

Allergic conjunctivitis

Subtypes and management strategies

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Allergic conjunctivitis is a common chronic disease, particularly in childhood, and often presents in general practice as a recurrent red eye. Allergic conjunctivitis is underdiagnosed and suboptimal treatment can result in potentially hazardous consequences to vision. Treatment of allergic eye disease involves a stepwise approach of minimisation strategies, nonpharmacological interventions and pharmacological treatments.

Only a small proportion of individuals with allergic disease tend to seek help, despite it affecting one in five people in Australia.¹ One of the most common allergic diseases is allergic conjunctivitis, affecting about 10% of people in Australia, with 80% of cases occurring in patients under 30 years of age.^{1,2} Although symptoms are often considered minor, allergic eye disease tends to have a chronic course with multiple recurrent episodes. There are well-established links between allergic conjunctivitis and other atopic conditions, such as asthma, rhinitis, eczema, food allergy and eosinophilic oesophagitis. Most patients with allergic conjunctivitis experience concomitant allergic rhinitis, with only 6% of patients experiencing isolated ocular symptoms.³

Patients with allergic conjunctivitis experience negative impacts on their quality of life, including tiredness, loss of

KEY POINTS

- Allergic diseases affect one in five people in Australia and are more common in children. People who experience allergic conjunctivitis report adverse effects of this condition on their quality of life.
- The most common type of allergic conjunctivitis is seasonal allergic conjunctivitis.
- Itching is the hallmark symptom of ocular allergy. If it is not a prominent symptom, the diagnosis of a red eye should be reconsidered.
- Rarer and more severe forms of ocular allergies that may threaten vision include atopic keratoconjunctivitis and vernal keratoconjunctivitis.
- Topical mast-cell stabilisers are the mainstay of treatment in managing ocular allergy; however, there are new management strategies to consider in refractory cases.
- There is no role for corticosteroids in treating patients with seasonal or perennial allergic conjunctivitis. The use of corticosteroids in other forms of allergic disease should always be under the supervision of an ophthalmologist, due to the potential of adverse effects.

productivity in work and school and adverse effects on mental health.⁴ Specific indicators of this include poor quality sleep and emotional distress due to unrelenting symptoms. There is also a significant economic cost to the healthcare system and an added financial burden of treatment to individuals.⁴

Less common but more severe forms of ocular allergy can threaten vision, such as vernal keratoconjunctivitis (VKC) and atopic keratoconjunctivitis (AKC). A good working knowledge on the spectrum of ocular allergic disease will facilitate GPs in managing routine cases and identifying complex presentations requiring referral for specialist care. Common ocular anatomy and pathology is described in Box 1.

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1. OCULAR TERMINOLOGY

- Chemosis – swelling of the conjunctiva
- Papillae – bumpy elevations and oedema of the conjunctival surface with infiltration by inflammatory cells and eosinophils
- Follicle – focal conjunctival swelling caused by aggregation of T-cells
- Tarsal/palpebral conjunctiva – the conjunctiva lining the inner surface of the eyelid
- Limbus – the anatomical junction of the conjunctiva/sclera and the cornea

Acute allergic conjunctivitis

Acute allergic conjunctivitis occurs at a hyperacute rate and is self-limiting, with resolution typically occurring within 24 hours.² Symptoms result from inoculation of the conjunctival sac by exposure to allergens (Figure 1). Acute allergic conjunctivitis can occur at any age but is most common in childhood. Symptoms include mild to debilitating pruritis, chemosis and periorbital oedema. Tearing, redness, foreign body sensation and mucous discharge may also occur. Occasionally, the eyelids may be swollen shut due to oedema. Acute conjunctivitis is further categorised as seasonal or perennial, with the former being more common. The difference between the two entities is the chronicity of symptoms, dictated by individual patient sensitivity to various allergens. It is important to note that the patient may be asymptomatic at the time of presentation; therefore, it is important to ask about the time of year when symptoms are at their worst.

