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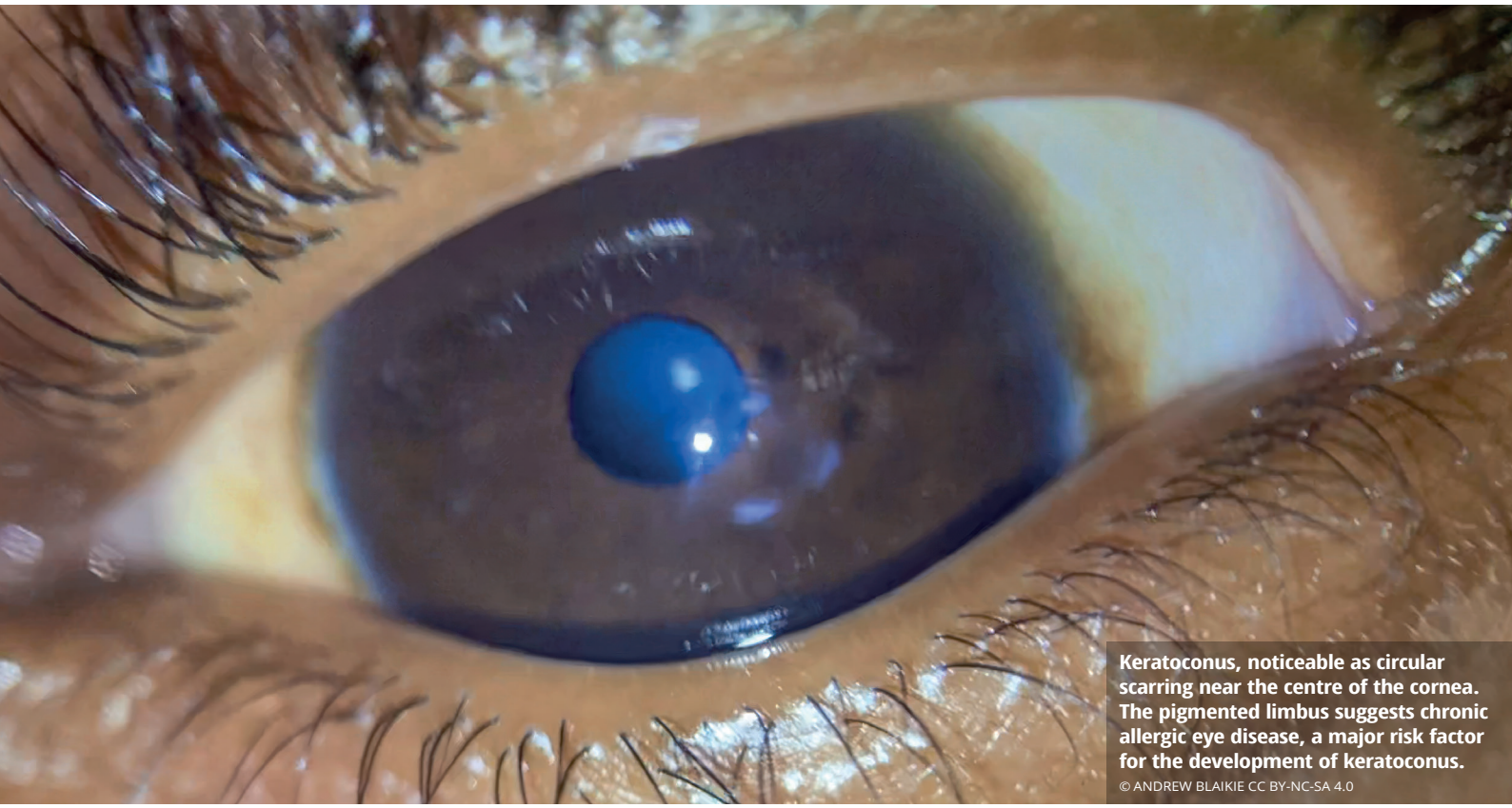

Keratoconus, noticeable as circular scarring near the centre of the cornea. The pigmented limbus suggests chronic allergic eye disease, a major risk factor for the development of keratoconus.

Common conditions affecting the ocular surface

Improving our understanding and management of ocular surface conditions, and educating patients about what they can do, will enhance patients' quality of life and protect their sight.

Victor Hu
International Centre for Eye Health, London School of Hygiene and Tropical Medicine UK.

The ocular surface consists of the ocular structures which are directly in contact with the outside world, including the cornea, conjunctiva, eyelids and eyelashes, the tear film, and any associated glands. A healthy ocular surface is vital for both comfort and clear vision.

Many patients with conditions affecting the ocular surface – such as dry eye and allergic conjunctivitis – do not experience significant sight loss. However, they often make up the greatest number of patients seen by eye care services. Even in relatively mild forms, these conditions can cause significant discomfort and affect patients' quality of life. If left untreated, they can cause changes to the corneal surface that may permanently impair vision in one or both eyes.

Dry eye disease is estimated to affect between 5% and 50% of people, often resulting in constant, debilitating irritation for those affected.[1] Children and some adults commonly experience ocular allergies, which can cause intense itching and inflammation. These symptoms can be distressing, leading to social withdrawal and children missing school. Ocular allergy and eye rubbing are also strongly associated with keratoconus, a condition in which progressive thinning of the cornea occurs, potentially resulting in loss of vision.

This issue offers practical, clear guidance on managing dry eye, allergic eye disease, and keratoconus, including recent advances such as corneal cross-linking.

Image courtesy of Andrew Blaikie, University of St Andrews.

Reference

1 Stapleton F, Alves M, Bunya VY, Jalbert I, Lekhanont K, Malet F, et al. TFOS DEWS II Epidemiology Report. Ocul Surf. 2017;15(3):334-65.

About this issue

Although many patients with conditions affecting the ocular surface – such as dry eye and allergic conjunctivitis – do not have significant sight loss, these conditions can cause great discomfort and affect patients' quality of life, even in relatively mild forms. If left untreated, they can cause changes to the corneal surface, including keratoconus, that may permanently impair vision in one or both eyes.

Contents

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Managing ocular allergy

Ocular allergy is debilitating and potentially blinding, and it most commonly affects children and young adults. Successful step-wise treatment can, however, be life-changing.

Ocular allergy is more common in hot, dry and dusty regions. It can particularly affect children and young people, causing social withdrawal and loss of schooling. Eye rubbing due to allergy can lead to keratoconus, so controlling the condition is important to prevent long term complications such as vision loss. In this article, we suggest a pragmatic management approach based on the severity of the condition. For more detailed information on the classification and management of ocular allergy, see the previous *Community Eye Health Journal* articles in the panel.[1,2]

Useful articles from the *Community Eye Health Journal*

Bore M. Managing ocular allergy in resource-poor settings. *Community Eye Health*. 2016;29(95):47-49. **https://bit.ly/3WIe43N**

Rathi VM, Murthy SI. Allergic conjunctivitis. *Community Eye Health*. 2017;30(99):S7-S10. **https://bit.ly/4ciwiP7**

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INTERNATIONAL CENTRE FOR EYE HEALTH

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Features and types of ocular allergy

Ocular allergy is a broad term that encompasses different types of allergic inflammation of the conjunctiva and/or cornea in response to allergens and irritants in the patient's environment.

It is usually **bilateral**, with symptoms and signs varying according to the patient and the type of ocular allergy.

The distinctive feature of ocular allergy is **intense itching** of the eyes. Patients may also experience burning sensation, sensitivity to light, and irritation.

More mild forms of ocular allergy affect the conjunctiva only. Patients with mild ocular allergy usually have one of the following two conditions:

- **Seasonal allergic conjunctivitis.** This usually occurs during the summer months, when pollen and other allergens are released.
- **Perennial allergic conjunctivitis.** This occurs throughout the year and may be a response to house dust mites, animal dander, or feathers.

Signs of mild ocular allergy include:

- Watering
- Red eyes (hyperaemia, see Figure 1)
- Mild blister-like swelling of the conjunctiva (chemosis, Figure 2)
- Small papillae inside the eyelids (less than 0.3mm in diameter, see Figure 3)

Ocular allergy is considered **more severe** when there is corneal involvement. This can be the result of seasonal or perennial allergic conjunctivitis that has not been managed well, or if the patient has one of the following conditions:

- **Vernal keratoconjunctivitis.** This typically affects young males and tends to be worse in the spring/summer months.
- **Atopic keratoconjunctivitis.** This is more common in adults and is associated with eczema on the eyelid skin.

Signs of mild ocular allergy

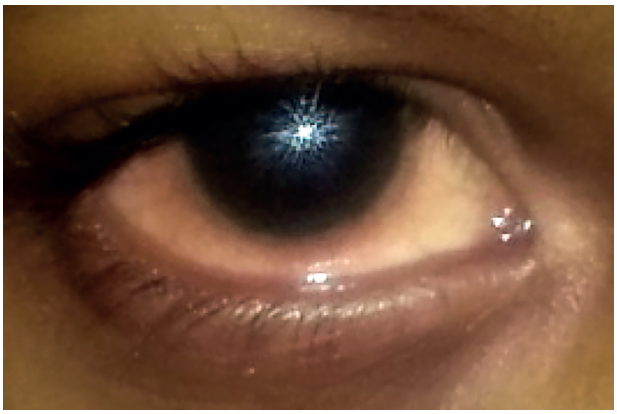

Figure 1 Red eyes (hyperaemia and limbal pigmentation)

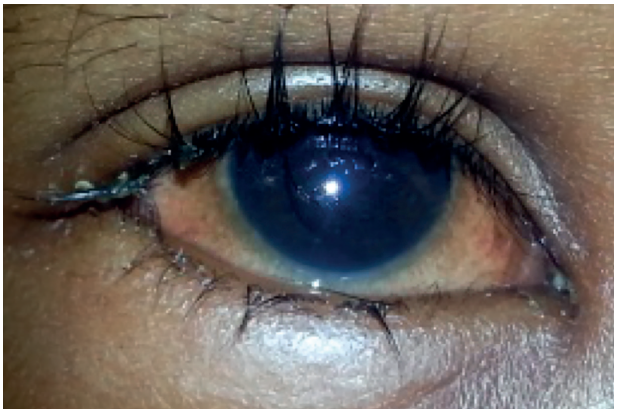

Figure 2 Mild, blister-like swelling of the conjunctiva (chemosis)

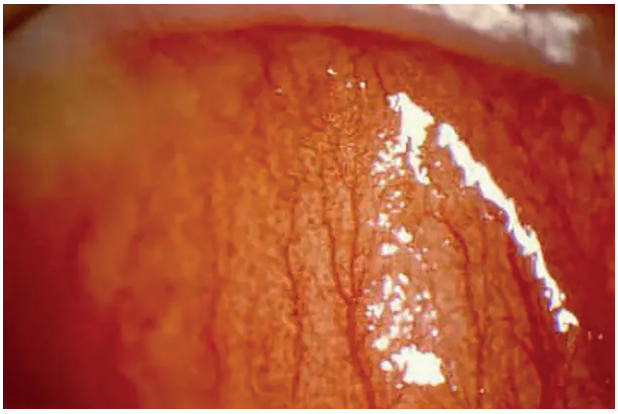

Figure 3 Slit lamp image showing small papillae in the upper eyelid. This patient has perennial allergic conjunctivitis.

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Signs of more severe ocular allergy include:

- **Large papillae** (cobblestones) inside the eyelids (Figure 4); anything bigger than 0.3 mm is considered severe.
- **Limbal thickening** or inflammation, including small nodules known as Horner-Trantas dots (Figure 5).
- **Shield ulcer**. Papillae inside the eyelids can damage the surface of the cornea, eventually leading to the formation of a shield ulcer (Figure 6).

Note: Any type of ocular allergy can result in sight loss if not managed well. Patients can develop keratoconus, or exacerbate it, if they excessively rub their eyes; advise all patients with ocular allergy to avoid eye rubbing and monitor them for signs of keratoconus (see articles in this issue). It is important to refer patients with more severe forms of ocular allergy, as well as patients with mild forms that do not respond to treatment, so they can be managed by an ophthalmologist.

