular surface abnormalities, contact lenses and, in some cases, preservatives used in certain multi-purpose contact lens solutions.

Dry eye can be associated with systemic diseases, chemicals, drugs, inflammation, allergic reactions, and contact lens wear. Severity of symptoms often poorly correlates with severity of dry eyes. The symptoms of dry eye typically include: burning, stinging, redness, foreign-body sensation, tearing and intermittent blurred vision. Signs include inflammation of the ocular surface. Severe dry eye is usually a contraindication for contact lens wear in community optometric practice and so treatment strategies for this will not be included in this article.

**TABLE 1**
**Examples of solutions marketed as contact lens rewetting drops**

| Contact lens rewetting drops specifically for use with soft and RGP lens *in situ* | Ingredients | Preservative |
|---|---|---|
| Clerz Plus | Tetronic 1304 helps the contact lens retain moisture and shields from protein build up | Polyquad |
| Optifree Express rewetting drops | Sterile buffered, isotonic aqueous solution. No hydrogel lubricants | Polyquad |
| ReNu rewetting drops | Poloxamine removes dirt and protein deposits | Sorbic acid |
| Lens Plus rewetting drops | Sterile, buffered isotonic solution. No hydrogel lubricants. Preservative free | Preservative free |
| Aquify Comfort drops | Sodium hyaluronate 0.1% | Sodium perborate |
| Complete blink N clean | Hydroxylpropyl methylcellulose (HPMC) is the lubricant, tyloapol is the surfactant | Polyhexamthylene biguanide |
| Glycerine artificial tears which may also be used with soft or RGPs lenses *in situ* | | |
| Systane | Polyethylene glycol 400 (0.4%) is the lubricant, Hydroxypropyl guar is the gel forming matrix | Polyquaternium-1 |
| Carboxyl Methylcellulose (CMC) artificial tears | | |
| Refresh tears | 0.5% CMC | Purite |
| Refresh liquigel | 1% CMC | Purite |
| Thera tears | 0.25% CMC. Hypotonic | Preservative free |

For many patients, contact lens intolerance is often a consequence of dry eye, with up to 50 per cent of soft contact lens wearers complaining of dryness. This rises to 68 per cent in presbyopes. A person with mild dry eye may not experience symptoms until they attempt to wear contact lenses, as contact lenses can disrupt the delicate balance of tear film dynamics and can precipitate dry eye symptoms. Some dry-eye patients can only wear contact lenses comfortably for short periods of time, while others are unable to tolerate them at all. Dryness and discomfort are the primary reasons why people permanently discontinue contact lens wear.

Management of dry eye involves identifying the underlying cause. In contact lens wear this is commonly a poor tear film due to meibomian gland disease. There are several ways to manage this problem. In particular there are several types of artificial tears available with varying ingredients. These include:

- Hydroxypropyl methylcellulose (HMPC)
- Carboxyl methylcellulose (CMC)
- Polyvinyl alcohol (PVA)
- Glycerine artificial tears
- Oil-containing eye drops – prevent evaporation of tears.

However, improving tear quality will not necessarily improve symptoms if the underlying cause is one of poor tear quantity. For the contact lens patient with marginal dry eye symptoms there are a number of different contact lens rewetting agents available to use in conjunction with contact lenses. These are usually a temporary solution but do offer some relief. Some examples are given in Table 1.

The use of artificial tears with contact lenses gives significant relief from symptoms for the marginal dry-eye patient. However, they are not a perfect substitute for natural tears which ▶

consist of an inner mucin layer, a central aqueous portion and an outer lipid layer. Artificial tears only add volume to the aqueous layer of the tear film. To be effective, artificial tears include hydrogels, agents which act to increase viscosity. Hydrogels increase the contact time on the eye, as well as swelling in water and retaining moisture. Examples of hydrogels used in artificial tears include: hydroxypropyl methylcellulose (HMPC), polyvinyl alcohol (PVA), polyvinyl pyrrolidone, hyaluronic acid or carbomer 940.

Certain products such as Systane (Alcon) also include other ingredients found in natural tears such as glycine, magnesium chloride and zinc chloride as well as ingredients with 'bioadhesive properties'. Systane contains HP-Guar, which forms a thin protective gel layer on the eye between blinks, but then turns to liquid on blinking.

Making artificial tears more viscous can reduce their ability to drain easily from the eye through the nasolacrimal ducts. In some patients, and particularly with contact lens wearers, the more viscous products may cause unacceptably blurry vision, despite manufacturers' claims to the contrary.

Preservatives are added to increase the shelf life of artificial tears. Some artificial tears still use benzalkonium chloride (BAC) which is well known to cause ocular irritation if instilled repeatedly into the eye. In contact lens wearers, these products are to be avoided and instead solutions containing other preservatives – such as polyquad or cetrimide – should be used as these cause much less irritation. Where preservatives must be avoided completely, products such as saline Minims, Clerz or Refresh tears are available in preservative-free, single-use vials. This is particularly important for patients fitted with extended wear soft hydrogel therapeutic bandage contact lenses, for example. This is because certain preservatives such as benzalkonium chloride can be absorbed into the lens matrix. With repeated instillation, the preservative concentration may build up to toxic levels and cause irritation.

