



CLINICAL UPDATES

Allergic eye disease

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Allergic eye diseases include conjunctivitis and occasionally keratitis in response to an allergen. The diseases affect 10%-20% of people globally^{1,2} and have a negative impact on quality of life and productivity.³⁻⁶

Early diagnosis and appropriate treatment is essential to reduce the frequency of relapses, to avoid complications that are potentially sight threatening, and to enhance patient self care. This article provides guidance on recognising the different forms of allergic eye disease and on their management.

Who gets allergic eye diseases?

Children and adolescents are more commonly affected by atopic disease in general, which tends to diminish with age. People with asthma, eczema, and rhinitis often experience concurrent ocular allergy.⁷ Europe, North America, and Japan report higher prevalence than developing countries.¹

How do they present?

Itching is the hallmark of allergic eye disease, which is accompanied by redness and watering of the eyes (fig 1⇓). Symptoms may occur in acute episodes which are generally recurrent or may be persistent in a chronic form.

What are the different types of allergic eye disease?

Table 1⇓ summarises the different types.

Common allergic eye diseases

Seasonal and perennial allergic conjunctivitis are the commonest forms of allergic eye disease and are associated with childhood atopy. Seasonal conjunctivitis is triggered by pollen and frequently occurs in spring and summer. It is often associated with nasal symptoms (rhinoconjunctivitis).

Perennial allergic conjunctivitis is triggered by environmental allergens such as house dust mites, animal dander, fungal spores, or moulds, and does not follow a seasonal pattern.^{8,9}

Both types of conjunctivitis involve a type I (immunoglobulin E mediated) hypersensitivity response, with degranulation of conjunctival mast cells in response to airborne allergens and

release of inflammatory mediators including histamine.¹⁰ Patients might present with persistent low grade symptoms or acute exacerbations.

Rarer causes

In vernal and atopic keratoconjunctivitis, contact dermatitis, and giant papillary conjunctivitis both type I and type IV (delayed, cell mediated) hypersensitivity reactions are implicated. The latter involves migration and activation of T-helper cells, which confers chronicity.

Vernal keratoconjunctivitis is a severe form of allergic eye disease commonly seen in young men. It is relatively rare in Western Europe¹¹ but the prevalence and severity increases in warm climates.¹² Classically it presents in the spring pollen season, but acute exacerbations can occur at any time after exposure to allergens. In vernal keratoconjunctivitis, goblet cells are increased, causing copious mucus production.¹³ Flares are characterised by bilateral intense ocular itching, redness, a thick mucous discharge, and symptoms of keratitis including pain, photophobia, and loss of vision.¹⁴ Chronic eye rubbing contributes to the development of keratoconus and other corneal ectasias.¹⁵⁻¹⁷ In severe cases, a corneal ulcer (shield ulcer) might be visible, which stains with fluorescein (fig 2⇓).

Atopic keratoconjunctivitis is a chronic inflammatory disease affecting young adults.¹⁸ Most patients have concomitant atopic dermatitis of the lids. Chronic itching and redness are typical, which can progress to cicatrization, ie, conjunctival scarring and eventually corneal opacification.^{18,19} Atopic keratoconjunctivitis leads to a decrease in goblet cells secreting mucin-5AC, which exacerbates ocular surface dryness and cicatrization.^{13,20}

Contact dermatitis is caused by exogenous irritants such as eye drops, contact lens solutions, and cosmetics, which can trigger lid dermatitis and a persistent conjunctivitis in non-atopic individuals (fig 3⇓).²¹ In contact dermatitis, a pure type IV hypersensitivity reaction occurs, which accounts for its poor response to topical antihistamines and mast cell stabilisers.²²

What you need to know

- Allergic eye disease is usually bilateral and itching is the predominant symptom
- Uncomplicated disease can be managed in primary care with one or more of cold compresses, lubricants, topical and/or oral antihistamines, and topical mast cell stabilisers
- Topical and oral steroids and immunomodulatory agents should be prescribed only under the care of an ophthalmologist in refractory cases

Giant papillary conjunctivitis is caused by both allergy and mechanical irritation triggered by a foreign material such as contact lenses, ocular prostheses, or exposed sutures.¹⁹ Subtarsal papillary hypertrophy is seen with a mucous discharge that remits with removal of the offending agent.⁸

How is it diagnosed?