Managing patients with mild ocular allergy

Mild ocular allergies can often be managed in the community or at primary care level, by following steps 1–4 as set out below. However, if there is no improvement with treatment, any suspicion of corneal involvement, or any other signs of severe ocular allergy, refer your patient to a specialist eye care unit.

Step1. Supportive therapy and patient education

Educating patients and their caregivers is a vital component of the management of ocular allergy.

Avoid allergens, both confirmed and suspected. This may be obvious, such as avoiding certain animals, including cats, or certain grasses. More frequent washing of pillowcases or bedding may also help. Testing for specific allergens can also be done where available (either by skin prick testing or blood testing), usually in an allergy clinic.

Avoid eye rubbing. This is critical, as rubbing sets off a vicious cycle of inflammation and further itching. It can also cause sight-threatening complications such as corneal infections and keratoconus. Cold compresses can help to relieve itching. These may be commercially available and are stored in the fridge or can be made by putting a clean face cloth into cold water, wringing out the excess water, and placing the cold compress on the closed eyes for 5–10 minutes. Alternatively, the face cloth can be wrapped around ice placed in a clean plastic bag.

Use artificial tears. This can help flush out allergens and inflammatory mediators and help soothe the eyes. Preservative-free formulations should be used. If patients are receiving multiple drops for severe allergy treatment (see step 3) artificial tears may be omitted to simplify treatment and to reduce costs.

Never self-medicate using over-the-counter steroid drops. If used inappropriately, or if their use is not monitored, these can have serious complications including corneal infections, glaucoma, and cataract.

Step 2. Oral antihistamines

These are often available over the counter and can be helpful, especially in more mild disease such as seasonal allergic conjunctivitis and/or when there is associated allergic disease, such as eczema or rhinitis.

Signs of more severe ocular allergy

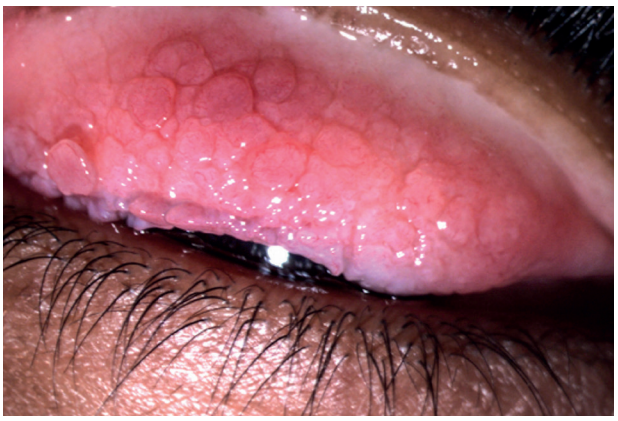

Figure 4 Large papillae, with a typical 'cobble-stone' appearance, in a patient with vernal keratoconjunctivitis.

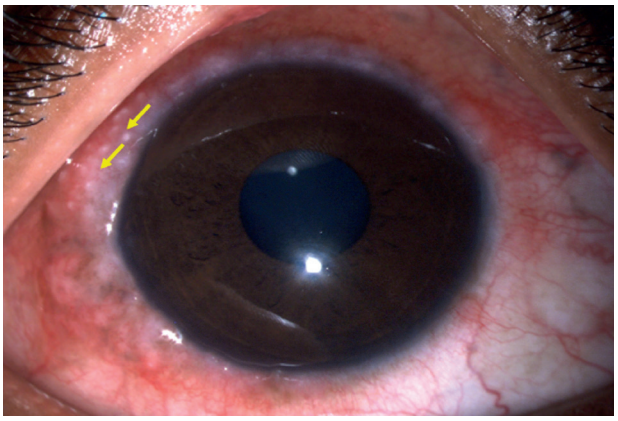

Figure 5 Limbal thickening due to inflammation. The small inflammatory nodules are known as Horner-Trantas dots.

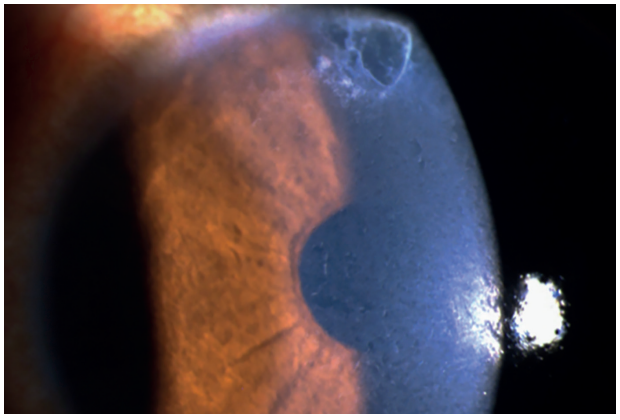

Figure 6 Shield ulcer in the upper part of the cornea.

They generally have few side effects and can be used long term, although some antihistamines are known to cause drowsiness and should be used with care.

Step 3. Topical anti-allergy medications

Anti-allergy eye drops include antihistamines and mast cell stabilisers, and are also available as a combined formulation known as dual-acting agents.

Antihistamines have a very rapid onset of action; however, the duration of effect is very short. Hence, these medications are rarely used in isolation. Conversely, **mast cell stabilisers** can take 2–6 weeks to start working, yet they offer sustained benefits over time due to their membrane-stabilising effects.[1,2] **Dual-acting agents** combine the properties of both agents, providing rapid onset and prolonged duration, and are generally preferred when available. Several molecules exist under each category and various meta-analyses have shown that the clinical efficacy of each drug is comparable to the other.[3] These drops are generally safe, well tolerated, and can be used in the long term. As with other eye drops, preservative-free formulations are preferred.

Managing patients with severe ocular allergy

When to refer

Refer patients for specialist care if:

1 There is no improvement after the treatment recommended in steps 1–3
2 There is any corneal involvement
3 There are signs of more severe disease, such as large (cobblestone) papillae or persistent limbal inflammation.

These patients are likely to need further treatment (see steps 4–8).

Managing ocular allergy in the eye department

In a specialist care setting, continue providing the treatment detailed in steps 1–3. Beginning at Step 4, work through the steps until the disease process is controlled. Treatment can then be cautiously stepped down.

Note: Adherence with treatment is particularly important for patients who have more severe forms of ocular allergy. Explain to patients and their caregivers that their condition needs long-term treatment, and that they should continue their treatment even if their eyes are feeling better. See our previous issue on 'Medicines for eye health' for useful guidance on adherence (**https://www.cehjournal.org/medicines/**).

Step 4. Topical corticosteroids

Steroid eye drops are rapid and effective in treating ocular allergy. However, due to their side effects, their use needs to be limited.

Steroids are used frequently at the start of treatment (e.g., 4–8 times a day); they are then rapidly tapered (e.g., over 4–6 weeks) to bring the disease under control.

Some steroid drops appear to have less severe side-effects (e.g., on intraocular pressure) and are generally preferred.These include loteprednol, hydrocortisone, and fluorometholone drops. Within this group, loteprednol is recommended for eyes requiring repeated doses. This is because it is only active on the corneal surface, where it is needed. Because it is unable to enter the eye, complications such as cataract and glaucoma are less common.[6]

Step 5. Topical calcineurin inhibitors

Cyclosporine and tacrolimus can be used as topical immunosuppressants in the eye and are useful as a long-term therapy. Because it takes a few months for them to take full effect, steroid drops are often started at the same time, as a short-term measure. Several studies have shown the efficacy of cyclosporine and tacrolimus in reducing the signs and symptoms of ocular allergy. Limited literature exists comparing these medications directly, but available studies have demonstrated no discernible difference in outcomes between them.[4,5] Cyclosporin eye drops have been licensed in Europe and the USA for the treatment of allergic eye disease. Tacrolimus ointment, formulated for ocular use, is also available several countries; its once-nightly dosage is easier to use and can improve compliance among paediatric patients.

Step 6. Supratarsal steroid injection

This surgical intervention is indicated in patients with severe papillary conjunctivitis with corneal changes, such as a shield ulcer. A long-acting steroid such as triamcinolone (0.5ml of a 40mg/ml preparation) is generally preferred, although a shorter acting steroid such as dexamethasone (0.5ml of a 4mg/ml preparation) can be used. The upper lid is everted and a cotton bud soaked in local anaesthetic used to numb the area around the upper tarsal border. The cotton bud can be used to lift the everted lid away from the globe. The steroid is injected with a 30 gauge (or similar) needle, just above the upper tarsal border. Children may require general anaesthesia, but with careful counselling, and establishing a good rapport, even young children can tolerate this procedure. The intraocular pressure should be monitored in case of a pressure rise, but this does not seem to be common. Although supratarsal steroids can effectively control the allergy, the effect is usually temporary and relapse of the disease may be noted after 4–6 months.[7] Close monitoring is needed, and systemic immunosuppression may offer a better alternative.

Step 7. Systemic immunosuppression

Where the above measures have been tried and the inflammation is not controlled, then systemic treatment to reduce the immune response may be required (where available), especially if there is corneal involvement and a risk of vision loss. This would normally involve a multidisciplinary team approach, in partnership with other specialties who are experienced with immunosuppression, such as immunologists or rheumatologists. A careful systemic evaluation is needed, as well as frequent monitoring after treatment has been started. There is little evidence or widely accepted guidelines on the choice of agent or duration of therapy. However, cyclosporine is commonly used, and discontinuation is considered if no relapses occur after 6–12 months.

Step 8. Surgical intervention

A shield ulcer may be seen in severe ocular allergy, typically vernal keratoconjunctivitis (Figure 3). This usually develops on the superior cornea and an inflammatory infiltrate can develop in the base of the ulcer, requiring surgical debridement. The severe limbal variant of vernal keratoconjuntivitis can result in limbal stem cell deficiency. Patients with limbal stem cell deficiency with sparing of the visual axis are managed with systemic immunosuppression and scleral contact lenses.[8,9] Limbal stem cell transplantation is required in patients with severe limbal stem cell deficiency involving the visual access.[8,9]

Newer therapy modalities

Numerous emerging avenues of treatment are under investigation for managing ocular allergies. One of the most promising avenues is **allergen-based therapy**, which involves identifying the specific allergen to which the patient is sensitive and implementing tailored desensitisation therapy.[10] **Conjunctival immunotherapy**, which targets the condition directly at the affected site,[11] may help prevent systemic complications associated with these treatment modalities. The use of **anti-IgE monoclonal antibodies** and **interleukin inhibitors** may provide additional steroid-sparing alternatives.[1,12] Future studies exploring the role of these novel therapeutic options will hopefully help to expand the armamentarium of ocular allergy management.

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Keratoconus: an introduction

Knowing how to identify and refer people with keratoconus is an important first step in reducing the risk of visual impairment from this progressive condition.

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Keratoconus is a condition characterised by progressive thinning and weakening of the cornea, leading to a cone-shaped appearance that distorts vision, usually in both eyes. It typically develops in young people around the age of puberty and is more common in boys and men. Keratoconus is very rare in some countries, and common in others. In Iran, for example, more than 3 out of every hundred people have the condition; in Russia, only 2 out of every million people are known to be affected.

Risk factors

Although the exact cause of keratoconus is not known, there are multiple risk factors associated with it, including chronic eye inflammation, eye rubbing, a family history of keratoconus, and other genetic factors such as Down syndrome, connective tissue disorders, and Leber congenital amaurosis.

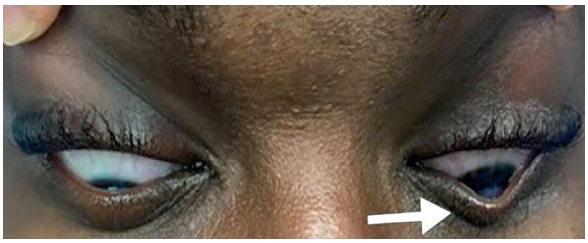
Presentation: symptoms and signs

The first signs of keratoconus are likely to be a slight blurring of vision, often in a person who is **atopic** (prone to allergies and eczema) and may excessively rub their eyes (see panel).

Other symptoms include blurred or distorted vision, often needing new spectacles (due to irregular astigmatism), difficulty seeing at night, sensitivity to light, and glare (seeing haloes around lights).

> **"Although the exact cause of keratoconus is not known, there are multiple risk factors associated with it."**

Figure 1 The conical shape of the cornea, outlined by the lower eyelid, is known as Munson's sign – a sign of severe keratoconus.