### Which artificial tears should be used with contact lens-wearing marginal dry eye patients?

Tear osmolarity increases in dry eyes and hypermolarity has been linked with increasing incidence of ocular surface inflammatory disease. Moderately hypotonic tears have been shown to promote disease healing in severe dry eyes. Examples of hypotonic artificial tears are TheraTears and Hypotears.[5]

Products containing gelling agents, such as Systane, or a viscous eye drop, such as Celluvisc and Liquigel, are useful where contact time needs to be prolonged without causing unacceptably blurry vision.[6] In patients with an element of meibomian gland dysfunction, oil-containing eye drops may be beneficial by helping to replenish the lipid layer of the tear film, for example Refresh Endura (Castor oil, polysorbate-80, carbomer1342, glycerine and no preservatives).[7]

Under the new medicines legislation, it is now possible for optometrists to sell and or supply these products to patients. Alternative management options include:

- Re-soaking contact lenses during the day. This can sometimes help relieve dry eye symptoms and enable individuals to wear their lenses comfortably for longer after re-insertion. It has been shown that certain lens materials can produce less discomfort and corneal staining if used in conjunction with certain contact lens solutions.[8]
- Cleaning and soaking lenses thoroughly and replacing lenses as often as is prescribed also contributes to overall contact lens comfort in patients with marginal dry eyes. Protein removing tablets are helpful for some patients but nowadays, with frequent replacement of lenses, these are not really necessary.
- Making frequent and complete blinks to rewet contact lenses helps reduce dry eye symptoms. Often visual display unit and personal computer users complain of lens dryness due to the reduced blink rates associated with concentrating on near vision tasks.
- There are many contact lens brands now manufactured from modern materials which specifically provide greater dehydration resistance and increased comfort for those who suffer contact lens-related dryness.
- Decreased aqueous tear production and decreased tear clearance can lead to chronic inflammation of the ocular surface. Prescription eye drops are now commercially available in the US which reduce this inflammation, for example Restasis (cyclosporine 0.05 per cent). However, this does not yet have a UK product licence.

Restasis is an anti-inflammatory eye drop prescribed for moderate to severe dry eyes and has proven to be effective in cases where inflammation is the underlying cause of the dryness symptoms, for example in keratoconjunctivitis sicca.

Although well outside the scope of the primary care practice, there are developments in the treatment of dry eyes that optometrists should be aware of. These include corticosteroids, androgenic therapy and autologous human serum. With regard to the latter, recent advances in biotechnology have enabled the production of tear film substitutes containing recombinant forms of growth factors. However, it is not yet clear whether these will be as efficacious as serum-derived growth factors. Further discussion of these is beyond the scope of this article.

### Punctal plugs

Punctal plugs may be considered for patients with chronic dry eye (particularly aqueous deficiency), in the absence of infection or other pathology, where the symptoms are not adequately controlled with tear supplements. This may include contact lens wearers and these can be fitted by an optometrist.[9] These punctal inserts maintain the tears on the eye, keeping it moist. This can be done on a temporary basis with a dissolvable collagen plug, usually lasting four to seven days, or more permanently with a silicone plug, which can be removed if necessary. Examples of silicone plugs include Eagle Vision and Oasis Soft Plugs. Herrick plugs, manufactured by Lacrimedics, are dissolvable intracanalicular plugs used for medium term (three months).

### Smart plugs

A Smart Plug (Medennium Inc, Irvine, California) is a temperature-sensitive punctal occlusive device that can be inserted painlessly and cannot be rubbed out like ordinary punctal plugs. Made from a thermodynamic acrylic polymer, at room temperature the device is a thin rigid rod 10mm long and 0.4mm in diameter. Using special forceps, the device is inserted into the tear duct where, at body temperature, it shortens and expands, transforming into a soft, gel-like glue which fills the punctal cavity. Unlike traditional plugs, no part of the Smart Plug lies above the surface of the eyelid after insertion.[10]

## Allergic conjunctivitis and contact lens wear

Allergy is a common cause of conjunctivitis, and this is certainly true among the contact lens population. Ocular allergic disorders include seasonal allergic conjunctivitis (SAC), perennial allergic conjunctivitis (PAC), vernal keratoconjunctivitis (VKC), giant papillary conjunctivitis (GPC) and atopic keratoconjunctivitis (AKC). Patients often present with a range of non-specific symptoms, though itching is usually present. Associated symptoms include redness, swelling, tearing

and occasional discharge. Differential diagnosis is important as many of these symptoms can occur with contact lens-related marginally dry eye. A complete history prior to fitting contact lenses is important as many allergic conjunctivitis patients report associated systemic environmental allergies.