Seasonal allergic conjunctivitis

Seasonal allergic conjunctivitis is the most common type of ocular allergy.^{5,6} Seasonal symptoms are triggered by fluctuating levels of aerosolised allergens, such as tree or grass pollens. This contrasts with perennial symptoms, which are caused by indoor allergens. The disease is most common in spring and autumn and there is often a history of other atopic diseases, such as eczema, asthma or allergic rhinitis. History-taking and examination should assess for family history of atopic comorbidities, as well as symptoms and signs of other common allergic processes.

Itchy and watery eyes often occur with nasal or pharyngeal symptoms and are a prominent feature in seasonal exacerbations. On examination, the conjunctiva is often mildly injected and may be swollen with low-grade papillary hypertrophy (Figure 1). There can be oedema of the eyelids, which is usually mild and does not diminish the patient's vision. Symptoms are usually bilateral. Pain is not usually a symptom of simple allergic conjunctivitis and should alert the GP to more sinister pathology.

Perennial allergic conjunctivitis

Perennial allergic conjunctivitis is similar to seasonal allergic conjunctivitis but symptoms persist throughout the year. Perennial

Classification of ocular allergic disease

Ocular allergic disease covers a broad group of conditions, as shown in the Table. Simple acute allergic conjunctivitis is either seasonal or perennial. In regard to pathophysiology and treatment, there is considerable overlap with chronic, immune-mediated forms of conjunctivitis (VKC and AKC) and giant papillary conjunctivitis. Despite the similarity in initial treatment, the outcomes and rates of complications differ between subtypes. Assessment of allergic conjunctivitis is described in Box 2 and criteria for diagnosing allergic conjunctivitis are detailed in Box 3. All forms of ocular allergic disease have distinct clinical features and natural histories.

TABLE. CLASSIFICATION OF COMMON OCULAR ALLERGIC DISEASES

Type	Risk factors	Clinical signs	Natural history	Potential sequelae
Seasonal or perennial allergic conjunctivitis	Exposure to environmental allergens: <ul style="list-style-type: none"> • seasonal (tree, grass and weed pollens) • perennial (dust mites, animal dander, mould) 	<ul style="list-style-type: none"> • Bilateral conjunctival injection • Watery discharge • Chemosis 	Seasonal recurrence	Local inflammation that often completely resolves
Vernal keratoconjunctivitis	<ul style="list-style-type: none"> • Exposure to environmental allergens may incite acute exacerbations • genetic predisposition to atopic reactions with comorbid atopic dermatitis and asthma • Spring and summer months • Hot and dry environments • Male sex 	<ul style="list-style-type: none"> • Bilateral conjunctival injection • Watery and mucous discharge • Cobblestone papillary hypertrophy • Limbal Horner-Trantas dots • Vernal plaques • Shield ulcers 	<ul style="list-style-type: none"> • Onset during childhood • Peaks in early teenage years • Symptoms decrease with age 	<ul style="list-style-type: none"> • Conjunctival scarring • Corneal scarring, neovascularisation, ulceration and infection • Eyelid thickening • Ptosis • Keratoconus
Atopic keratoconjunctivitis	<ul style="list-style-type: none"> • genetic predisposition to atopic reactions with comorbid atopic dermatitis and asthma • Winter months • Male sex 	<ul style="list-style-type: none"> • Bilateral conjunctival injection • Conjunctival oedema • Watery or mucous discharge • Eyelid eczema ± scaling and cracking of periocular skin • Papillary hyperplasia of superior or inferior tarsal conjunctiva 	<ul style="list-style-type: none"> • Onset during childhood • Peaks in young adult years • Continues into the patient's fifth decade of life 	<ul style="list-style-type: none"> • Conjunctival scarring • Corneal scarring, neovascularisation, ulceration and infection • Distortion of the tear film • Eyelid thickening or tightening • Punctate keratitis • Loss of eyelashes • Cataracts • Keratoconus • Retinal detachment • Herpetic ocular infection
giant papillary conjunctivitis*	<ul style="list-style-type: none"> • Wearing of contact lenses, with poor hygiene or prolonged use • Wearing of ocular prostheses 	Papillary hypertrophy of superior tarsal conjunctiva with a fibrotic centre	<ul style="list-style-type: none"> • Directly associated with presence of risk factors • Most common in teens and young adults 	Acquired ptosis

* A repetitive mechanical irritation aggravated by concomitant allergy (not a true ocular allergy).