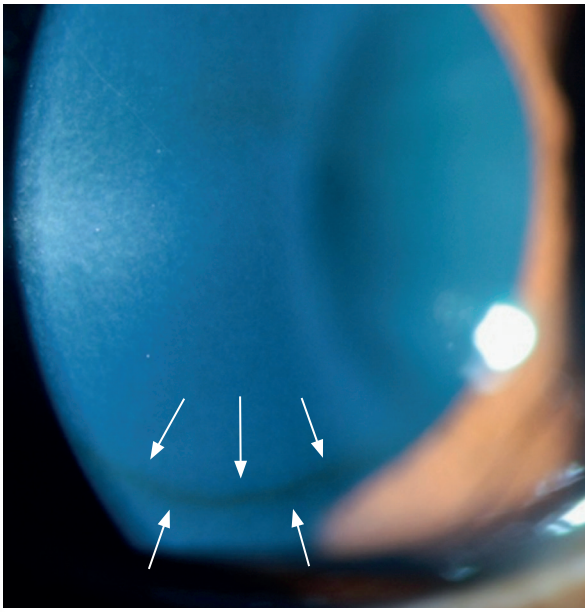
A visit to an **optician** or **optometrist** may reveal early changes that can be managed with glasses or contact lenses.

In addition to changes in refraction, more severe keratoconus may be visible when the patient looks down and the conical shape of the cornea is outlined by the lower eyelid, as shown in Figure 1. This is known as Munson's sign. These patients need specialist treatment.

If you have a slit lamp

In patients with moderate to severe keratoconus, typical slit lamp signs include corneal steepening and thinning, iron deposits in the cornea (Fleischer's ring, Figure 2), and whitish lines in the deep corneal stroma and Descemet's membrane (Vogt's striae, Figure 3). As the condition progresses, splits in Descemet's membrane can lead to corneal oedema and a whitish spot at the apex of the cone (hydrops) with subsequent poor vision and pain.

Figure 2 Slit lamp image showing an eye with Fleischer's ring: a curved, light-brown line caused by iron deposits in the cornea.



Atopy and eye rubbing

People with atopy, especially children and young people, are at greater risk of keratoconus. They may have **eczema** (**atopic dermatitis**), which can cause painful itching of the eyelids and surrounding skin. In people with eczema, the itching is worse when their allergies and eczema are not well managed, particularly when they are stressed, hot or exposed to an allergen such as nuts or pollen. They may also suffer from **eye allergies** (see page 2), which cause chronic eye inflammation and itching of the eyes.

People often rub their eyes in response to itching, as it can provide temporary relief. However, this usually makes the itching worse – leading to even more vigorous eye rubbing.

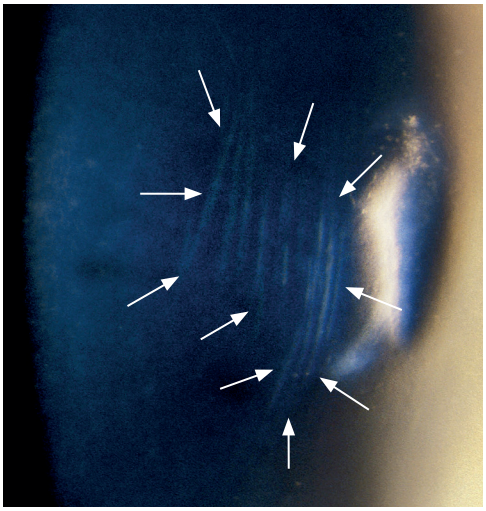
Children are more likely to rub their eyes, as they may not understand the risks of eye rubbing or may not be able to stop or control themselves.

What can patients and their caregivers do?

- To **reduce the severity of the itching over time**, seek treatment for the allergies and eczema, and adhere to any prescribed medication.
- For i**mmediate relief**, apply a **cool compress** to the eyes to relieve itching and inflammation. To make a cool compress, soak a clean cloth in water, wring it out, and place it over closed eyes. Repeat as needed.

Top tip for physicians: If a patient with atopy complains of blurred vision, ask whether they rub their eyes. If they say yes, this could indicate the onset of keratoconus. Refer them for an eye examination.

Figure 3 Slit lamp image showing Vogt's striaie: faint whitish lines in the deep corneal stroma and Descemet's membrane (see arrows).



Keratoconus is often progressive, but the condition can stabilise for many people when they reach the age of 30 or above.

What to do if you suspect your patient has keratoconus

If you think a patient may have keratoconus, refer them to a hospital with an eye department so their condition can be treated. Explain to the patient that rubbing their eyes will make the problem worse – and encourage them to stop.

If they have an eye allergy or eczema affecting the skin around the eyes (see panel), getting the right treatment for these conditions will help to reduce the itchy sensations that they are trying to relieve by rubbing their eyes.

Diagnosis and management in the eye department

In the eye department, a diagnosis of keratoconus is made by mapping the cornea to reveal areas of irregular corneal curvature and corneal thinning.

At first, keratoconus is often managed by prescribing spectacles or rigid (gas permeable) contact lenses to improve vision. When these are no longer adequate, corneal transplant surgery may be considered.

However, an approach known as corneal cross-linking, when available, is very effective at halting progression of the condition. It involves the use of UV light after the corneal epithelium has been removed and riboflavin drops applied. This causes the corneal surface to stiffen, slowing down further thinning of the cornea and worsening of the keratoconus.

For more on diagnosis and treatment, including cross-linking, please see the next article in this issue.

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Keratoconus: diagnosis and management

A new treatment for keratoconus – corneal cross-linking – can slow or halt progression; however, early and accurate diagnosis remains essential.

A definitive diagnosis of keratoconus is made using corneal topography and/or tomography.[1] In settings where sophisticated imaging systems are not available, a simple Placido disk (or keratoscope) can be used. This reveals the shape of the front surface of the cornea (the topography) as a series of concentric rings (mires). In keratoconus, an irregular shape of the mires mirrors the irregular corneal curvature. An area of increased steepening is indicated where the reflected mires are close to each other (Figure 1). Placido-based imaging systems can provide detailed topographic maps, allowing you to assess corneal irregularities.

"In settings where sophisticated imaging systems are not available, a simple Placido disk (or keratoscope) can be used."

Since these systems are based on reflection-based principles of topography, the posterior corneal surface is not directly mapped. However, it can be derived using mathematical calculations after carrying out ultrasound pachymetry to map corneal thickness. Two types of systems (available since the early 2000s) that can directly map the anterior and posterior surface of the cornea are Scheimpflug systems (e.g. Pentacam or Galilei) and scanning slit systems (e.g. Orbscan). These are generally more expensive.

Patients with keratoconus typically have asymmetric corneal steepening, coinciding with thinning and elevation in the same area (Figure 2).

Figure 1 Image of Placido rings in keratoconus. The mires are closer to each other inferiorly, indicating an area where the cornea is steeper.

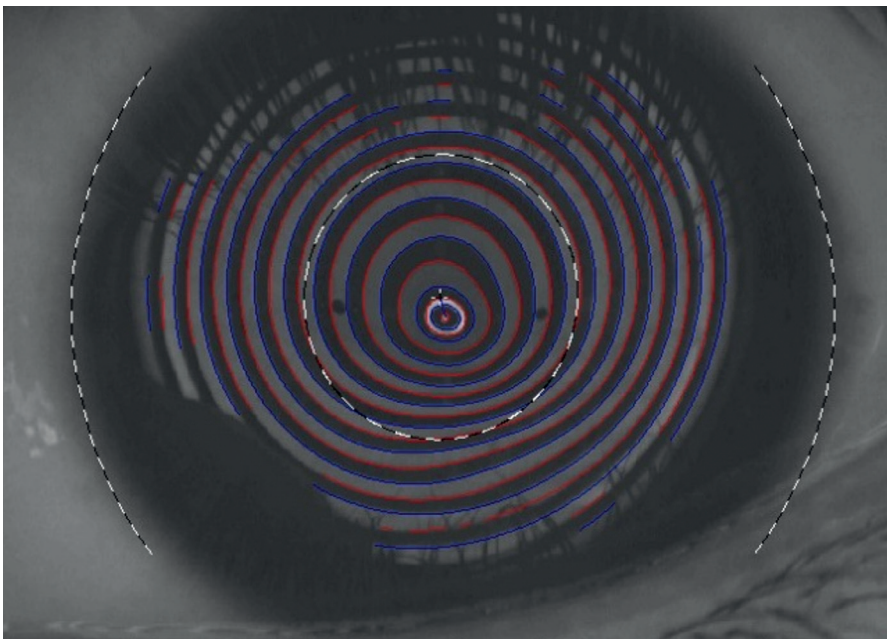
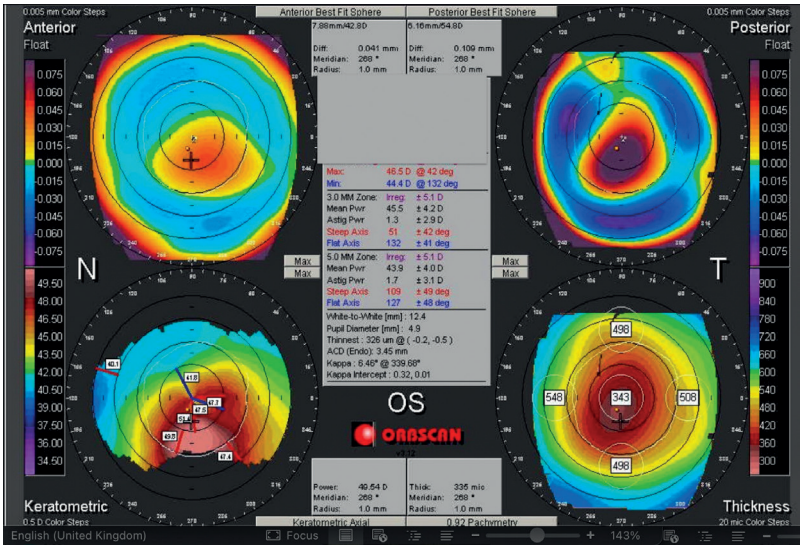


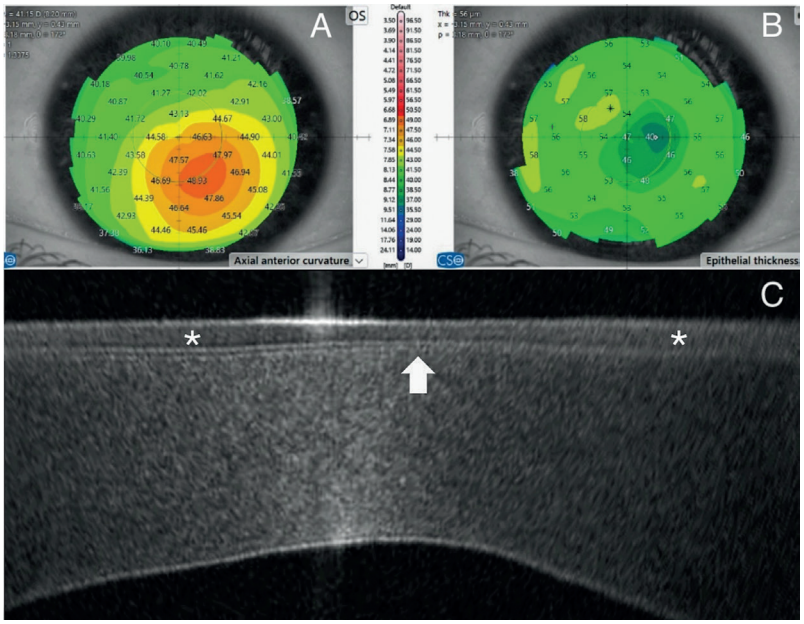
Figure 2 A quad map of a patient with keratoconus, produced using the Orbscan imaging system. Note the typical inferior steepening with abnormal elevation in the anterior and posterior elevation maps, as well as thinning in the same area.



In patients with advanced keratoconus, corneal optical coherence tomography (OCT) can show thinning. A relatively new device (MS-39, CSO Italy) combines Placido disk corneal topography with high resolution OCT-based anterior segment tomography. This can segment corneal thickness into epithelium and stroma (Figure 3).