A focused history can help differentiate allergic eye disease from other forms of red eye, which are summarised in table 2↓.

History

Ask about itching, the type of discharge, duration of symptoms, and exacerbating factors. Bilateral symptoms typically suggest an infective or allergic cause, although both can manifest asymmetrically. Red, watery, and itchy eyes recurring in the spring and summer is highly suggestive of allergic eye disease. Nasal symptoms might be present. Ask about recent coryzal illnesses or exposure to infected individuals, which can suggest an infective cause. A history of atopic diseases such as eczema or asthma favours an allergic cause. The use of eye drops should be established; this might be the cause of symptoms, as in contact dermatitis.

Ocular pain and loss of vision are unusual in simple allergic conjunctivitis. These symptoms might suggest vernal keratoconjunctivitis or conditions such as uveitis or an infective corneal ulcer, the latter being generally associated with contact lens use.

Importantly, ask about the impact of symptoms on quality of life. The functional effects of allergic eye disease can be profound, as highlighted by our *Patient's perspective* (boxes 1 and 2).

Examination

Assess visual acuity using the Snellen's chart. Examine the lids for swelling and dermatitis. Use a torch, preferably with a magnifier, to assess for conjunctival redness or swelling and any obvious corneal or limbal irregularities. Subtarsal upper lid papillae are often evident. Figures 1 to 3↓ show many of the findings in allergic eye disease.

Topical fluorescein can show signs of keratitis and can be used in primary care for any red eye associated with pain, loss of vision, or photophobia. (fig 2↓).

What treatment options are available in primary care?

Patients with uncomplicated allergic eye disease, which mostly constitutes seasonal and perennial allergic conjunctivitis, can be managed in primary care with oral and topical anti-histamines and mast cell stabilisers.

Box 3 lists red flags that should prompt referral to acute hospital eye services.

For acute symptoms, institute preventative measures and offer topical second generation anti-histamines. Figure 4↓ summarises

the recommended treatment algorithm for primary care management based on the National Institute for Health and Care Excellence (NICE) guidelines and our experience.

Assess for clinical and symptomatic improvement at 1-2 weeks. Topical mast cell stabilisers can be used for recurrent or persistent symptoms but the loading period makes them ineffective for acute symptoms. The topical preparations available are summarised in table 3↓.

Preventative measures

Cold compress and instillation of refrigerated preservative-free lubricant eye drops can potentially induce local vasoconstriction and relieve acute symptoms, although there is limited evidence for this.²³ Lubricants must be instilled regularly, at least four to six times a day.

For seasonal allergic conjunctivitis, advise reducing exposure to outdoor pollen and grasses by keeping house and car windows closed during high pollen counts. Sunglasses can be useful to reduce pollen exposure.²⁴

For perennial allergic conjunctivitis, if there is a known trigger, measures to control that trigger (house dust mites, mould, and animal dander) can be initiated. These include frequent replacement of pillow, blanket, and mattress covers, frequent floor cleaning and vacuuming, using bedding that is impermeable to house dust mites, air purifiers with high efficiency particulate air filters, and acaricide sprays.

Evidence for the utility of allergen avoidance in allergic eye disease is poor, and few studies report on ocular symptoms as the primary outcome. A Cochrane systematic review examined various preventative measures for nasal and ocular symptoms of allergic rhinitis. Nine trials (501 patients across nine trials) met inclusion criteria and were small and of poor methodological quality. House dust mite impermeable mattress covers and high efficiency particulate air filters can reduce the allergen load, but neither is associated with an improvement in symptoms. The review concluded that acaricide sprays might be the most effective single intervention in both reducing house dust mite loads and improving symptoms of allergic rhinitis.²⁵ In practice, multi-modal allergen avoidance methods might confer some benefit in perennial allergic conjunctivitis when the allergen is known, but the effectiveness is likely to be limited by patient compliance or financial constraints.