Adapted from Hernández-Sánchez MC, Montero J, Rondon C, et al. *J Invest Allergol Clin Immunol* 2015; 25: 94-106.⁵

allergic conjunctivitis is due to chronic exposure of the eyes to allergens, such as house dust mites, animal dander, mould spores, rodents and feathers. Seasonal exacerbations are common, which can make it challenging to distinguish from seasonal conjunctivitis.⁶

Vernal keratoconjunctivitis

VKC is a more severe form of ocular allergy and, in rare cases, can lead to vision loss. VKC is also known as 'spring catarrh' and is clinically distinct from perennial or seasonal allergic conjunctivitis. The aetiology is not well understood but is thought to be due to a combination of climate and allergen

exposure. It is more common in males than females (3:1) and children under 10 years of age. About 50% of patients who experience VKC have a coinciding history of asthma or atopy. VKC exhibits seasonal variation, is more severe in arid dry climates and has a clinical course of two to 10 years. Many patients have complete resolution without any symptoms after adolescence; however, about 5% of patients will develop AKC.⁵

In VKC, patients experience intense itching, photophobia and tearing. Clinical signs include a rosy, mucous discharge, upper eyelid swelling with large cobblestone-like papillae of the superior palpebral conjunctiva visible on lid eversion (Figure 2)

and Horner-Trantas dots (off-white deposits at the limbus that consist of eosinophils and cellular debris).

Corneal involvement may occur in severe cases, which is caused either by inflammatory mediators produced by eosinophils or by direct mechanical trauma of the inflamed papillary changes on the conjunctival surface. Corneal involvement ranges from a mild punctate keratitis to a shield ulcer (named for its shape). Shield ulcers can scar and commonly require debridement by an ophthalmologist. Patients often require specific therapy that may include topical corticosteroids, topical ciclosporin or sub tarsal triamcinolone to

2. CLINICAL ASSESSMENT OF ALLERGIC CONJUNCTIVITIS²

- Typical ocular or systemic symptoms of allergy, particularly itch
- Strong personal or family history of IgE-mediated diseases
- Exposure/environment history
- Recurrent intermittent or persistent symptoms
- The upper eyelids should be everted to assess appearance (lid oedema, ptosis, watery eye, sclera injection, conjunctival chemosis, and corneal clarity may all be observed without a slit lamp)
- Skin prick tests or in-vitro specific IgE tests to identify causative allergens
- Conjunctival scrapings for eosinophils is rarely necessary, but may be helpful

reduce conjunctival papillary inflammation, so early referral is imperative. VKC may be associated with the development of keratoconus, particularly due to chronic eye rubbing.⁷ Patients should be strongly advised against rubbing their eyes.

Atopic keratoconjunctivitis

AKC is a chronic, bilateral conjunctivitis associated with atopic dermatitis of the eyelids. Of the 3% of the population with atopic dermatitis, up to 25% will develop some degree of ocular involvement. A correct diagnosis of this condition is important as it can be associated with significant ocular morbidity.⁸

AKC usually occurs in patients between 30 and 50 years of age. It is also more common in men and tends to be perennial, with



Figure 2. Cobblestone papillae in a patient with vernal keratoconjunctivitis.