Early keratoconus is often characterised by epithelial thinning over the tip of the cone, with corresponding thickening around the base of the cone as the epithelium tries to mask the irregular stroma. In these eyes, just looking at the front surface (topography), may miss early ectatic changes underneath. Cross-sectional corneal OCT is also useful to assess the depth of the scar in patients with more advanced keratoconus with stromal scarring, who are due to undergo keratoplasty. It is also useful in patients with hydrops, to assess the tear in Descemet's membrane.

Figure 3 Combined Placido disk and OCT images of early keratoconus. **A.** Axial anterior curvature showing early ectasia. **B.** Epithelial thickness showing thinning over the corresponding area. **C.** Cross-sectional OCT image highlighting changes in epithelial thickness over the tip of the cone (white arrow) and at the base of the cone (asterisks).



Treatment

Historically, options to improve vision in keratoconus were limited to spectacles or rigid (gas permeable) contact lenses, corneal ring segment implants (since the 1990s), and corneal transplantation (penetrating or deep anterior lamellar keratoplasty) in patients with advanced keratoconus.

Wollensak first described corneal cross-linking (CXL) in 2003 as an approach to halt progression in cases of keratoconus and prevent worsening. Corneal cross-linking involves shining ultraviolet (UV) light at the cornea after the epithelium has been removed and riboflavin drops have been applied. This induces biochemical changes in the corneal stromal collagen, increasing the biomechanical stiffness, and halting further thinning and ectasia progression. Patients are typically monitored every 6–12 months with serial corneal scans to detect disease progression.

The standard approach is to offer corneal cross-linking to patients who are progressing. Corneal changes should be greater than the limits of repeatability for your scanning device (i.e., above machine noise). To improve the interpretation of scans, it is recommended to take three consecutive scans per eye per visit and ensure that contact lenses are removed for a consistent period prior to scanning (e.g., 1 week for soft contact lenses, 2 weeks for rigid gas permeable contact lenses). Unfortunately, there is no consensus on what constitutes a significant change, but an increase in keratometry values of more than one dioptre, or a reduction in corneal thickness of greater than 15 microns, might be considered significant.

Some patients are at a higher risk of progression, with young age considered the most important variable. In such high-risk patients, clinicians may opt to monitor more frequently (e.g. every 3 months) or consider offering corneal cross-linking at the point of diagnosis (i.e. without documented progression). The cornea naturally stiffens with age, and progression is unusual after people reach their mid-30s.

In patients with atopy, it is important to give them a short course of pre-operative steroid drops to make sure the ocular surface is quiet before corneal cross-linking is performed. Safety during pregnancy has not been established, but the hormonal changes during pregnancy can sometimes be associated with disease progression. Clinicians are advised to discuss these unknown risks with the patient, weighing them up against the potential benefits of preventing further deterioration in vision.

Protocols

The initial protocol described, known as the Dresden protocol, involves epithelial debridement in the central 8–9 mm of the cornea and soaking it with riboflavin drops every 2 minutes for 30 minutes, followed by ultraviolet-A (UVA) 370 nm radiation exposure at 3 mW/cm^2 for 30 minutes to achieve a surface dose of 5.4 J/cm^2.

There have been several protocols since then, including accelerated and pulsed protocols.

The protocol of administering 10 minutes of ultraviolet light, with an irradiance of 9mW/cm^2, is widely accepted

and is used, for example, at LV Prasad Eye Institute in India.[2] The protocol used at Moorfields Eye Hospital in London, UK is 30 mW/cm^2 for 4 minutes, with a 1.5-second on/off cycle (total energy 7.2 J/cm^2).[3]

Examples of corneal cross-linking devices include standard floor-mounted devices such as KXL (Glaukos Corp) and PXL (Peschke GmbH), as well as devices mounted on a slit lamp, such as the C-EYE device (EMAGine AG).

Choice of riboflavin

The choice of riboflavin depends on the corneal thickness. All the above protocols are described for corneas with a minimum stromal thickness of 400 microns (which would be approximately 450 microns on tomography when the epithelium has not been removed). Isotonic riboflavin, made with dextran, is used in these patients.

Stromal thickness and risk of endothelial damage

In patients with advanced keratoconus, where the stromal thickness is less than 400 microns, there is a potential risk of damage to the corneal endothelium. A number of approaches can be used in this situation, including using hypotonic riboflavin with physiological balanced salt solution, instead of dextran, which helps to increase the stromal thickness.[2] Before starting the UV irradiation, use an intraoperative ultrasound pachymeter, if available, to confirm the stromal thickness to be more than 400 microns. Other eye units reduce the amount of energy being used for thinner corneas.

The risk of endothelial damage from corneal cross-linking appears to be low, and in practice many units would accept a corneal thickness of 400 microns or over on tomography (i.e. with the epithelium on, so that the thickness will be 350-370 microns with the epithelium off) for their normal cross-linking protocol. Units setting up their own cross-linking service are advised to do their own research and investigation to help decide what protocol to adopt.

Postoperative care and pain management

Patients will experience pain in the initial 24-48 hours following the procedure. The pain can be severe, especially in younger in patients. Oral pain relief should be given, and some units give patients topical anaesthetic drops (e.g. 3 single-dose units) to use within the first 48 hours, although there is a risk of delayed healing if the eye is anaesthetised excessively. Although topical non-steroidal anti-inflammatory drugs (NSAIDs) have been described for pain relief, their use is not generally advised as there is risk of sterile infiltrates and stromal melts. Antibiotic drops or ointment are given for the first few days to prevent infection.

Postoperative monitoring is advised within the first week to monitor for complications. Early postoperative complications include poor epithelial healing, infective or sterile infiltrates, and central toxic keratopathy. Patients with a poor ocular surface from atopic disease are at particular risk of delayed epithelial healing. Delayed complications include haze and scarring. Spectacle prescription or contact lens trial may be given after 6 weeks of the procedure and these are likely to be needed for visual rehabilitation.

> **"Like many conditions, the focus has shifted from treating the disease to preventing and diagnosing it at an early stage."**

In patients with symptoms of poor visual quality due to irregular astigmatism and adequate corneal thickness, photorefractive keratectomy (PRK) can be used as an add-on procedure to regularise the cornea and improve visual quality. Epithelial removal using phototherapeutic keratectomy (PTK) has also been described.

Summary

It has become apparent that keratoconus is more prevalent than initially believed. Like many conditions, the focus has shifted from treating the disease to preventing and diagnosing it at an early stage. Corneal cross-linking has proven to be transformative in the management of progressive keratoconus, and it has led to a reduction in the need for corneal transplant surgery where it is being used.

Step-by-step guide for performing corneal cross-linking

A clean room is required for the procedure; it is not necessary to perform corneal cross-linking in an operating room with air filtration.

Corneal cross-linking can be performed by a single staff member – traditionally by ophthalmologists, but in a number of eye clinics this now undertaken by trained nurses.

Corneal cross-linking devices are generally floor mounted, such as the KXL (Glaukos Corp.) and PXL (Peschke GmbH) or – less commonly – mounted on a slit lamp, such as the C-EYE device (EMAGine AG).

1. Select the preferred protocol. The **accelerated protocol** of 9mW/cm^2 ultraviolet light for 10 minutes is widely used. (The total treatment time is 30 minutes: 5 minutes to set up and remove epithelium, 15 minutes for the riboflavin application, and 10 minutes of exposure to ultraviolet light.)
2. Instil topical anaesthetic drops into the eye(s) to be treated.
3. Debride the central 8-9 mm of corneal epithelium using a hockey knife or other blunt instrument. This is usually done with the patient lying down on a couch where the rest of the procedure will be performed, but it can be done using the slit lamp microscope. Epithelial debridement can be aided with applying 20% ethyl alcohol for 30 seconds in a corneal well, although this is not mandatory.
4. Soak the cornea with riboflavin for 10 to 20 minutes, applying drops every 1 to 2 minutes. In patients with thin corneas, where hypotonic riboflavin is being used, the stromal thickness can be checked according to the agreed protocol using a pachymeter.
5. Apply ultraviolet light of 370 nm using a cross-linking machine from an approved manufacturer. The light should be applied to the central part of the cornea, avoiding the limbus and potential damage to the limbal stem cells. Apply riboflavin drops every 2 to 5 minutes during irradiation.
6. At the end of the procedure, rinse the eye using sterile saline. A bandage contact lens (BCL) can be placed to improve comfort, but may increase the risk of sterile infiltrates forming. Alternatively, the eye may be padded along with antibiotic ointment.

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Dry eye disease: an introduction

Dry eye is uncomfortable and can impair sight, reducing quality of life. Early recognition, advice, and treatment can improve symptoms and prevent worsening of the condition.

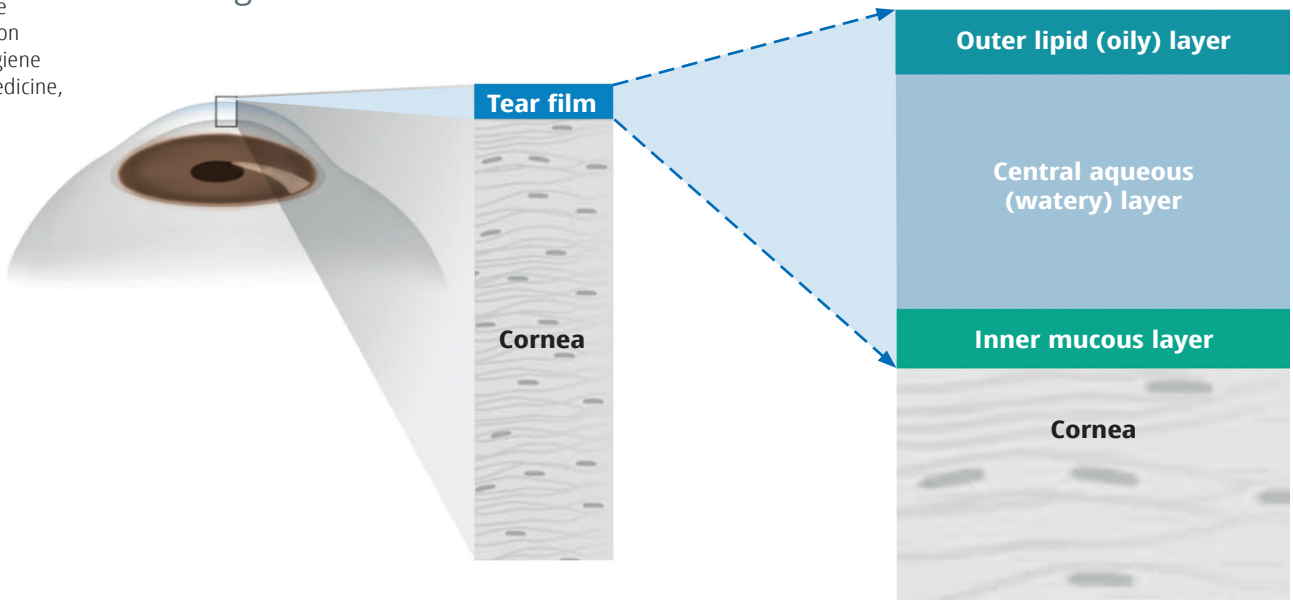


Figure 1 The position and composition of the tear film

The tear film protects, nourishes, and lubricates the eyes, keeping them healthy. It is made of three layers, all of which are important for the eye to function well (Figure 1):

- **The central aqueous (watery) layer.** The bulk of the tear film is made up of watery tears that are formed in the lacrimal glands, are spread over the ocular surface when blinking, and then drain away through ducts on the inner edge of the eyelids and out into the nose, in a continuous cycle.
- **The inner mucous layer.** This is a sticky layer which connects the watery layer of the tear film to the cornea, while allowing it to move freely across the ocular surface, reducing friction and preventing damage when blinking. The mucous layer is produced by cells in the ocular surface.
- **The outer lipid (oily) layer.** The oily outer layer seals the tear film and keeps it stable by reducing evaporation. This layer is also responsible for maintaining a smooth optical surface that allows light to refract through the cornea without distortion. This layer is produced by the meibomian glands in the eyelids.

Without a healthy tear film, eyes become dry, causing discomfort and blurred vision. The tear film can be affected for many reasons.