A variety of antigens have been implicated in allergic conjunctivitis, with seasonal pollens, animal dander, and dusts being the most common. In contact lens wearers, other potential antigens include denatured tear constituents or solution preservatives that may adhere to the lens surface and initiate an allergic response. Indeed, contact lens management of the allergic conjunctivitis patient can be quite challenging, due to the many potential antigens.

In contact lens patients with allergic conjunctivitis, often the most successful management strategies involve fitting lenses with reduced wearing times, frequent replacement lenses or daily disposables to reduce lens spoilage, and a change to preservative-free solutions. If the patient is currently wearing a disposable lens, then refitting with an alternative type of disposable with a different lens material (for example from group IV to group II or group I) may also help. Sometimes re-fitting patients with rigid gas-permeable lenses (RGP) is the only successful strategy. With keratoconics this is certainly the case as associated atopy – including allergic blepharoconjunctivitis, asthma and eczema – is common.

With contact lens-related allergic conjunctivitis, the contact lens clinician must always remember to optimally control non-lens related allergic conjunctivitis prior to fitting or before re-commencing contact lens wear.

Primary treatment of allergic conjunctivitis usually includes avoiding the allergen, cool compresses, ocular irrigation and lubrication (which helps remove and dilute the allergen). There are a wide range of suitable ocular lubricants available. Secondary treatment options available include topical decongestants, antihistamines and mast cell stabilising agents.[11] The range of products now available to additional supply (AS) optometrists has increased considerably.


**Figure 2** Treatments for allergic conjunctivitis

## Topical decongestants

Topical decongestants act primarily as vasoconstrictors that are highly effective at reducing erythema and are widely used in combination with antihistamines. Vasoconstrictors, such as phenylephrine and tetrahydrozoline, are sympathomimetic agents that decrease vascular congestion and eyelid oedema via adrenoceptor stimulation. They have no effect on diminishing any allergic response. Some decongestants may only be used for short periods of time, no more than four times a day for three consecutive days. Prolonged use may actually make symptoms worse, causing more swelling and redness that persists even after the drops are stopped. Tachyphylaxis, or a rebound effect, sometimes occurs.

## Antihistamines

A variety of topical ophthalmic antihistamines are available. These agents block the physiological responses to histamine release by acting as a competitive antagonist at the $H_1$ receptors. Otrivine-Antistin is a pharmacy (P) medicine and therefore can be supplied by all optometrists (Figure 2). This contains antazoline, which is an antihistamine, but only available in combination with the sympathomimetic naphazoline. This can be used by adults and children aged over five years, two or three times a day. It is particularly useful for contact lens wearers who suffer acute seasonal allergic conjunctivitis and who wish to continue wearing lenses during the summer months when pollen counts are generally high.

The newer second-generation topical antihistamines exhibit a selective affinity for $H_1$ receptors. They also inhibit the release of histamine and other inflammatory mediators from mast cells. Levocabastine, a highly selective receptor $H_1$ receptor antagonist, has now been discontinued despite being included on the AS list for optometrists. Emedastine is another useful alternative in this category and is available to AS optometrists. This can be used to treat patients from three to 65 years old with SAC for up to six weeks per year.

Initially, oral antihistamines were extensively used to systemically control the symptoms of allergic rhino-conjunctivitis. First-generation antihistamines were generally sedating, but recent second-generation, non-sedating agents, are frequently used to treat ocular allergy. However, the current evidence base demonstrates that the therapeutic effects directly on the eye of an orally administered antihistamine are no better than a placebo compared with topically administered agents. Oral antihistamine medications are therefore often only beneficial as an adjunct to topical treatments in more symptomatic cases of allergic conjunctivitis. All the non-sedating agents now have a relatively long half-life and only require once or twice daily dosing.

Loratidine (Clarityn), cetirizine (Benadryl) and chlorpheniramine (Piriton) are useful in the contact lens

wearer with typical hay fever-type symptoms. Before advising patients to use OTC oral antihistamines, a full drug history should be taken, as there are several potential interactions or allergic responses that may exacerbate the presenting problem. Drug dosage should be gradually increased (titrated) to achieve maximum therapeutic benefit with the minimum medication. Most allergic conjunctivitis patients will notice a significant improvement within the first 12 to 72 hours of commencing treatment.

### Mast cell stabilisers

Sodium cromoglycate, for example Opticrom, is the prototypic mast cell stabiliser and its efficacy is concentration dependent. The exact mechanism of its action remains unclear. Initially, this agent was licensed only for more severe forms of allergic conjunctivitis, such as GPC and VKC. However, this is now available for use by optometrists as a P medicine. Care should be taken to avoid sodium cromoglycate preparations that contain BAC as the preservative, however.