3. CLINICAL CRITERIA FOR SUSPICION OF SEASONAL OR PERENNIAL ALLERGIC CONJUNCTIVITIS⁵

Bilateral conjunctival hyperaemia and pruritis, with ≥ 3 of the following:

- ocular symptoms associated with exposure to suspicious allergens
- association with other allergic diseases (e.g. rhinitis, asthma, atopic dermatitis)
- response to topical pharmacologic therapy (e.g. antihistamines, mast-cell stabilisers, dual-action agents)
- absence of giant papillary conjunctivitis*
- absence of corneal involvement (e.g. Horner-Trantas dots)

* A repetitive mechanical irritation aggravated by concomitant allergy (not a true ocular allergy).

potential exacerbations in winter. Severe itching of both the ocular surface and eyelids is the hallmark symptom and may be debilitating. Clinical signs in the skin usually precede ocular involvement and include significant hyperaemia and oedema of the conjunctiva, scaling and cracking of the periocular skin and fine papillary hyperplasia (which tends to be more marked in the inferior regions). Corneal scarring and neovascularisation can occur in severe cases due to corneal inflammation, as well as disturbance of the tear film, subconjunctival scarring and distortion of the lid margin.

About 5 to 10% of patients with AKC will develop a cataract as a result of their condition.⁸ These patients are also at risk of other ocular disorders, such as keratoconus, retinal detachment and herpetic ocular infection.

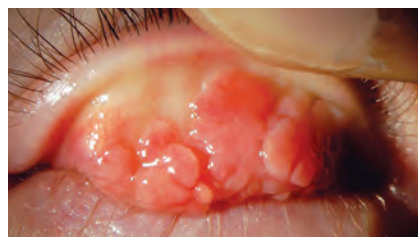
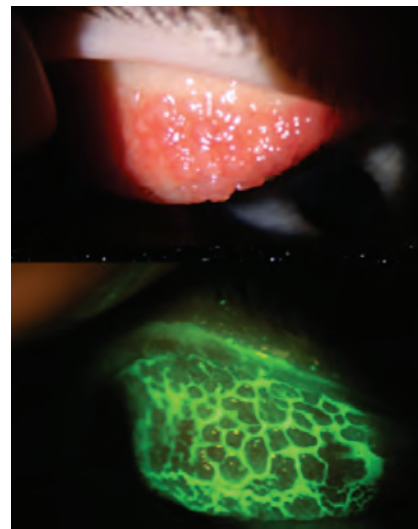


Figure 3. giant papillae in an infant due to the long-term use of aphakic lenses following congenital cataract surgery.



Figures 1a and b. Papillary hypertrophy in a patient with acute allergic conjunctivitis (a, top). Fluorescein staining and ultraviolet light view of the same patient's eye (b, bottom).

Giant papillary conjunctivitis

Giant papillary conjunctivitis occurs most commonly in teens and young adults, usually due to long-term contact lens use. The reaction of the superior tarsal conjunctiva to chronic exposure of contact lenses or foreign bodies results in papillary hyperplasia (Figure 3). It may also occur with ocular prostheses or following ocular surgery due to filtration blebs or loose or eroding sutures. Symptoms include itching, tearing, increased mucous production and ocular discomfort.

Differential diagnoses

The causes of an acute red eye are varied (Box 4). Itch is the hallmark symptom of all ocular allergies. Any patient with uncontrolled ocular pain or reduced vision warrants an urgent referral to an ophthalmologist, as these symptoms may suggest raised intraocular pressure from acute glaucoma, inflammation from uveitis or an infection of the cornea (e.g. microbial keratitis). Infections are particularly common in contact lens wearers.⁵ The use of topical corticosteroids should be avoided in patients with an acute, red eye, unless comanaged with an ophthalmologist and especially if there is any suspicion of infection.^{3,5}

Pathogenesis of ocular allergy

The ocular mucosa has a large surface area, mainly composed of the palpebral and bulbar conjunctiva. It is one of the most exposed and accessible sites with a dense population of mast cells and lymphocytes, allowing direct antigen deposition and leading to the initiation of the allergic cascade.