- **Ageing.** With age, people produce fewer tears, and the tear film composition changes.
- **Blepharitis.** A condition involving blockage of the meibomian glands. Blockage of the glands leads to inflammation and reduced production of the upper oily lipid layer, which increases evaporation of the tear film.
- **Hormonal changes.** Pregnancy or the menopause can alter tear production.
- **Medical conditions.** Diabetes, rheumatoid arthritis, or Sjögren's syndrome can affect the tear film composition, leading to dryness.
- **Medication.** Antidepressants and anti-anxiety tablets can contribute to dry eye. Some eye drops, such as glaucoma medication, can also cause dry eye – especially eye drops that contain preservatives.
- **Contact lenses.** Prolonged wear can worsen dry eye.
- **Environmental exposure.** Air conditioning, smoke, or pollutants can aggravate dry eye disease.
- **Digital screens.** Prolonged use can contribute to dry eye symptoms. This is because people tend to blink less often when looking at screens.

Dry eyes (eyes without a healthy tear film) can become inflamed and there can be damage to the surface of the cornea. If left untreated, a negative cycle can occur: blinking can result in increased friction between the eyelid and cornea, which can damage the cells that produce the mucous layer, further destabilising the tear film and leading to increased evaporation of tears and inflammation of the ocular surface. Eventually, corneal ulcers may develop and eyesight may be lost.

Symptoms of dry eye

Patients with dry eyes tend to complain of:

- Eye irritation – a gritty sensation or a feeling that their eyes are dry
- Excess mucous secretion – eyes are 'sticky', or the person notices dried mucous on waking
- Burning or stinging sensation
- Foreign body sensation
- Blurred vision
- Light sensitivity

Clinical signs

Some signs of dry eye, such as redness and reduced tear meniscus height, can be seen using magnification and a bright light. A slit lamp is ideal, although it is possible to use the anterior segment loupe of an Arclight or traditional direct ophthalmoscope and a +20 dioptre lens.

The key signs are best seen by instilling fluorescein and examining with either a bright white light or (better yet) a blue light:

1 Look for punctate epithelial erosions (Figure 2), a key sign of dry eye. Figure 3 shows an eye with a healthy appearance; there are no erosions.
2 Observe how long it takes for the tear film to break up after blinking; more than 10 seconds is healthy. Figure 4 shows what it looks like when the tear film breaks up.
3 Estimate the meniscus height: 0.2 mm to 0.3 mm is normal. (see Figure 5); less than 0.2 mm is a sign of dry eye.

Figure 2 Punctate epithelial erosions.

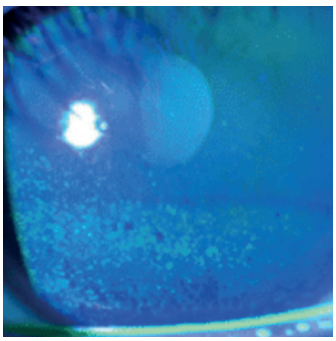


Figure 3 A healthy eye – there are no erosions.

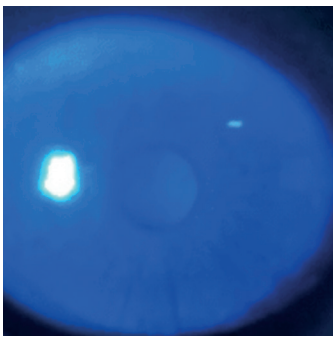


Figure 4 The tear film has started to break up.

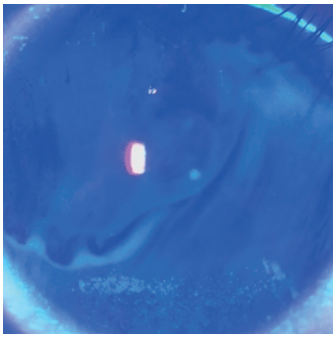
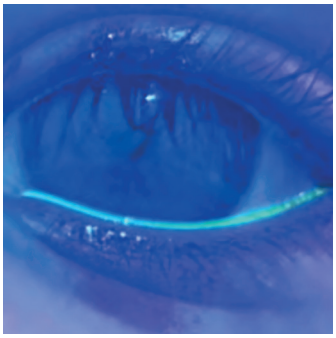


Figure 5 Normal tear meniscus height is 0.2 to 0.3 mm.



What to do

All patients with dry eye will benefit from **artificial tears**; preservative-free drops are less likely to worsen the condition. The frequency of use depends upon the severity of the symptoms.

Patients will also benefit from **advice** about avoiding air conditioning, smoke, or other pollutants, reducing the time spent looking at computer or phone screens, and altering their diet by drinking more water and eating foods with omega-3 fatty acids, (such as oily fish, nuts, and seeds) as well as green, leafy vegetables.

Advice about **eyelid care** (warm compresses, eyelid cleaning and massage) can also be helpful first-line treatment, especially in those with blepharitis (see panel).

Symptoms of dry eye can be due to other conditions. If symptoms and signs persist, despite treatment, and there is pain, redness, photophobia, and blurred vision, **refer the person to an eye clinic**. It is important to exclude other causes and to consider different treatments.

The article that follows covers dry eye disease in more detail, including treatments that will not be available in many eye care centres. However, it is helpful to have a thorough understanding of the condition that affects so many people and, in some cases, can be debilitating and cause blindness.

ADVICE FOR PATIENTS: Lid hygiene to improve meibomian gland function

Daily eyelid hygiene, such as applying warm compresses, followed by eyelid cleaning and massage, can help to improve meibomian gland function, thereby improving symptoms.

1. Warm compress
Dip a clean cloth in warm water (not hot), then wring out most of the water and fold the cloth to create a rectangle of approximately 5 cm by 20 cm. Apply gently to the eyelids while lying down or sitting with the head tilted back (Figure 6). Reheat the pad when it cools, so that heat is applied to the lids for a total of 10 minutes. This can help the oily meibomian gland secretions to flow more easily.

2. Cleaning
Use cooled boiled water and a clean face cloth, cotton wool pad, or cotton bud to clean the eyelid margins. Rubbing along the margin can unblock the opening of the glands.

3. Massage
Massage the lids towards the lid margin (Figure 7). This can help express the oily meibomian gland secretions, improving dry eye when blepharitis is present.

Figure 6 Applying a warm compress to the eyes.

Figure 7 A patient massages their eyelids using a clean fingertip.

This video by the Arclight Project shows how to do this for a patient; patients can also learn to do this for themselves. **tinyurl.com/4a8vs66s**

Managing dry eye disease

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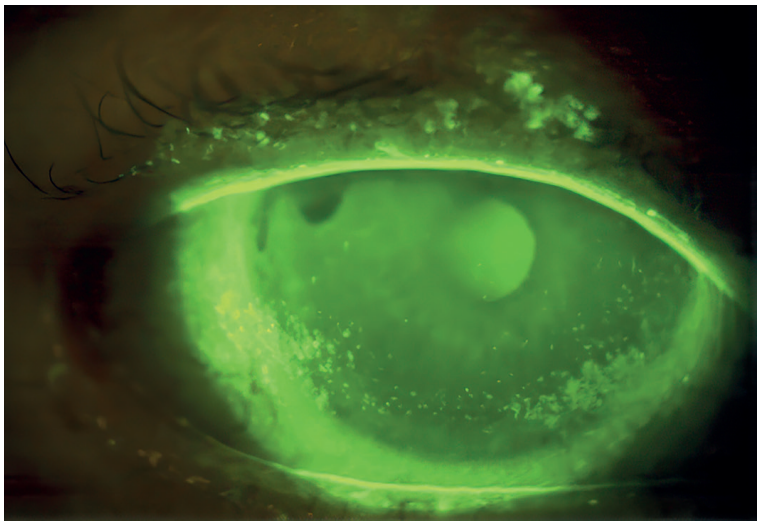
The treatment of dry eye disease aims to interrupt the vicious cycle of damage and inflammation of the ocular surface and restore the tear film.

Dry eye disease is a common, debilitating disorder of the ocular surface and one of the main reasons patients seek ophthalmic care. It affects millions of people worldwide, causing symptoms that directly impact patients' eye health and quality of life.[1–5] This article will concentrate on the management of dry eye disease, including recent developments.



Punctate epithelial erosions characteristic of dry eye. Image taken using blue light and a yellow filter, after instilling fluorescein. UK

Dry eye disease is classified based on the types of physical changes responsible (its pathophysiology). Aqueous-deficient dry eye and evaporative dry eye may overlap in variable combinations and coexist in the same clinical presentation: the mixed dry eye.[3] In all forms, tear hyperosmolarity (when the tears are too concentrated) — whether due to reduced tear secretion, excessive evaporation, external factors, or systemic diseases — acts as a triggering factor for a cascade of events, resulting in ocular surface inflammation and damage. Tear film instability and epithelial damage stimulate and chronically damage corneal nerve endings, resulting in symptoms such as pain, increased blink rate, compensatory increase in reflex tear secretion, limitations in performing daily activities, and – often – depression.[7]

Dry eye disease diagnosis

Dry eye disease can be distinguished from other ocular surface diseases through screening questionnaires and tests. Several diagnostic protocols have been proposed.[8] Scores higher than 6 on the Dry Eye Questionnaire-5 (**tinyurl.com/r2t35sc8**) or higher than 13 on the Ocular Surface Disease Index (**eyecalc.org/osdi/**) may suggest dry eye disease and the need for a more detailed evaluation. The presence of reduced tear film breakup time, elevated or large differences in tear osmolarity (concentration) between eyes, or superficial ocular staining of the cornea, conjunctiva, or eyelid margin (for example, with fluorescein) are all signs of ocular surface instability that confirm the diagnosis.

Definition of dry eye

The Dry Eye WorkShop II (DEWS II) of the Tear Film and Ocular Surface Society defined dry eye as follows (known as the DEWS II definition):

"Dry eye is a multifactorial disease of the ocular surface, characterised by a loss of homeostasis (stability) of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity (concentration), ocular surface inflammation and damage, and neurosensory abnormalities play etiological (causative) roles."[6]

After determining the presence of dry eye disease, based on positive questionnaire results and one or more positive results on eye examination, further tests — such as meibography, lipid interferometry, and tear volume measurement — may be performed (when available) to determine disease subtype and severity, and to guide management.

Dry eye disease management

Dry eye disease management is challenging as the causes are often complex. Treatment aims to interrupt the vicious cycle of damage and inflammation by restoring tear film and ocular surface stability. In this article, we propose a 4-step approach to the management of dry eye disease.

Step 1. Laying a good foundation

The strategies in this step are the foundation of dry eye disease management. They must be continued alongside any other treatment the patient may receive in future.

Education & counselling

Start by educating the patient about the disease, including what can make it worse, and how to manage it at home. Encourage patients to reduce the time spent looking at computer or phone screens and/or to take breaks when using screens. Taking regular exercise, and avoiding air conditioning, smoke, or other pollutants, can also help.

Tear supplementation

Prescribing preservative-free artificial tears is a common strategy.

- **Aqueous eye drops** can contain agents such as hyaluronic acid and hydroxypropyl guar; these make the eye drops more viscous (thicker), which keeps them on the ocular surface for longer.
- **Lipid-based eye drops** and **liposomal sprays** have become more popular for the management of signs and symptoms associated with meibomian gland dysfunction and lacrimal lipid deficiency.[1]

All formulations should be preservative free if at all possible as preservatives in eye drops can cause toxicity and worsening of the dry eye disease.

Eyelid care
Eyelid hygiene practices such as warm compresses (followed by eyelid massage), and eyelid cleaning (e.g., using cooled boiled water and a clean face cloth or cotton wool pad) help alleviate blepharitis and meibomian gland dysfunction symptoms, thereby promoting tear film stability. Such strategies should be used from the beginning and often help improve dry eye disease when performed properly. See the previous article in this issue for more information.

Dietary modifications
Encourage patients to drink plenty of water and eat more foods that contain essential fatty acids (EFAs) such as oily fish, nuts, seeds, and green, leafy vegetables. EFAs, particularly omega-3 and omega-6, play a significant role in modulating inflammatory mechanisms in the human body. While laboratory studies demonstrate the anti-inflammatory properties of omega-3 and its positive effect on lacrimal gland function and the ocular surface, clinical trials investigating oral EFA supplementation for dry eye disease treatment have shown varied results; there are also controversies surrounding the ideal dosage, formulation, and duration of treatment. Nevertheless, omega-3 supplementation is widely used and is part of the authors' list of initial therapies proposed for the treatment of dry eye disease.