Nedocromil (Rapitil) and lodoxamide (Alomide) are more modern forms of sodium cromoglycate (Opticrom) and should be tried if Opticrom has not sufficiently helped. Lodoxamide is a mast cell stabiliser that is claimed to be approximately 2,500 times more potent than sodium cromoglycate in *in vitro* studies in the prevention of histamine release. In clinical practice, however, this is certainly not the case. Lodoxamide is also available as a P medicine for use by optometrists. Originally, nedocromil was thought to be just a mast cell stabilising agent, but now it is recognised to have multiple actions including antihistamine properties. This is available for use by AS optometrists as are a number of other agents which possess dual properties. These include: Olopatadine (for patients aged three years and above, twice daily instillation for up to four months), Ketotifen (for patients three years and above, twice daily instillation with no treatment limit), and Azelastine (also available as a P medicine but this is restricted to the treatment of patients 12 years and older in this category).

Topical non-steroidal anti-inflammatory agents (NSAIDs) can benefit the allergic conjunctivitis patient. However, diclofenac is the only NSAID available to AS optometrists. NSAIDs exert their therapeutic effect on the cyclo-oxygenase pathway by the non-selective inhibition of cyclo-oxygenase-1 (COX-1) and cyclo-oxygenase-2 (COX-2) isoenzymes. This prevents prostaglandin and thromboxane formation which both play a key role in the inflammatory process.

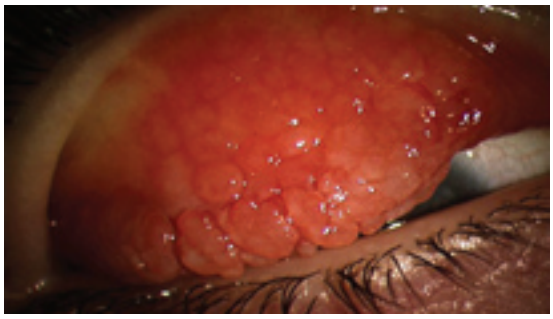

**Figure 3** Giant papillary conjunctivitis, courtesy of SJ Morgan

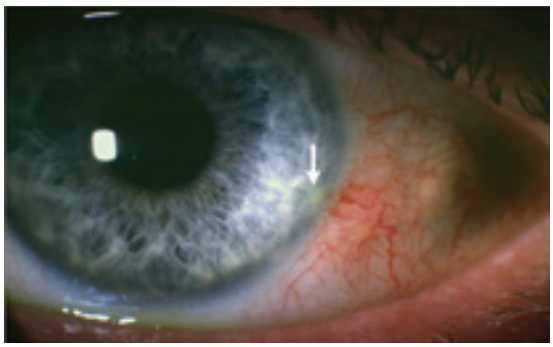

**Figure 4** Peripheral infiltrate

In more severe allergic presentations, topical steroids are required which inhibit, among other things, prostaglandin production. Topical steroids are outside the remit of the contact lens clinician who should, however, be able to recognise when referral for such treatment is indicated.

## Giant papillary conjunctivitis

Giant papillary conjunctivitis (GPC) (Figure 3) was previously a condition frequently seen in soft contact lens patients and, to a lesser extent, RGP lens wearers. Patients with exposed suture knots and ocular prostheses may also develop this condition. Atopic patients – those with asthma, hay fever or animal dander allergies – may be at greater risk. The aetiology of GPC is thought to be immunological, where contact lens deposits act as allergens, as well as mechanical. With current lens wearing regimes, this condition is much less common.

In the past, temporary discontinuation of lens wear was often required. Nowadays, using frequent replacement or daily disposable lenses minimises lens deposition and therefore subsequent immunological reaction leading to papillae formation. Mechanical irritation may also be reduced by fitting lenses with a relatively low modulus of elasticity, as the higher the Young's modulus of elasticity the stiffer the material. For example, Focus Night & Day (1.4Mpa) is a relatively stiff lens compared with Acuvue Advance (0.4Mpa). A lens with a low modulus may still be relatively stiff if it has a thick and chunky design, however. Where contact lens discontinuation is not a viable option, such as with keratoconics, then appropriate lenses (usually RGPs) should be fitted in combination with medical therapy.

Topical decongestants and mast cell stabilisers are a reliable modality for treating GPC and are the treatment of choice for chronic GPC. The use of ocular lubricants (see above) is a useful adjunct to this therapy. In more serious cases, aggressive management may be required to prevent tissue damage and this may include corticosteroid therapy.

## Contact lens-related trauma

Manipulation of a contact lens during insertion and removal can traumatise the epithelium, creating corneal abrasions. These abrasions usually heal quite rapidly with simple lubrication or patching. Debris trapped under a contact lens, or a chip or tear in the edge of a lens, can produce dramatic curvilinear abrasions. Removal of the debris or replacement of the damaged contact lens is all that is needed to treat this problem. With corneal abrasions, consideration should always be given to supplying a prophylactic antibiotic, such as chloramphenicol or fusidic acid. Chloramphenicol 0.5 per cent drops are recommended during the day and 1 per cent ointment at night.