Advise patients to avoid eye rubbing as this can worsen redness and conjunctival swelling.^{26,27}

Contact lenses can trigger giant papillary conjunctivitis but can also exacerbate other forms of allergic eye disease. Contact lens wearers with an acute red eye should be assessed by a trained optician or ophthalmologist and offered guidance regarding optimal care of their lenses. Avoid or reduce contact lens use until acute symptoms subside. If this is not feasible, a second generation anti-histamine eye drop should be used as described below.

Box 1: Patient's perspective

I never really had eye problems when growing up. I wore glasses in primary school for reading but stopped at around the age of 15.

The serious eye issues started during university. All the while I still had serious eczema, which seemed to flare up when exposed to the allergens I knew about. I felt my eyes were also irritated the same way, but was given no clear reason why this was nor did anything given at my local practice help. My vision would get very blurry, and my eyes would become red and painful to the point that I couldn't keep them open. I ended up taking a lot of time away during my first year of university, similar to the time I had to take off school for my bad eczema and all the hospital appointments that came with it.

I played a lot of sport and it became a problem because I literally couldn't keep my eyes open at times. Also, going out with friends became a chore, and I found myself wearing dark sunglasses just to hide my puffy eyes. The shades also lessened the pain I would feel as my eyes became very sensitive to light.

After a summer of the worst symptoms I had ever experienced, I was referred to the hospital ophthalmology department. Suddenly I had a whole array of drops—ones for inflammation, antibiotics, lubricants, and drops for pain on exposure to light. I took oral steroids for a short time and was made aware of other new treatments, should things worsen. Thankfully the drops helped and my condition has completely settled. When flare-ups occur I now get referred directly to the ophthalmologist for steroid drops and I also know the signs to look out for before things worsen.

Box 2: Physician's perspective

This patient had been lost to follow-up for 12 months after starting university. In the interim he was managed by his local general practitioner and walk-in centres with over-the-counter lubricants and antibiotics. By the time he presented, his vernal keratoconjunctivitis was very active. He had a shield ulcer in one eye and bilateral Horner-Trantas dots with acute drop in vision. We quickly escalated the therapeutic ladder from topical steroid drops, to oral steroids with adjuncts. He remained under close observation of the multi-disciplinary teams with immunology and dermatology input and was weaned off oral steroids. We eventually saw his condition improve and he was discharged with advice to return for any flare-ups.

The importance of inquiring about the impact of disease was highlighted by this patient, particularly if at school, college, or university. The patient's disease affected university attendance and examinations, sports, and social activities.

Box 3: Red Flags

- Pain +/- photophobia
- Blurring or loss of vision
- Red eye in a contact lens wearer
- Evidence of corneal involvement: ulcer, opacity or spots, limbal changes
- Recent eye surgery

Pharmacological eye drops**Topical second generation antihistamines**

These are well tolerated and are dual acting, with secondary mast cell stabilising properties that make them effective for both acute symptoms and long term control.²⁸ Agents in this class include emedastine, epinastine, azelastine, ketotifen, and olopatadine which are licensed for twice daily use. The dosing schedule of topical second generation antihistamines makes them practical for children with allergic eye disease as it eliminates the need for drop instillation during school hours.

Evidence from a small randomised controlled study suggests that olopatadine is safe and effective in contact lens wearers.²⁹ Preservatives in eye drops can irritate the eye when wearing contact lenses. Advise using the drops 15 minutes before lens insertion and then after lens removal.

Mast cell stabilisers

These drugs inhibit mast cell degranulation which is responsible for symptoms in seasonal and perennial allergic conjunctivitis. Drugs include sodium cromoglicate, lodoxamide, and nedocromil sodium. Aside from frequently reported burning, all three are well tolerated.²⁸ However, they need to be instilled four times a day. Additionally, they take several weeks to become effective and might not treat acute symptoms.²⁰ Both these issues often culminate in treatment failure because of poor compliance.³⁰ Hence, they are usually reserved for long term prophylaxis once there is adequate symptom control.