Environmental and behavioural control measures
Certain behavioural and environmental conditions can also play a role in the development and progression of dry eye disease. Exposure to dry or polluted air can aggravate dry eye symptoms, as can excessive screen exposure time and sedentary habits. Therefore, it is important to advise patients about their habits and environment and seek ways to reduce or compensate for harmful factors, such as scheduled breaks during screen use, environmental adjustments (e.g., the use of humidifiers in very dry environments), taking regular physical exercise, and avoiding air conditioning, smoke, or other pollutants.

Review of medications
The use of systemic medications for other purposes can affect the ocular surface. For instance, antihistamines, antidepressants, anxiolytics, and isotretinoin (for acne) are known for their adverse effects on the ocular surface. Depending on the severity and significance of the adverse effects, both physician and patient may choose to reduce, replace, or discontinue the medication. Long term use of glaucoma drops is often associated with dry eye disease, especially prostaglandin analogue drops. Any eye drops being used should also be reviewed and reduced or changed to preservative-free formulations if possible.

Step 2. Stepping up treatment

In patients where the measures in Step 1 prove ineffective or insufficient, there is a need to step up treatment. In this stage, it is possible to increase lubricating measures, evaluate the possibility of *Demodex* infestation, and consider the use of tear conservation devices, meibomian gland dysfunction treatment therapies, and other specific topical prescriptions.

Tear supplementation
Increase lubricating measures by prescribing aqueous or lipid-based gels and ointments.

Treatment for *Demodex*
The infestation of the eyelid margins by the *Demodex folliculorum* mite might be considered in patients with resistant blepharitis. This a common condition that can cause symptoms such as itching, redness, and irritation. Management often includes **topical tea tree oil-based solutions or ointments** and **eyelid hygiene** practices (see Step 1), as well as oral medication containing **ivermectin**.

Tear conservation
Interventions that aim to promote tear conservation can also be valuable in this stage of treatment. **Temporary punctal occlusion** with punctal plugs involves closure of the proximal tear drainage ducts in order to retain natural tears and prolong contact with the ocular surface. **Moisture chamber spectacles or goggles** can be used to create a barrier and help reduce tear evaporation; they can also promote comfort and improve patients' quality of life during treatment.

Meibomian gland dysfunction treatment
In patients for whom the clinical approach in Step 1 is not enough, there may be a need for further interventions, although access to these may be limited. **Intense pulsed light** (IPL) can be used to target dysfunctional blood vessels and decrease inflammation in the eyelids and surrounding tissue, thereby improving tear film stability. **Thermal pulsation therapy**, often followed by **mechanical gland expression**, helps address meibomian gland dysfunction by applying controlled heat to the eyelids; this helps the release of meibum. Eyelid treatments such as debridement and exfoliation aim to remove debris and biofilm from the eyelid margins, promoting healthier tear production and relieving symptoms.[5] These strategies might be used alone or in combination, depending on the patient's needs.

Other drug options
Other options can be added, e.g. if there are specific signs, progression or acute worsening of symptoms, or if there is no response to previously described treatment.

- **Topical corticosteroids** play a crucial role in managing various inflammatory conditions, including dry eye disease, by inhibiting the inflammatory cascade. It must be administered for a limited duration and in a tapering regimen, as long-term use is associated with potential complications such as cataract, ocular hypertension, and opportunistic infections.
- **Non-steroidal drugs that affect the immune system** (immunomodulators) offer a promising alternative to corticosteroids. Cyclosporine A, the most studied immunomodulator so far, has been approved for moderate to severe dry eye disease as it showed significant reduction in inflammatory markers and improvement in tear osmolarity.[4] Tacrolimus, a substance with superior immunosuppressive potential, has emerged as a viable therapeutic option for patients that are intolerant of, or unresponsive to, cyclosporine A. However, tacrolimus is not widely available.[1]

- A wide range of **topical formulations for lacrimal secretion stimulation** (known as secretagogues) are known but not widely available. These vary in mechanism of action, stimulating aqueous, mucous, and/or lipid secretion. Notable topical secretagogues include diquafosol tetrasodium and lacritin, which stimulate aqueous-mucous secretion and promote lacrimal gland secretory processes, respectively.
- **Topical mucolytics** are often used as adjunctive therapy, especially those with antioxidant properties, such as acetylcysteine. These work by breaking down mucous (or mucin) molecules. These medications may also be used to treat filamentary keratitis, a potential complication of dry eye.
- Finally, **systemic and topical antibiotics**, such as tetracyclines and azithromycin, are prescribed not only for their antimicrobial effects but also for their anti-inflammatory properties in conditions associated with dry eye disease, such as blepharitis and meibomian gland dysfunction.[5] Optimal dosages and protocols for these antibiotics remain controversial, and further research is needed to determine their efficacy and long-term effects.[1] Examples of commonly used regimens include doxycyline 50–100 mg, or lymecycline 408 mg, used once a day for several months. Note their contraindications, including use in pregnancy and young children.

Step 3. Long-term management

In this step, there is an even greater concern about the long-term effects and sequelae of the disease. Further approaches have to be considered and potentially added to the overall treatment in very severe cases.

Oral secretagogues

Oral secretagogues can be used to help increase tear secretion, although their effective role remains controversial. **Pilocarpine** and **cevimeline** are cholinergic agonists that can be administered orally to manage especially moderate to severe dry eye disease.[1]

Biological tear substitutes

Biological tear substitutes have also been extensively used in treating severe ocular surface diseases due to their biochemical similarities to tears. Examples include **autologous and allogeneic serums**, derived from the blood of the patient or from another human being, respectively. While complications are rare, concerns over contamination, lack of manufacturing standardisation, and immune response risks tend to limit its widespread use. The use of **platelet-rich plasma** (PRP) is also a valuable therapeutic option due to its superior growth factor content compared to fresh frozen plasma or serum. However, there is also a lack of consensus on manufacturing protocols, which means further research is needed to fully assess their benefits and indications in dry eye disease treatment.[1]

Therapeutic contact lens options

Therapeutic contact lenses can be helpful, providing symptomatic relief and improving ocular comfort for patients with moderate to severe dry eye disease. **Soft bandage lenses** provide a soothing barrier over the cornea, retaining tears for a longer period and playing a role in the healing of epithelial lesions. On the other hand, **rigid scleral lenses** can create a vault over the corneal extension and provide a tear reservoir between the lens and the epithelium, thereby hydrating and protecting the ocular surface.

Step 4. More permanent solutions

The final step of treatment for severe dry eye disease consists of long-term topical and/or oral medications, as well as more invasive approaches such as surgical procedures involving permanent punctal occlusion, amniotic membrane graft, tarsorrhaphy, and salivary gland transplantation. Fortunately, only a small number of patients tend to present with such severe forms of dry eye disease.

Prescription drug options

After all the clinical attempts mentioned in the previous steps, the use of long-term **topical/oral corticosteroids and oral immunosuppressants** need to be considered.

Surgical approaches

Surgical alternatives for dry eye disease include various approaches to alleviate symptoms and improve ocular surface health. Correction of eyelid malposition with **ectropion or entropion surgery** should be considered if appropriate. Permanent occlusion of the lacrimal puncta with **punctal cautery** can be considered if there is significant aqueous deficiency, e.g., in Sjögren's syndrome, and if a trial of punctal plugs does not cause watering of the eyes (initially on the lower puncti only). **Tarsorrhaphy** to reduce (partially or completely) the exposure of the ocular surface and to decrease tear film evaporation would normally be reserved for patients with serious, vision-threatening disease. Surgical procedures utilising **amniotic membrane grafts** can restore tissue integrity and reduce inflammation, but these are temporary measures and are normally only considered in very severe disease. **Major salivary gland transplantation** and **autotransplantation of minor salivary glands** from oral and nasal mucosa can also aid in reconstructing the fornices and in managing dry eye disease symptoms; however, this requires a very specialised service to be available.[1]

Regular monitoring and careful long-term evaluation are crucial for ensuring the effectiveness of the proposed therapies, making it possible to modify or complement them as needed. Additionally, patient education and participation in decision-making have a significant impact on treatment success and adherence, as well as assisting in the prevention of relapses and complications.

Summary

This article represents a synthesis of the current knowledge about dry eye disease, with a focus on management. It is important to understand the multifaceted nature of this condition and the variety of therapeutic approaches available.

There are numerous opportunities for further research and many fields of innovation and investigation are yet to be explored. Commitment to clinical excellence and continuous medical education are essential if we want to promote the wellbeing and quality of life for our dry eye disease patients.

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Complications in patients who have undergone laser refractive surgery

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Refractive surgery is a relatively safe procedure. Although complications are rare, being familiar with the signs and symptoms can support early detection and appropriate, timely referral and treatment.

A patient is ready to undergo laser refractive surgery. INDIA

Although refractive surgery is generally safe and effective, it is not free of complications. Due to its rising popularity, an increasing number of people are travelling long distances for refractive surgery and returning home for postoperative management; local eye care professionals may therefore be faced with any complications that occur. The aim of this article is to help you to recognise common complications after refractive surgery and guide management or referral, as appropriate.

Refractive surgery involves reshaping the cornea by cutting a hinged flap in the central part of the cornea, removing some corneal tissue, and then replacing the flap.There are different types of refractive surgery, such as laser-assisted in situ keratomileusis (LASIK), laser epithelial keratomileusis (LASEK), small incision lenticule extraction (SMILE), and photorefractive keratectomy (PRK). Complications can vary depending on the type, so it would be helpful to ask your patient if they know which they received.

Dry eye disease

Dry eye disease manifests in the immediate postoperative period and is observed in over 90% of patients who have undergone corneal laser refractive surgery; it is particularly common in patients who have undergone laser-assisted in situ keratomileusis (LASIK) as the corneal nerves are cut. Dry eye symptoms are most bothersome in the first month after surgery and gradually improve over 3–12 months. Improvement in corneal sensation and dry eye disease occur by 3–6 months, but corneal re-innervation can be delayed by 2–5 years. Postoperative dry eye also predisposes patients to potentially sight-threatening complications such as refractive regression and microbial keratitis (see below).[1]

Symptoms

Ocular dryness, pain, stinging, photophobia, redness, visual fatigue, and fluctuating vision.

Clinical signs

Decreased tear film stability, reduced tear secretion, fluorescein staining of the ocular surface, and laser-induced neurotrophic epitheliopathy.

Management

At community or primary level, initial management consists of lubricating eye drops, warm compresses, and lid hygiene. If this does not address symptoms, patients need to be managed by an ophthalmologist who can prescribe different lubricant drops, topical cyclosporine, and slow tapering of topical steroids. Temporary punctal plugs can also be considered in patients with severe dry eye disease. See the article on dry eye disease in this issue for more information and guidance.

Keratitis

Keratitis is relatively uncommon, but it is a potentially sight-threatening complication of refractive surgery procedures.[2]

It is important to distinguish **microbial (infective) keratitis** (Figure 1, overleaf) from **inflammatory (sterile) keratitis**. The most common type of inflammatory keratitis after refractive surgery is **diffuse lamellar keratitis** (Figure 2), which normally manifests as infiltrates in the LASIK interface. This typically starts

Table 1 Typical features of inflammatory and infective keratitis.

Clinical features	Inflammatory keratitis	Infection: microbial keratitis
Symptoms	No pain, redness, or watering Decreased vision when infiltrates involve the visual axis	Associated with pain, watering, redness, photophobia, and decreased vision if there is visual axis involvement
Ciliary congestion	Absent	Present
Corneal infiltrates	Whitish, may be diffuse (corneal stromal haze) There may be generalised corneal oedema	Yellowish, possibly dense, clustered area of infiltrates There may be dense corneal oedema, localised to a smaller area of the cornea
Anterior chamber inflammation	No cells or flare	Cells with or without flare in the anterior chamber; possible hypopyon
Microbiology (if available)	Negative	Positive for causative organisms, such as bacteria, fungi, *Acanthamoeba*, or Herpes simplex virus

at the periphery of the flap and progresses along the interface, towards the visual axis. Table 1 compares the typical clinical features of these two types.