## Keratitis and corneal infiltrates

Despite the shift in the contact lens market to the use of frequent replacement and daily wear contact lenses, and advances in contact lens technology, contact lens-related keratitis continues to be a serious problem.

Keratitis may present in many different forms. Superficial keratitis generally does not produce corneal scarring, whereas deeper stromal keratitis does. Corneal infiltrates are a common feature in keratitis of many different causes. Corneal infiltrates consist of single or multiple discrete greyish white cell accumulations of mainly polymononuclear leukocytes (neutrophils) as well as lymphocytes and macrophages. These migrate through the cornea from the limbus or tear fluid into the cornea. Infiltrate formation is in response to local tissue damage and secondary chemotactic factors, from antigens and toxins, for example, from a contact lens or an infective cause. Accurate clinical assessment of both symptoms and signs is important and scraping the cornea for cultures makes the diagnosis much easier. Important diagnostic factors include:

- Reported symptoms (pain, photophobia)

- Size and location of the lesion
- Corneal staining
- Any anterior chamber activity (with or without hypopyon)
- Conjunctival injection (circumferential in severe cases but more sectoral in less severe cases).

Corneal infiltrates associated with contact lens wear may present from a variety of causative factors. In contact lens wear, infiltrates are most often sterile (non-infectious), but may also be infectious. A recent study showed infiltrates tend to occur in the superior cornea of patients with extended wear silicone hydrogel lenses, in the central cornea of patients with daily wear disposable lenses and in the peripheral cornea of patients with daily wear hydrogel (excluding daily disposables). Infiltrates that appear near the limbus are generally less severe.[12]

Soft daily wear frequent replacement contact lenses are the most common type of lens associated with corneal ulcers in which the most common causative organism is *Pseudomonas aeruginosa*, followed by other Gram-negative bacteria and *Acanthamoeba*.[13] The contact lens practitioner should be aware of the limitations of OTC antibiotic eye drops that have their limitations for the treatment of anything other than relatively minor infections. Although Chloramphenicol and Fusidic acid are now available for use in practice, neither of these is effective against *Pseudomonas aeruginosa*. One Polymixin B combination (Polyfax) does, however, have some effect against *P aeruginosa* and is available to AS optometrists to treat ocular bacterial infections.[3] These conditions, in theory, include conjunctivitis, keratitis, corneal ulceration and ulcerative blepharitis. Where appropriate, the ointment should be used two to three times a day, depending on the severity of the condition, with treatment being continued for at least two days after the eye has apparently fully recovered.

The importance of discontinuing contact lens wear and discarding contaminated contact lenses and contact lens cases in instances of contact lens-related infection cannot be over-emphasised. However, it is important to stress that, in practice, wherever *Pseudomonas* infection is suspected these should all be referred immediately to secondary care for treatment with fluoroquinolones.

In contact lens practice it is important to be able to distinguish between relatively benign conditions that may be managed by the optometrist, from the less common but potentially sight-threatening microbial keratitis (MK). The various types can be summarised as follows:

- Contact lens-induced peripheral ulcer (CLPU)
- Contact lens acute red eye (CLARE)
- Infiltrative keratitis (IK)
- Asymptomatic infiltrative keratitis (AIK)
- Asymptomatic infiltrates (AI)
- Sight-threatening microbial keratitis (MK).

## CLPU

CLPU gives rise to usually unilateral single or multiple whitish/grey focal anterior stromal infiltrates in the periphery or mid-periphery of the cornea (Figure 4). These are often seen in extended and continuous wear contact lens patients but may also be seen with daily wear contact lenses. They are caused by an inflammatory reaction to toxins released by Gram-positive bacteria, such as *Staphylococcus aureus* and *S epidermidis* that colonise the contact lens surfaces (and are also responsible for causing blepharitis – see above). The resultant round infiltrates can range in size from 0.1mm to 2mm in diameter and, on acute presentation, will involve a full-thickness loss of epithelium. Symptoms vary from none at all to moderate foreign-body sensation, redness and epiphora.

## Differential diagnosis

The differential diagnosis for CLPU includes:

- Early MK
- Marginal keratitis
- Corneal phlyctenulosis.

The signs which distinguish sight-threatening keratitis (which requires urgent referral) from CLPU include:

- Increasing severity of signs and symptoms after lens wear has been discontinued
- Irregular infiltrates with raised edges and sometimes associated satellite lesions
- Mucopurulent discharge, adherent to the lesion (particularly in *Pseudomonas* infection)
- Lid oedema
- Severe diffuse bulbar and limbal hyperaemia
- Marked anterior chamber reaction (flare and cells, possible hypopyon).