A Cochrane review (30 trials, 4344 participants) found that topical antihistamines and mast cell stabilisers reduce symptoms in allergic conjunctivitis compared with placebo and are well

tolerated. Reporting of symptoms was variable across studies and treatment success was poorly defined, making estimates on efficacy difficult. Levocabastine, azelastine, and sodium cromoglicate improved symptoms when compared with placebo. A meta-analysis was only possible when comparing olopatadine and ketotifen, which showed a statistically significant reduction in itching with olopatadine at 14 days. A single study also suggested a significant benefit of olopatadine over sodium cromoglicate for itching. Overall, there was insufficient evidence to recommend one agent over the other because of study heterogeneity. No serious adverse events were reported.³³ Switching between antihistamines and mast cells stabilisers can therefore be considered when there is treatment failure or intolerance, as outlined in figure 4.

Topical vasoconstrictors

Alpha-adrenoceptor agonists (eg, xylometazoline) can reduce conjunctival swelling, redness, and lid oedema. They are generally combined with topical first generation anti-histamines (eg, antazoline phosphate). These combination drops are short acting and require frequent use, which can result in ocular discomfort, tachyphylaxis, and rebound redness on cessation.^{20,31} Over-the-counter availability has led to widespread use by self medicating patients but long term use should be avoided. Avoid use in patients with cardiovascular disease and hypertension because of the sympathomimetic action of topical vasoconstrictors.³²

Systemic medications

Oral second generation antihistamines are less sedating than first generation, and are associated with a lower risk of cardiac

arrhythmias.³⁴ Drugs include fexofenadine, cetirizine, loratadine, levocetirizine, and desloratadine. All have shown comparable efficacy and safety in the context of allergic rhinoconjunctivitis, although studies looking specifically at ocular symptoms are lacking.³⁴

For isolated ocular symptoms, there is some evidence from two small randomised controlled trials (155 patients across two trials) that topical second generation antihistamines alone are, in general, more effective than oral ones, and are associated with fewer side effects. The combination of the two can however produce greater control of ocular symptoms.^{35 36} Of note, oral second generation antihistamines can worsen dry eye more than topical agents through reduced tear production and quality and this can, paradoxically, worsen allergic eye symptoms.³⁷ With isolated ocular symptoms, use topical medications as a first line, reserving oral second generation antihistamines for those with inadequate control on topical treatment or for those with concurrent rhinitis. As for topical treatments, oral second generation antihistamines can be used during acute episodes and continuously for long term prophylaxis.

What specialist management might help in refractory cases?

Consider referral to specialist eye services if symptoms do not settle, red flag signs appear (Box 3), or in patients with chronic symptoms refractory to treatment.

Pharmacological eye drops

Topical corticosteroids

Topical steroids are useful in seasonal and perennial allergic conjunctivitis refractory to the above measures, and are generally needed to suppress flares of vernal and atopic keratoconjunctivitis.³⁸ However, their association with cataract and elevated intraocular pressure leading to glaucoma is well documented.³⁹ The national ophthalmic associations in the UK and the USA^{40 41} recommend the use of topical steroids only under the care of an ophthalmologist or those trained to measure intra-ocular pressures and perform a slit lamp exam to assess for cataract, glaucoma, and potential contraindications such as herpes simplex and fungal keratitis.

Fluorometholone and loteprednol etabonate are weaker topical steroids which are effective for this indication^{39 42} and are relatively low risk for these side effects.⁴³ For sight threatening disease flares, potent steroids such as dexamethasone and prednisolone acetate might be required. Short courses tapered over a few weeks are preferred to reduce the risk of complications,⁴⁴ though some patients might require long term low dose topical steroids to control symptoms.