What to ask the patient

- Ask about pain and photophobia – these are typical of microbial keratitis
- Ask about adherence with postoperative steroid medications. Non-adherence can increase the risk of diffuse lamellar keratitis
- Ask about the type of surgery, if they know – diffuse lamellar keratitis is associated with LASIK and SMILE.

Management

If **infection** is suspected, start broad-spectrum antibiotics immediately. Refer the patient to an eye clinic if symptoms worsen or do not improve in 48 hours, ideally somewhere that can carry out a full microbiology workup.

If **inflammation** is suspected, continue topical corticosteroids. If infiltrates are worsening and/or involve the visual axis (leading to decreased vision), refer the patient to a corneal specialist for flap lift and interface wash.

NOTE: Corneal stromal haze that does not clear with increased doses of topical corticosteroids should alert you to the possibility of pressure-induced stromal keratitis (see the section on **increased intraocular pressure**). The treatment of pressure-induced stromal keratitis is to reduce the steroid drops, rather than maintaining or increasing the steroid drops, as you would with diffuse lamellar keratitis.

Figure 1 Microbial (infectious) keratitis with ciliary congestion, central corneal infiltrates, and irregular margins.

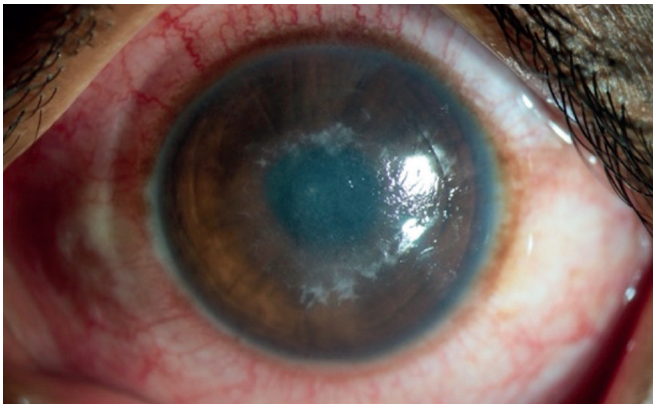
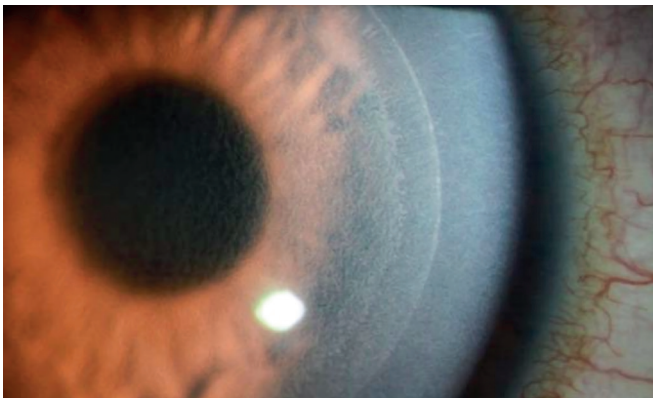


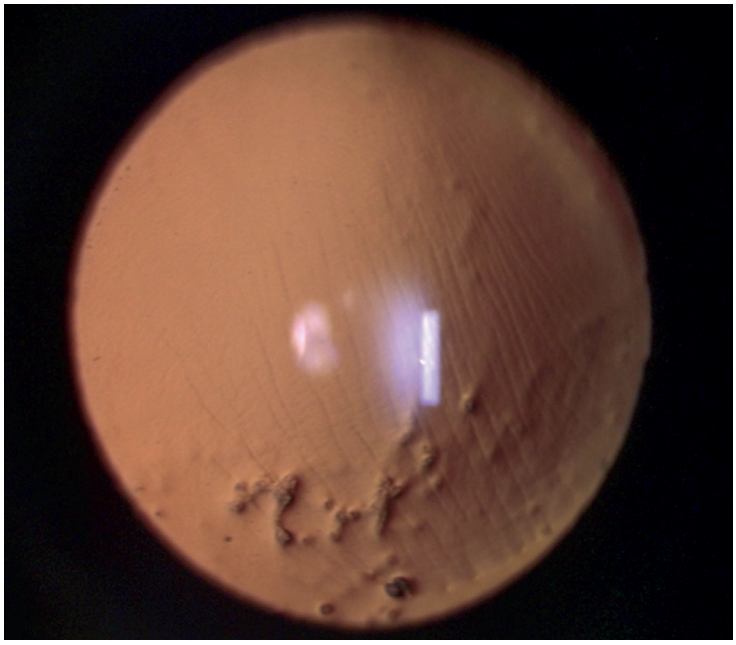
Figure 2 Diffuse lamellar keratitis starting at the periphery of the LASIK flap and progressing to the centre of the visual axis.



Post refractive surgery ectasia

Post refractive surgery ectasia involves changes to the shape of the cornea, similar to what is seen in keratoconus, as a result of refractive surgery. It may manifest months to years after laser vision correction and is relatively rare, occurring in between 0.04 and 0.5% of patients, most commonly those who are young and have high myopia.

Figure 3 LASIK Flap macrostriae visualised with retro-illumination using a slit lamp.



Symptoms

Typically presents as blurred vision and a progressive increase of the refractive error.

Clinical signs

See the article on keratoconus in this issue.

Management

- Counsel the patient and advise them to avoid eye rubbing
- Consider using rigid gas permeable contact lenses to improve vision
- Consider collagen cross linking (see the article in this issue) and/or (less commonly) inserting intracorneal stromal ring segments.

Avoid further refractive surgical procedures in patients who have abnormal corneal tomography suggestive of ectasia.

Flap striae

Flap striae are commonly seen after LASIK. If seen within the first few weeks after surgery, this can be due to:

- Intraoperative drying and distortion of the flap
- Dislodgement of the flap during removal of the speculum at the end of surgery
- Rubbing of eyes by the patient
- Sleeping without topical lubricants, which may dry up the flap, especially so in patients with incomplete closure of eyelids during sleeping. The dried-up flap sticks to the eyelid and gets disturbed on waking up.

Delayed appearance of flap striae could be due to mechanical dislodgement of the flap, perhaps by a blunt trauma, and may present at any time after surgery.

Symptoms
Blurring of vision, poor visual acuity, and monocular diplopia (double vision).

Signs
Wrinkling of a LASIK flap can be seen using a slit lamp, ideally with retro-illumination (Figure 3). This can be either peripheral or finely distributed in the central portion of the flap. Disruption of the tear film may be seen after fluorescein has been put in the eye.

Management
- **Microstriae** are fine wavy folds in the LASIK flaps, caused by fine wrinkling of the Bowman's layer and epithelium. Microstriae do not affect vision and may be observed.
- Patients with **macrostriae** have large folds on the LASIK flap. These are caused by dislocation or poor apposition of the flap. Macrostriae cause distortion of vision. In these patients, the flap needs to be lifted and repositioned.

Raised intraocular pressure
There is a risk of the intraocular pressure (IOP) going up after laser refractive procedures, with the main cause being the use of steroid eye drops.

Risk factors
- Frequent use of steroid eye drops, e.g., more than 4 times a day
- Patients with a history of pressure rise with steroid use
- Family history of glaucoma.

Symptoms
- Patients may be asymptomatic, so the IOP must be monitored after the procedure, at least while the patient is on steroid drops
- Vision may be blurred if pressure-induced stromal keratitis develops (see below).

Signs
- High IOP measurement
- A diffuse and fine stromal haze may also develop, similar in appearance to pressure-induced stromal keratitis. This is often initially diagnosed as diffuse lamellar keratitis. However, diffuse lamellar keratitis occurs earlier than pressure-induced stromal keratitis, which is usually seen more than a week after surgery.

NOTE: Fluid may accumulate underneath a LASIK flap; this can cause the intraocular pressure measurement to be falsely low so that the high IOP is missed. Looking for fluid clefts with a slit section on the slit lamp is important. Fluid pockets may be seen under the flap with anterior segment OCT if available (Figure 4).

Management
Corneal stromal haze that does not clear following an increased dose of topical corticosteroids should alert the physician of pressure-induced stromal keratitis. Prompt lowering of the IOP with pressure-lowering medications, shifting to low potency topical steroids, or tapering and stopping topical corticosteroids may help reduce IOP and control this condition.

Figure 4 OCT of interface fluid syndrome with fluid cleft (arrow).

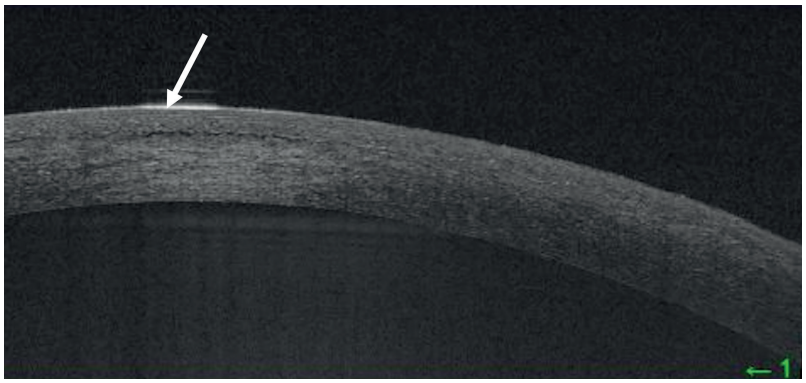
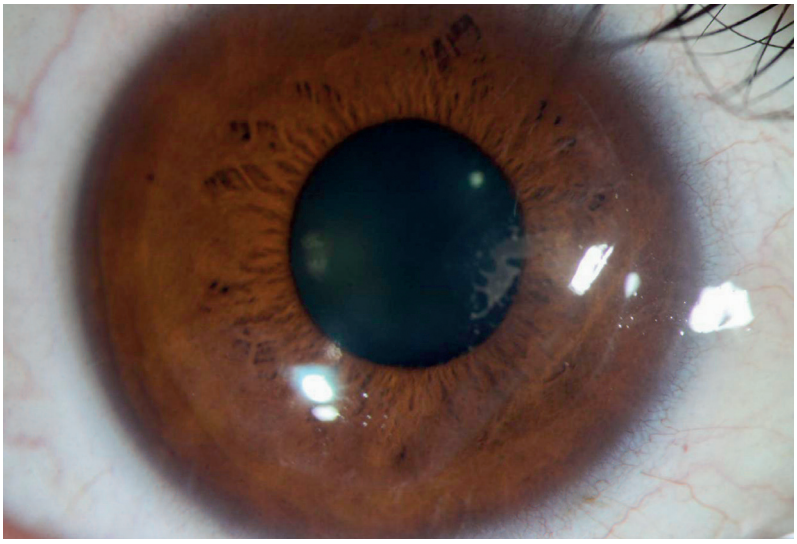


Figure 5 Slit lamp photography showing an area of grade 1 epithelial ingrowth with epithelial pearls.



Epithelial ingrowth
Epithelial ingrowth occurs in up to 3.9% of patients receiving refractive error surgery for the first time, and in 10–20% of re-treated patients. It is more common in patients who received manual LASIK surgery.

Most symptoms appear within four weeks, although delayed presentations are not uncommon. The condition arises from the implantation of epithelial cells during surgery, or their later migration from the flap edge after surgery.

Symptoms
Early symptoms include foreign body sensation and reoccurrence of glare due to ocular surface irregularity, while later stages may involve blurring of vision. Early epithelial ingrowth is usually hard to diagnose accurately by symptoms alone, since the symptoms may overlap with normal post-surgical discomfort.

Clinical signs
Slit lamp examination is more important than symptoms for early diagnosis and to grade the severity. Typical signs of epithelial ingrowth include epithelial pearls or nests (i.e., large epithelial pearls), white boundary lines along the nests at the flap-stromal interface, and flap melting (see Figures 5, 6, and 7).

Management

Patients with suspected epithelial ingrowth should be referred to an ophthalmologist who can grade the severity and begin treatment if needed. Action should be taken within 2–3 weeks, or sooner if possible.