Unlike MK, CLPUs have milder symptoms and quickly resolve with lens discontinuation, in the absence of therapeutic intervention. As the clinical presentation of CLPU and early MK can be so similar, it is usual to treat CLPU cautiously. This involves discontinuing lens wear immediately, but also treating with topical fluoroquinolone

monotherapy, such as ciprofloxacin 0.3 per cent (Ciloxan). Provided the clinical signs and symptoms are relatively mild (usually with no anterior chamber activity), the patient is instructed to instil the medication at home and is reviewed again within two to three days.

Marginal ulcers (marginal keratitis) caused by peripheral corneal hypersensitivity to Staphylococcal exotoxins are typically oval in shape and located at the 2, 4, 8 and 10 o'clock positions and run parallel to the limbus. There is usually a clear gap between the infiltrate and limbus, but this can be spanned by blood vessels. CLPUs, however, can occur at any position in the peripheral cornea. Occasionally, there is no clear interval, as infiltrates are seen to stream from the limbal vasculature to the focal infiltrate. In these cases, treatment of the underlying lid condition should be addressed. Sometimes it is necessary for the community optometrist to refer for topical steroid treatment, for example Predsol N drops four times a day. Where steroids are concerned, intraocular pressure (IOP) should always be recorded prior to commencing treatment so that appropriate action can be taken if the IOP is found to be subsequently raised due to steroid use.

## CLARE

This is a non-ulcerative sterile keratitis associated with colonisation of Gram-negative bacteria on contact lenses. Typically, the patient (mainly wearing continuous or extended wear lenses or sometimes poorly fitting immobile lenses of any type) wakes up in the early morning with uniocular discomfort/pain, photophobia, watery discharge, bulbar and limbal hyperaemia. Slit-lamp examination will reveal:

- Sub-epithelial to anterior stromal infiltrates in the periphery of the cornea distributed either focally or diffusely, with an interval between the limbus
- Reduced vision will occur if infiltrates develop in the central cornea but otherwise this remains unaffected
- No staining or ulceration
- Pronounced circum-limbal injection
- Occasionally, in severe cases, flare and keratic precipitates will be involved, but this is not usual.

It is vitally important to differentiate CLARE from MK, which is potentially blinding. Therefore, if there is any doubt about the diagnosis, the patient should be referred. As CLARE is non-ulcerative and non-infectious, it will subside with removal of contact lenses. Temporary discontinuation, along with ocular lubrication, should facilitate reduction of signs and symptoms. If in any doubt then referral for fluoroquinolone mono-therapy (see above) should be made. Re-assessment of contact lens fit should be undertaken in cases where tight-fitting lenses are the underlying cause. Switching to daily wear monthly replacement lenses or daily disposables in recurrent cases is also recommended.