Topical immunomodulatory therapies

The issues with topical steroids have led to the advent of topical immunomodulatory therapies such as ciclosporin and tacrolimus. A robust meta-analysis of seven trials (153 participants, 306 eyes) compared topical ciclosporin to a placebo. The outcomes measured were clinical signs, patient reported symptoms, usage of steroid drops, and adverse effects such as stinging and burning. Topical ciclosporin reduced scores for signs and symptoms in the meta-analysis but there was considerable study heterogeneity. Three studies enrolled patients with topical steroid dependent allergic eye disease and a statistically significant reduction in the use of steroid drops was observed in two of these. A pooled odds ratio of adverse events did not show increased burning or stinging with ciclosporin.⁴⁵

The use of topical tacrolimus, a newer and more potent calcineurin inhibitor, has been explored in patients with severe allergic eye disease in a small randomised controlled trial (30 participants) comparing tacrolimus with ciclosporin, an observational study (1436 patients) and a non-blinded cohort study (791 patients). All studies showed an improvement in signs and symptoms, with two studies demonstrating efficacy in ciclosporin resistant cases.⁴⁶⁻⁴⁸

The use of both agents in allergic eye disease remains off-label although ciclosporin, under the name "Ikervis," is approved by NICE for the treatment of severe dry eye.⁴⁹ The prescribing of both agents is likely to increase as novel uses are found, particularly where there are concerns regarding the side effects of steroids.

Systemic medication

Oral prednisolone is used when the above measures have failed to suppress a flare.

Both oral ciclosporin and tacrolimus can be used for long term control in severe cases. Systemic medications are also useful when there is concurrent lid disease, as with atopic keratoconjunctivitis.^{50 51} Subcutaneous omalizumab, a monoclonal antibody directed towards immunoglobulin E, which is approved by NICE for treating severe allergic asthma and chronic urticaria^{52 53} also confers symptomatic benefit in vernal and atopic keratoconjunctivitis.⁵⁴⁻⁵⁹ Long term use of these systemic medications is rarely required from the authors' experience. If required, they are best managed under joint care between ophthalmology and rheumatology, paediatrics, or immunology services.

In severe or poorly controlled eye disease, particularly in the presence of concurrent asthma or rhinitis, referral to local allergy services might be indicated for skin prick testing to identify allergens which might be amenable to treatment with sublingual immunotherapy.⁶⁰

What is the long term outcome?

Seasonal and perennial allergic conjunctivitis tend to have a chronic course with recurrent exacerbations. They are not usually associated with visual loss, although if untreated they can manifest with reversible corneal epithelial changes.⁶¹

Managing the patient's expectations is paramount. Explain that the aim of treatment is to relieve symptoms and allow them to resume normal activity. It might take several weeks to suppress symptoms and complete elimination might not be possible.

Preventative measures can be adequate to control symptoms in a minority. In most patients, outcomes depend on adherence to treatment, which might be better with the twice daily topical second generation antihistamines, particularly in children. The severity and frequency of episodes tend to diminish with age, as with most allergic diseases, but flares can still occur into adulthood. Most patients have predictable flares and should be advised to use treatment continuously several weeks before and during certain periods eg, spring and summer rather than as needed. Patients with unpredictable flares, severe disease, or symptoms throughout the year might require long term treatment with trials of therapy cessation or switching to other drops if there is poor tolerance.

Vernal keratoconjunctivitis tends to remit after puberty and persistence is rare after 25 years of age, although evidence from case series suggest that it can reduce vision in 6-55% of patients depending on the study region. This is generally related to corneal changes or injudicious use of corticosteroids.^{14 44} Atopic

keratoconjunctivitis tends to have a protracted course and corneal problems might be seen.⁶² The prognosis for resolution in contact dermatitis and giant papillary conjunctivitis is very good, provided the allergen is identified and eliminated.⁶³

For all allergic eye disease, if there is good symptom control with a topical second generation antihistamine or mast cell stabiliser, regular follow-up is not essential. Advise patients to return to primary care if their symptoms are not adequately controlled or if they develop pain or loss of vision.

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How patients were involved in the creation of this article

A patient with allergic eye disease reviewed the article and suggested amendments, specifically to include information on the psychological and functional impacts of allergic eye disease. He also provided his story included in the box on "patient's perspective." Patients also provided clinical images for this article, which have been used with due consent.

Education into practice

Think about the last time you saw a patient with symptoms suggestive of allergic eye disease

Are there aspects of how you would question the patient that you might alter as a result of reading this article? For example, do you routinely ask about contact lens use and a history of atopy?