The management of epithelial ingrowth varies according to its location, clinical features, and severity, as described in the 4-level grading system proposed by Probst and Machat.[3] Please note that it is necessary to grade according to the most severe characteristics present to avoid delays in treatment. Detailed grading standards for each level are as follows:

- **Grade 1** epithelial ingrowth is defined as "thin growth, 1–2 cells thick, non-progressive, difficult to detect, well-delineated with a white line along the advancing edge, no flap change, and 2 mm within the flap edge." Fortunately, since such ingrowth is not likely to be progressive, there is no treatment needed for patients with grade 1, which is the most common type seen in clinics. Figure 5 is an example of grade 1 epithelial ingrowth.
- In **grade 2**, the following characteristics (seen by slit lamp examination) would differentiate it from grade 1: thicker growth, discrete cells within an epithelial nest, no demarcation line along the nest, and an easily detectable rolled or grey flap edge with no stromal melt. Although no urgent treatment is needed, follow the patient up in 2–3 weeks; if some progression is detected, the patient should be referred to an ophthalmologist for further evaluation and treatment. Figure 6 is an example of grade 2 epithelial ingrowth.
- **Grades 3 to 4** would show much more severe clinical signs, such as pronounced/aggressive growth that is several cells thick, a rolled flap with thickened whitish-grey appearance, confluent haze at the flap edge, and flap melt beyond 2 mm from the flap edge, invading towards the visual axis. Figure 7 is an example of grade 3–4 epithelial ingrowth. Possible treatment for grades 3 and 4 include mechanical debridement, flap suturing, fibrin glue, ocular hydrogel sealant, and non-invasive neodymium-doped yttrium aluminum garnet (Nd:YAG) laser.[2] Urgent treatment is needed.

Figure 6 Slit lamp photography showing an area of grade 2 epithelial ingrowth with epithelial nests.

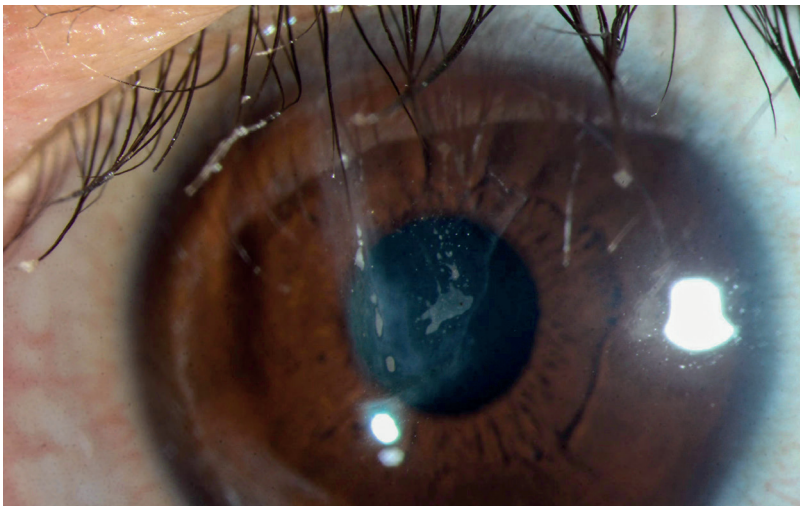
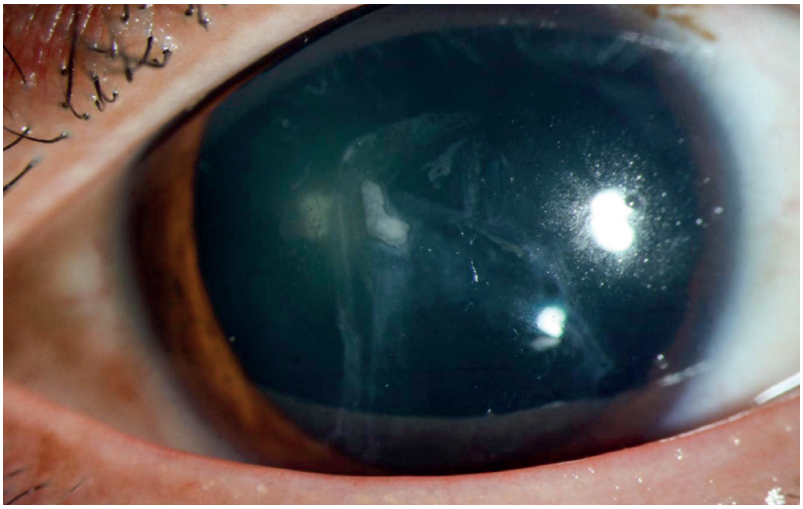


Figure 7 Slit lamp photography showing grades 3 to 4 epithelial ingrowth.



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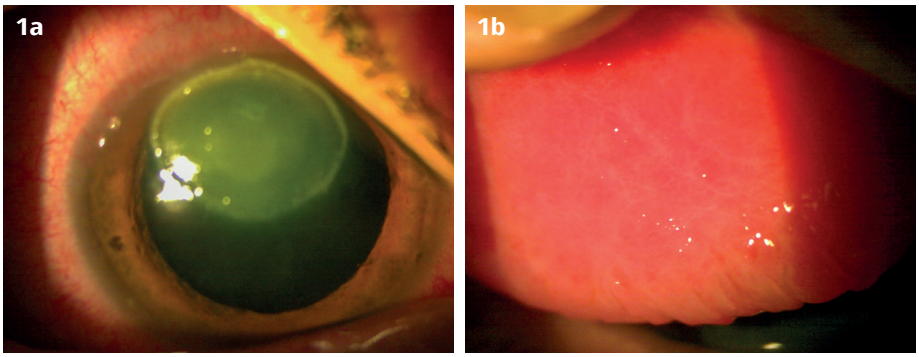
Picture quiz

This quiz is based on a real patient. Read the information, then use your knowledge and clinical skills to answer the questions. We suggest you use a separate sheet of paper, then compare your answers with those provided further down.

A 21-year old man presents with a history of a red, sore, itchy right eye. Clinical pictures were taken (Figure 1 a and b). He reports having had itchy eyes for the past 5 years and he frequently rubs his eyes. He also has eczema, including on the periorbital skin.

Figure 1 a and b Initial presentation in a 21-year old man. UK



Question 1
What signs can you see on the images?

Question 2
What are your thoughts on what is going on with this patient?

Question 3
What is your management approach for this patient?

ANSWERS

1. Conjunctival hyperaemia; a superior corneal oval-shaped epithelial defect with a white deposit at the base; marked tarsal conjunctival papillae with fine scarring.

2. This patient likely has severe allergic conjunctivitis. A more thorough history and examination are needed, but the presentation is consistent with atopic keratoconjunctivitis. This patient also has a shield ulcer on the cornea (something more commonly associated with vernal keratoconjunctivitis). An inflammatory plaque has formed at the base of the ulcer, formed of secreted proteins and mucin.

3. This patient needs urgent treatment for severe allergic conjunctivitis. A shield ulcer is a vision-threatening complication because corneal scarring, vascularisation, infection, or even perforation may develop.

The eye shown in the image is likely to need many or all of the treatments listed below, and the other eye is likely to need some of them, depending on its clinical status. The patient should be monitored closely to assess his response to treatment, and treatment should be tapered gradually once there has been improvement. All drops should be preservative-free if possible, to avoid toxicity.

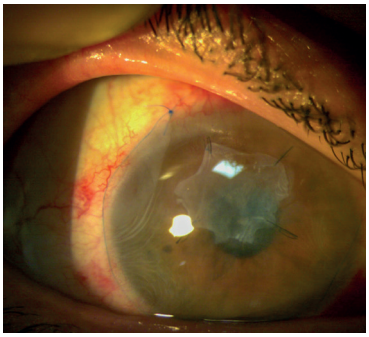
- Conservative measures such as avoidance of triggering allergens; discussion about the importance of not rubbing the eyes, and use of cold compresses instead; lubricating eye drops; trial of oral antihistamine.
- Antihistamine and mast cell stabiliser combination eye drops.
- A course of steroid eye drops, initially very frequently and then tapering to minimise side-effects.
- A topical calcineurin inhibitor, if available; either ciclosporin or tacrolimus.
- Broad-spectrum antibiotic eye drops to prevent infection developing in the ulcer.
- A supratarsal steroid injection. This can be considered immediately or after a few days, depending on the response to the other treatment.

Shield ulcers often require surgical debridement, especially if there is a dense plaque at the base of the ulcer.[1] This should be considered after 1–2 weeks if the above treatment is not successful. The procedure is done in theatre, with good anaesthesia, using a number 15 surgical blade or similar to debride the plaque down to clear cornea. If available, an excimer laser can be also used to perform a superficial keratectomy.[2]

The addition of an amniotic membrane graft can help to reduce the inflammation and allow the cornea to re-epithelialise.[3] Figure 2 shows the ulcer after the plaque was removed and with two layers of amniotic membrane in place: an inner layer over the area of shield ulcer and an outer one over the whole of the cornea and limbus.

If available, amniotic membrane contact lenses can also be used as an alternative to sutured amniotic membrane. These are relatively quick to insert but provide only a single layer of amniotic membrane and tend to be expensive.

Figure 2 Amniotic membranes in place over the ulcer. UK



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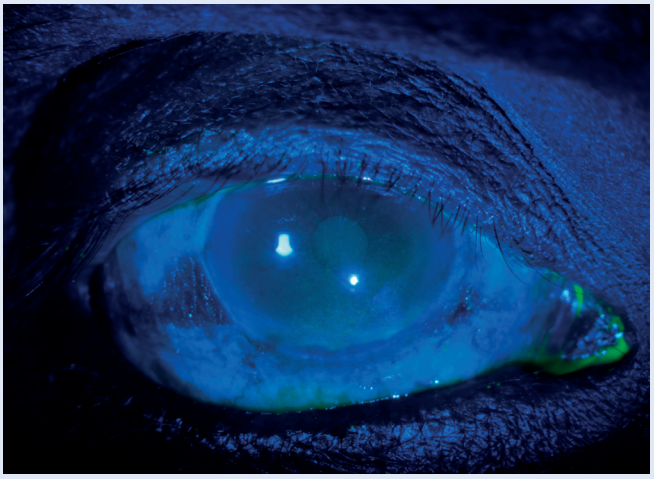
Key community eye health messages

Preventing keratoconus following ocular allergies:

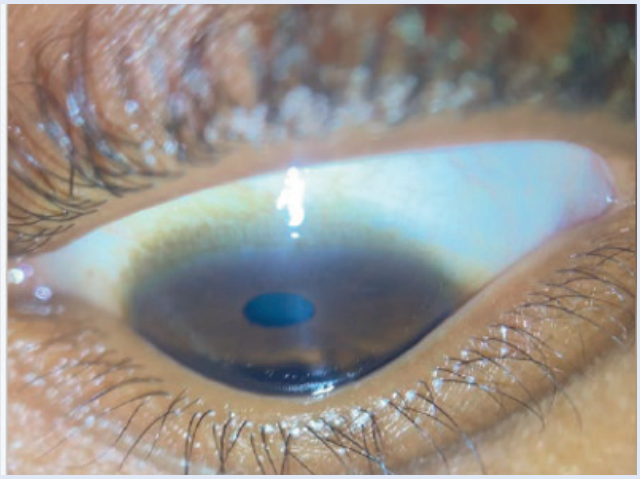
- Avoid rubbing your eyes – rubbing can thin the cornea, increasing the risk of keratoconus and potential vision loss.
- Treat allergies promptly – both seasonal and perennial allergies should be managed to prevent corneal damage or complications like shield ulcers.
- Recognise red flags – refer patients to an ophthalmologist if they report severe pain, sudden vision loss, persistent symptoms, or signs of infection.

Managing dry eye:



- Recognise and treat early symptoms – early intervention helps prevent symptoms from worsening.
- Maintain a balanced tear film – the tear film consists of three layers essential for comfort and clear vision.
- Adopt lifestyle changes – reduce screen time, stay hydrated, and maintain good eyelid hygiene to improve dry symptoms.

Preventing the progression of keratoconus:



- Monitor regularly – frequent corneal scans and check-ups help detect early signs of disease progression.
- Tailor treatment to corneal thickness – treatment protocols, including riboflavin and UV exposure, should be carefully adjusted to ensure safety.
- Consider corneal cross-linking – this procedure can halt or slow the progression of keratoconus, preserving vision over time.