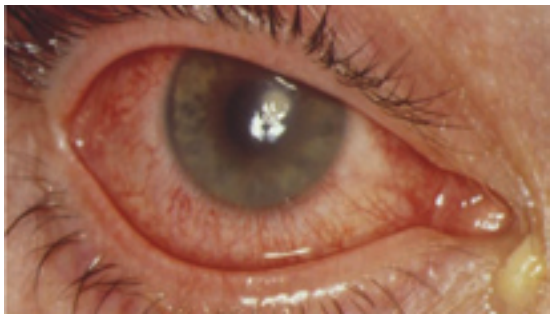

**Figure 5** *Pseudomonas* corneal ulcer, courtesy of SJ Morgan

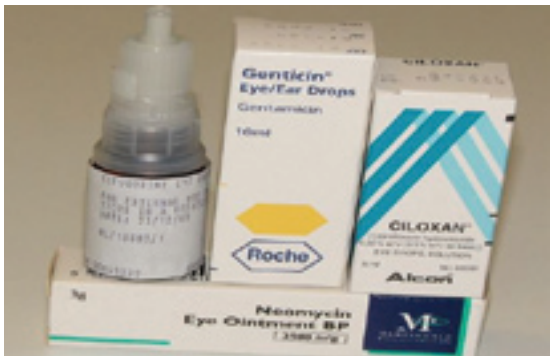


**Figure 6** Antibiotics used to treat corneal ulcers

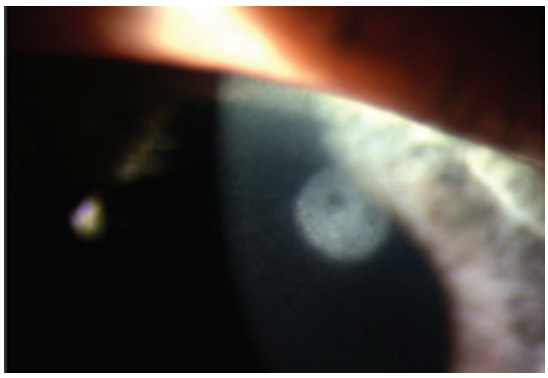

**Figure 7** Peripheral ulcer, courtesy of SJ Morgan

## Infiltrative keratitis (IK)

The term IK, or infiltrative keratitis, applies to conditions other than CLPU, MK and CLARE, in which there is sudden onset of infiltrative events. Where there are no symptoms, this is termed asymptomatic IK (AIK). Unlike CLARE, which occurs during sleep, IK symptoms occur later in the day. The inflammatory events of IK may develop from a variety of causative factors, including mechanical trauma, Gram-positive bacterial exotoxins, and even from a minor foreign body trapped under the lens. Symptoms may vary widely, from severe to non-existent. IK is usually managed by temporarily discontinuing lens wear. Lens wear should not be resumed until all signs and symptoms are completely resolved. Medication is usually unnecessary in most cases of IK, with palliative use of preservative-free ocular lubricants if required.

## Microbial keratitis (MK)

MK (Figure 5) is a very serious complication of contact lens wear. It can occur with any type of lens, with the highest incidence in hydrogel extended wear, then silicone hydrogels and the lowest incidence with RGP lenses. Although numerous micro-organisms have been associated with MK, it is the Gram-negative *Pseudomonas*, especially *P aeruginosa*, that has been implicated in the majority of infections involving extended wear hydrogels and silicone hydrogels.

Stromal necrosis occurs in *Pseudomonas* infections from the liberation of exotoxins, endotoxins, and numerous proteolytic enzymes. The stromal infiltrates associated with pseudomonal MK are dense, and accompanied by significant oedema, large central epithelial excavation and a mucopurulent discharge adherent to the ulcerated area. There may also be a ring infiltrate from the release of endotoxins.

Patients (particularly contact lens wearers) presenting with signs and symptoms consistent with MK require immediate referral for medical management. It is important for optometrists to be familiar with secondary care treatment regimens, so that once patients have been referred, they can discuss likely treatments in an informed way and offer accurate advice to patients returning to their practice for further advice or reassurance once treatment has been instigated. A selection of antibiotics used in the treatment of corneal ulcers are shown in Figure 6.

Small (<2mm) peripheral ulcers (Figure 7) in the anterior stroma usually respond well to topical fluoroquinolone monotherapy (which inhibits action of DNA gyrase, an enzyme essential for bacterial DNA synthesis), prescribed according to locally agreed protocols, eg ciprofloxacin 0.3 per cent (Ciloxan) which has a broad spectrum of activity, including *Haemophilus* species. In these cases, patients may be allowed to instil their drops at home and advised to return immediately if the eye worsens. Larger (>2mm) and more severe ulcers, and those that are on the visual axis, should be treated aggressively with topical modern fluoroquinolones in combination with fortified aminoglycosides (particularly

effective against Gram-negative rods).

At Sunderland Eye Infirmary, for example, this involves a standard first-line treatment of fortified gentamicin 1.5 per cent and cefuroxime 5 per cent drops, each used hourly. Cycloplegics/mydriatics are used to relieve pain and temper the anterior chamber reaction, as well as to prevent posterior synechiae.[14] Patients are usually admitted for this treatment. Gentamicin is itself highly toxic and epithelial healing is the primary goal. Therefore preservative-free drops should always be used. Treatment can be divided into two main phases:

- Sterilisation – where intensive antibiotic therapy is given
- Healing phase – where the aim of treatment is to promote healing and minimise any inflammation present. This may take several weeks.

Although cultures are not always taken with small peripheral ulcers, they should be obtained whenever lesions are:

- Larger than 2mm diameter
- More than one-third the thickness of the cornea.
- On the visual axis
- And particularly when contact lenses are implicated.

Cultures should always be taken of the patient's contact lenses and solutions, if available, to increase the chance of obtaining positive identification of the pathogen. Early and aggressive treatment of MK can lead to good visual outcomes, although a permanent scar will almost always be present.

In contact lens wearers presenting with any atypical keratitis, and particularly if associated with severe pain and chemosis, *Acanthamoeba* keratitis should always be considered. In the early stages no ulceration may be present but instead stromal keratitis perineural infiltrates (often mimicking herpes simplex dendritic ulcers) occur, which later give rise to central or paracentral ring infiltrates and abscesses. Scleritis and glaucoma are later complications of *Acanthamoeba* keratitis. Therapy is usually with topical polyhexamthylene biguanide (PHMB 0.02 per cent) or chlorhexidine (0.02 per cent), with or without propamide 0.1 per cent, which are instilled initially every hour. Any accompanying bacterial infection also requires separate treatment as described above. In severe cases therapeutic keratoplasty (corneal graft) is necessary when medical treatment is not successful. Recently the multi-purpose solution Complete MoisturePlus by Advanced Medical Optics (AMO) was linked with an outbreak of *Acanthamoeba* keratitis (AK) among soft contact lens wearers in the US and patients have been advised to avoid its use.[15]

## Fungal keratitis

In the past couple of years, certain contact lens solutions (such as Bausch & Lomb ReNu MoistureLoc) have been implicated in outbreaks of fungal keratitis (keratomycosis) in various parts of the world caused by *Fusarium* species. Although such cases are rare, contact lens practitioners should be aware of this condition that is often diagnosed late in its clinical course, resulting in a poor prognosis. Typically infiltrates tend to be grey (sometimes pigmented) and elevated with feathery borders. Satellite lesions are common. Treatment involves use of polyenes such as amphotericin B, natamycin and azoles (fluconazole and ketoconazole). Steroids are indicated later in the treatment course to control inflammation which may be causing significant damage.