How might you better explain conservative measures to improve the patient's symptoms?

How might you better explain to patients what allergic eye disease is and set up expectations for a trial of treatment?

Project suggestion: Is the introduction of leaflets on allergic eye disease for patient education in the community associated with a reduction in emergency department attendances for these ocular complaints?

Sources and selection criteria

We searched PubMed and the Cochrane Library using the phrases "allergic eye disease" and "allergic conjunctivitis" in addition to search terms relating to the different sub-sections including epidemiology, pathophysiology, classification, management, and prognosis. Literature from the past five years was used preferentially, particularly where this was a randomised controlled trial, systematic review, or meta-analysis. With more established treatments such as topical antihistamines and mast cell stabilisers, we found that many of the studies conducted were older. Guidelines from the Royal College of Ophthalmologists, the American Academy of Ophthalmology, and the National Institute for Health and Care Excellence have been incorporated.

Additional educational resources

For healthcare professionals

National Institute for Health and Care Excellence Clinical Knowledge Summary on Allergic Conjunctivitis. Evidence based eye care resource providing cross-reference to NICE approved therapeutics and guidelines for management and referral. Free to access. Available at: www.cks.nice.org.uk/conjunctivitis-allergic

Medscape. Classification of Ocular Allergy. CME accreditation available upon completion of modules. Registration required, free to access. Available at www.medscape.org/viewarticle/565791

American Academy of Ophthalmology Preferred Practice Pattern Guideline on Conjunctivitis. Evidence-based guideline updated by the Cornea and External Eye Disease PPP Committee providing information on recognition, and recommendation for care and evidence-based management options. Free to access. Available at: www.aao.org/preferred-practice-pattern/conjunctivitis-ppp-2013

For patients

Patient. Allergic Conjunctivitis. Free to access. Available at: <http://patient.info/doctor/allergic-conjunctivitis-pro>

Allergy UK. Allergic Eye Disease. Free to access. Available at www.allergyuk.org/allergic-eye-disease/allergic-eye-disease

UpToDate. Patient education: Allergic conjunctivitis (Beyond the Basics). Free to access. Available at: www.uptodate.com/contents/allergic-conjunctivitis-beyond-the-basics

NHS Choices. Conjunctivitis. Free to access. Available at: www.nhs.uk/Conditions/Conjunctivitis-infective/Pages/Introduction.aspx

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Tables

Table 1 | Clinical presentation and features of allergic eye disease subtypes

Disease subtype	Natural history	Allergens and risk factors	Seasonal?	History of atopy?	Clinical signs	Complications	Visual impairment	Pathophysiology
Seasonal allergic conjunctivitis (SAC)	Onset in childhood, diminishes with age. Recurrent. Both sexes affected equally	Pollens and grasses	Yes	Common	Bilateral. Conjunctival redness and swelling. Watery or mild mucous discharge	Minimal	+/-	Type I hypersensitivity
Perennial allergic conjunctivitis (PAC)	Onset in childhood, diminishes with age. Both sexes affected equally	Dust mites, animal dander, air pollutants, moulds	No	Common	As for SAC	Minimal	+/-	Type I hypersensitivity
Vernal keratoconjunctivitis	Onset in childhood or adolescence. Chronic with acute seasonal exacerbations. Predominantly males. Tends to diminish over several years	Allergens as for SAC and PAC. Higher prevalence in warm and dry climates	Yes	Possible	Bilateral. Giant papillary hypertrophy of upper lid conjunctiva, conjunctival redness, watery and mucoid discharge. Horner-Trantas dots or limbal papillae, corneal erosions	Eyelid thickening, ptosis, corneal ulceration, scarring, and neovascularisation, keratoconus	++	Type I and IV hypersensitivity
Atopic keratoconjunctivitis	Onset in late adolescence or middle age. Predominantly males. Chronic with acute exacerbations	Allergens as for SAC and PAC. Strong predisposition for atopy	No	Always	Bilateral. Atopic dermatitis, blepharitis, eyelid oedema, corneal erosions	Eyelid tightening, loss of lashes, corneal ulceration, scarring, and neovascularisation, keratoconus, early onset cataract	+++	Type I and IV hypersensitivity
Giant papillary conjunctivitis	Onset at any age. Both sexes affected equally. Chronic. Resolves after removal of allergen	Contact lens use (soft lenses more than hard lenses): poor lens hygiene, prolonged lens wear time (>8-10 hours/day), infrequent lens replacement. Exposed sutures after eye surgery, scleral buckles (for retinal detachment repair), ocular prostheses (after eye removal)	No	Possible	Laterality dependent on location of foreign body. Giant papillary hypertrophy, mucoid discharge	Ptosis	+/-	Type I and IV hypersensitivity
Contact dermatitis conjunctivitis	Onset at any age. Both sexes affected equally. Chronic. Resolves after removal of allergen	Eye drops, cosmetics, soaps	No	Possible	Lid dermatitis. Periocular oedema and erythema	Minimal	+/-	Type IV hypersensitivity