Seasonal allergic conjunctivitis and perennial allergic conjunctivitis are the only ocular conditions known to involve solely type 1 hypersensitivity reactions. In individuals who have previously been sensitised, immune cells release inflammatory cytokines that stimulate immunoglobulin E (IgE) production by B cells, resulting in the IgE binding to mast cells. Subsequent cross-linking by allergens triggers mast-cell degranulation and release of histamine and other inflammatory mediators. Airborne allergens typically contact the conjunctiva via the tear film. The early phase of the allergic cascade usually begins within seconds to minutes after allergen exposure and will clinically last 20 to 30 minutes.^{2,6,8} These changes

result in vasodilation, oedema and the recruitment of other inflammatory cells (e.g. eosinophils). The late phase begins a few hours later. Activation of the cyclooxygenase pathway and lipoxygenase pathway triggers the release of prostaglandins, thromboxanes and leukotrienes, which attract additional inflammatory cells, leading to continued inflammation, persistent symptoms and increased changes associated with tissue damage. Progression results in hypersecretion of tears that increases drainage through the lacrimal ducts, carrying allergens directly into the nasal passage.

AKC and VKC involve a more complex pathogenesis of mixed type 1 and type 4 (cell-mediated) hypersensitivity.^{2,6-8} There are published reports of their association with IgE-mediated atopic disease but the association is not necessarily causal.² There is a plethora of increased cytokines and chemokines in VKC and AKC compared with seasonal allergic conjunctivitis and giant papillary conjunctivitis.¹¹ There is florid infiltration of CD4 T-cells, eosinophils and mast cells, which leads to

4. COMMON CAUSES OF A RED EYE

Allergies

- Acute
 - seasonal allergic conjunctivitis
 - perennial allergic conjunctivitis
- Chronic
 - vernal keratoconjunctivitis
 - atopic keratoconjunctivitis
 - giant papillary conjunctivitis

Infections

- Viral infection
- Bacterial infection
- Other (e.g. fungal infection)

Immune disorders

- Intraocular disorder (uveitis)
- Extraocular disorder (e.g. episcleritis, scleritis)

Nonspecific causes

- Dry eye
- Rosacea
- Foreign body in the eye
- Chemical injury
- Medication
- Vasomotor disorder

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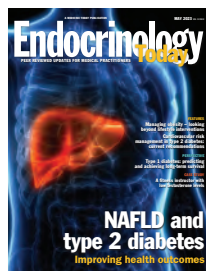
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5. THERAPIES FOR ALLERGIC EYE DISEASE

Minimisation strategies

- Sunglasses as a barrier to airborne allergens
- Hypoallergenic bedding
- Sheets washed in hot water (to denature allergenic proteins such as dust mite faeces)
- Animal exposure minimised (if implicated)
- Allergic consultation may be of benefit to identify specific allergens, for a systemic review of atopic disease and for consideration of immunotherapy, which may benefit selected patients with seasonal and perennial allergic conjunctivitis^{9,10}
- Immunotherapy does not benefit patients with vernal or atopic keratoconjunctivitis

Nonpharmacological therapies

- Cool compresses – to alleviate itch
- Avoidance of allergens
- Avoidance of eye rubbing – can traumatise conjunctiva and release inflammatory mediators
- Pollution avoidance and climate control – air conditioning might be of benefit particularly with vernal keratoconjunctivitis, which is exacerbated by heat
- Artificial lubricants to dilute allergens and inflammatory mediators, and to lessen mechanical trauma. Avoid preservatives in eye drops where possible
- Refrigeration of eye drops may enhance the subjective relief of symptoms

Pharmacological therapies*

- Topical ocular therapies – antihistamines, vasoconstrictors, mast-cell stabilisers, NSAIDs, dual-activity agents, corticosteroids, ciclosporin
- Oral antihistamines
- Nasal topical corticosteroids
- Systemic or local depot corticosteroids (ophthalmologist use only)
- Immunotherapy (ophthalmologist use only)

* Specialist advice should be sought for children 3 years of age and under.

chronic inflammation with fibrosis and tissue destruction.