## Conclusion

With the recently expanded access to therapeutic agents through AS and SP, optometrists can now self-treat a wider range of contact lens-related

ocular complications. A rapid and accurate diagnosis of more severe, sight-threatening complications is vital so urgent referrals can be made for appropriate treatment to prevent vision loss. Contact lens practice will be further enhanced by independent prescribing, now that its introduction by the Department of Health has been officially announced.

In Part 8, Professor John Lawrenson and Lucy Titcomb look at the range of drugs available to optometrists with and without further training.

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## MULTIPLE-CHOICE QUESTIONS – take part at opticianonline.net

**1 Which of the following statements on the rate of complications in contact lens wear is correct?**
**A** 6 per cent of patients will develop problems each year
**B** 16 per cent of patients will develop problems each year
**C** 26 per cent of patients will develop problems each year
**D** 36 per cent of patients will develop problems each year

**2 Which of the following antibiotics is not available to additional supply optometrists?**
**A** Fusidic acid
**B** Chloramphenicol
**C** Ciprofloxacin
**D** Polyfax

**3 Which of the following statements is incorrect? Blepharitis:**
**A** Is exacerbated by lens spoilage
**B** Is a common cause of lens intolerance
**C** Is caused by Staphylococcal colonisation of the lid margins
**D** Is a contraindication to all contact lens wear

**4 Which of the following statements on dry eyes and contact lens wear is incorrect?**
**A** 68 per cent of presbyopes suffer contact lens intolerance due to marginal dry eyes
**B** 50 per cent of soft contact lens wearers suffer marginal dry symptoms
**C** Patients benefit from hydrogel-containing ocular lubricants
**D** Solutions containing benzalkonium chloride preservative are recommended

**5 All the following are ocular lubricants except:**
**A** Systane
**B** Refresh Endura
**C** Restasis
**D** TheraTears

**6 Which one of the following punctual plugs is made from a thermodynamic acrylic polymer?**
**A** Eagle Vision
**B** Oasis Soft
**C** Smart
**D** Herrick

**7 Which of the following drugs is available for use by additional supply optometrists but not by entry-level optometrists?**
**A** Otrivine-Antistin
**B** Lodoxamide
**C** Optrex allergy eye drops
**D** Olopatadine

**8 Which of the following statements on allergic conjunctivitis in contact lens wearers is incorrect?**
**A** Patients may be fitted with daily disposable lenses
**B** Preservative-free solutions should be used
**C** Diclofenac may be used by AS optometrists
**D** Over-the-counter (OTC) oral antihistamines are just as effective as topical agents in the treatment of allergic conjunctivitis

**9 Which of the following is not a management option for GPC?**
**A** Fit daily disposable lenses
**B** Consider lens materials with higher Young's elastic modulus
**C** Consider changing to lenses from different groups eg IV to II
**D** Use mast cell stabilisers

**10 Which of the following statements on the treatment of keratitis is incorrect?**
**A** Chloramphenicol and fusidic acid have no effect on *Pseudomonas aeruginosa*
**B** CLPU should always be scraped prior to treatment with ciprofloxacin 0.3 per cent
**C** Ulcers larger then 2.0mm should initially be treated with fortified amino-glycosides and fluoroquinolone antibiotics
**D** In contact lens wearers presenting with any atypical keratitis, and particularly if associated with severe pain and chemosis, *Acanthamoeba* keratitis should always be considered

**11 Which of the following statements is incorrect?**
**A** Silicone hydrogels are rarely implicated in microbial keratitis
**B** RGP lens wear carries the least risk associated with microbial keratitis
**C** CLARE is sometimes seen with immobile daily wear lenses
**D** Soft lens CLPUs can occur at any position in the peripheral cornea

**12 Which of the following statements is incorrect?**
**A** Infiltrates may be caused by an inflammatory reaction to toxins released by Gram-positive bacteria
**B** Infiltrates with irregular edges are commonly associated with CLPU
**C** CLARE-associated infiltrates are typically sub-epithelial to anterior stromal infiltrates in the periphery of the cornea
**D** In a contact lens wearer with asymptomatic infiltrative keratitis infiltrates may take a few weeks to clear

Successful participation counts as two credits towards the GOC CET scheme and one towards the Association of Optometrists Ireland's scheme. **Deadline for response is October 18**