Table 2| Differentials of allergic eye disease

Differential	History and presentation	Clinical findings
Infective conjunctivitis: - Bacterial - Viral - Fungal - Parasitic	Eyes involved sequentially. Infectious contacts. History of upper respiratory tract infections	Preauricular lymphadenopathy. Copious mucinous or green discharge
Dry eye syndrome: - Tear film instability - Aqueous tear deficiency	No itching unless coexisting allergic eye disease. Review medication history for side effects	Overlapping features of ocular allergy
Autoimmune disease: - Uveitis - Scleritis	No itching. Systemic symptoms may be present (back, joint, or tendon pain). Floaters. Severe eye pain. Loss of vision	Decreased vision. Unilateral or bilateral. Systemic signs
Infective corneal ulcer (microbial keratitis)	No itching. Contact lens wear in the majority. Severe eye pain	Decreased vision. Unilateral. White corneal deposit (infiltrate)

Table 3| Commonly used topical medications in allergic eye disease

Topical agent	Mode of action and use	Side effects	Dosing
Topical second generation antihistamines			
Emedastine Epinastine Azelastine Ketotifen Olopatadine	Dual acting with antihistamine and secondary mast cell stabilising properties. Well tolerated and ideal for acute symptoms and long term control	Preservatives (benzalkonium chloride) can irritate the ocular surface	Twice daily dosing allows continuous contact lens wear during the day and is practical for parents who can instil drops outside school hours
Mast cell stabilisers			
Sodium cromoglicate Lodoxamide Nedocromil sodium	Inhibit mast cell degranulation and have a role in long term prophylaxis once symptoms adequately controlled. Might not treat acute symptoms and can take several weeks to become effective due to slow onset	Burning sensation often reported	Requires four times a day instillation, which can result in non-compliance. Available as a preservative-free formulation
Topical vasoconstrictors			
Xylometazoline	α adrenoceptor agonists. Can have sympathomimetic effects, so avoid in patients with cardiovascular disease and hypertension. Available over the counter	Frequent use results in ocular discomfort, tachyphylaxis, and rebound redness on cessation	Short acting, necessitating frequent use. Often combined with first generation antihistamines such as antazoline phosphate
Topical corticosteroids			
Fluorometholone Loteprednol etabonate	Weaker topical steroids effective for suppressing flares of seasonal and perennial allergic conjunctivitis	Use of topical steroids associated with increased risk of cataract and elevated intraocular pressure leading to glaucoma, particularly in children.	Used four to six times a day for acute flares and less frequently for long term control
Dexamethasone Prednisolone acetate	Potent topical steroids for sight threatening disease flares	Contraindications include herpes simplex and fungal keratitis	Might be required hourly for severe disease flares and tapered over a few weeks. Long term use requires close monitoring
Topical immunomodulatory therapies			
Ciclosporin	Calcineurin inhibitor used off licence as a steroid sparing agent and for steroid resistant disease	Stinging and burning, local erythema and oedema, conjunctival hyperaemia and blurred vision	Generally once daily but may be used more often. Patients should keep eyes closed for 2 minutes after instillation to increase local drug action and reduce systemic absorption
Tacrolimus	More potent calcineurin inhibitor, might be effective in ciclosporin resistant cases of severe allergic eye disease	Transient burning sensation. Systemic adverse reaction unlikely	Twice daily administration

Figures

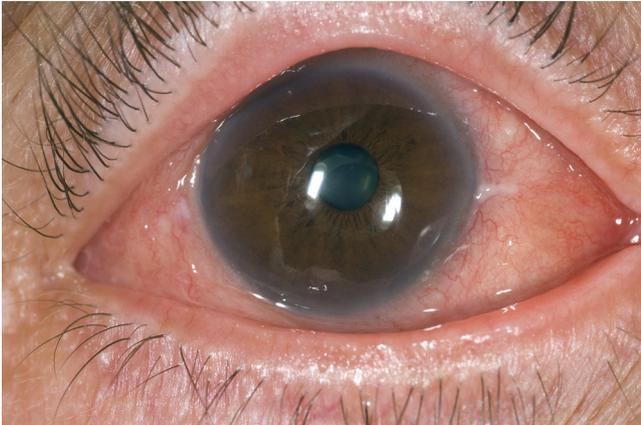


Fig 1 Seasonal allergic conjunctivitis presenting acutely, with conjunctival redness and swelling (chemosis). Note that the cornea is clear, with no signs of keratitis



Fig 2 (Top left) A mid-peripheral white corneal "shield ulcer," characteristic of severe vernal keratoconjunctivitis. (Top right) The same ulcer fluorescing green under cobalt blue filtered light after fluorescein staining of the ulcer. (Bottom left) Subtarsal fine papillae seen on upper lid eversion. These papillae can coalesce to form giant papillae, which are associated with vernal keratoconjunctivitis and giant papillary conjunctivitis. (Bottom right) Limbal papillae are gelatinous lumps at the corneal limbus. The white nodules within the papillae are Horner-Trantas dots. Both are characteristic of vernal keratoconjunctivitis

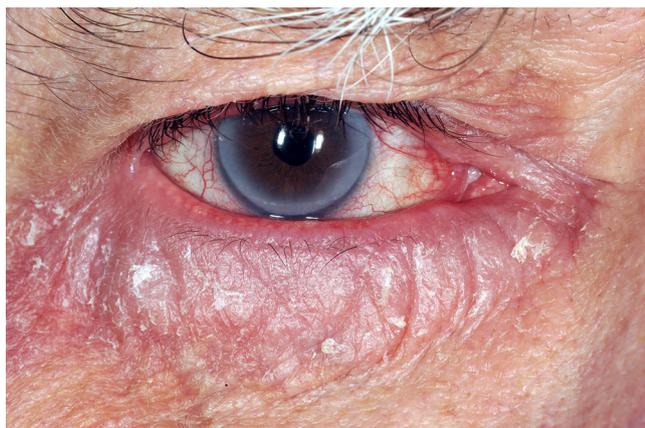


Fig 3 Contact dermatitis secondary to glaucoma eye drops. There is lid dermatitis and mild conjunctival redness

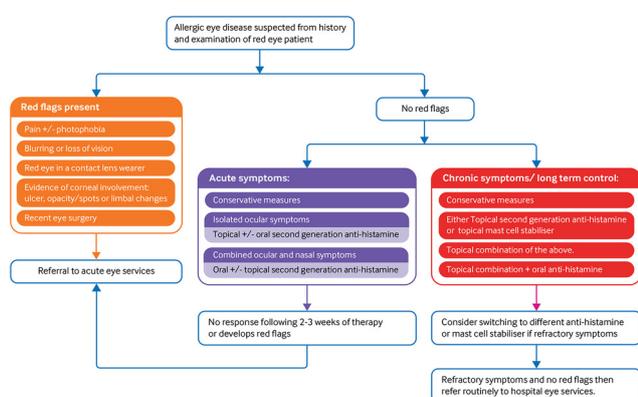


Fig 4 An algorithm for the management of allergic eye disease in primary care, based on NICE guidelines and the authors' experience