Giant papillary conjunctivitis is not a true ocular allergy but is instead a repetitive

mechanical irritation aggravated by concomitant allergy. Mixed populations of inflammatory cells are produced in response to a foreign body, with elements of a hypersensitivity reaction and chronic inflammation. However, the reaction usually resolves after the inciting foreign body is removed.

Treatment

Treatment of allergic eye disease involves a stepwise approach of minimisation strategies, nonpharmacological interventions and pharmacological treatments (Box 5). Although initial treatments are often empiric, selecting therapies that are tailored to the patient's symptoms can improve adherence and the response to treatment. Specialist advice should be sought for the treatment of children under 3 years of age as most pharmacological treatments for allergic conjunctivitis are contraindicated in this age group. All patients should be educated about good general eye care for allergic conditions and discouraged from rubbing their eyes, as it causes mast-cell degranulation and worsening of symptoms.¹² Patients should also be advised to frequently apply artificial tears and cool compresses. Known allergen exposures should be avoided and contact lenses should be removed (if applicable). Patients should be asked about allergies to cosmetics and other eye medications and the use of low allergenic cosmetics can be helpful.

Patients with giant papillary conjunctivitis will respond best to the removal of the offending foreign body, in conjunction with the measures described in Box 5. If the patient's condition is related to chronic contact lens use, changing the lens type or the cleaning solution can be beneficial. Patients should be recommended to have a break from wearing contact lenses.

Antihistamines

Both topical and oral antihistamines can be used with good effect. First-generation oral antihistamines should be avoided as they produce anticholinergic side effects, such as confusion, sedation, urinary retention, constipation, dry eyes and dry mouth.⁵

Topical antihistamines target the ocular tissues directly and, as such, have a faster onset of action and are better tolerated with fewer side effects. Mild symptoms of itch and erythema are relieved with regular instillations of drops (up to four times a day). Improved control can be achieved by a combination of short-term topical vasoconstrictive and antihistamine therapies, such as naphazoline plus antazoline, naphazoline plus pheniramine or naphazoline plus hamamelis extract. It is important to note that chronic use of vasoconstrictors can lead to tachyphylaxis and rebound hyperaemia or vasodilation when discontinued.⁵

Topical mast-cell stabilisers and dual-activity agents

Topical dual-activity agents have the combined properties of antihistamines and mast-cell stabilisers. They are clinically superior to and better tolerated than topical mast-cell stabilisers or antihistamines, alone, and should be considered first-line treatment. Immediate relief is provided by antihistamines and prophylactic effects are achieved by mast-cell stabilisers, with some inhibition of eosinophil migration and other mediators of inflammation.^{3,12} Dual-activity agents have largely replaced topical mast-cell stabilisers alone, such as levocabastine, sodium cromoglycate and antihistamines. They are best used on a prophylactic basis and require a loading period of several weeks prior to allergen exposure.

Olopatadine and ketotifen have multiple actions as mast-cell stabilisers, anti-inflammatory agents and selective H1-antagonists. Olopatadine 0.1% and ketotifen 0.025% are the mainstays of treatment for most ocular allergic diseases and their use is supported by extensive clinical research and experience. Ocular surface toxicity can occur in rare cases due to benzalkonium chloride (a surfactant preservative), so drops should be instilled 30 minutes prior to contact lens use or after removal and should not be applied while the patient is wearing contact lenses.³ Ketotifen is also available in a preservative-free form.

6. AUSTRALIAN TGA CATEGORIES FOR PRESCRIBING IN PREGNANCY²⁰

- **Category A** – no observed increase in harm to fetus, in a large number of women
- **Category B1** – no observed increase in harm to fetus, in a small number of women or in animal studies
- **Category B2** – no observed increase in harm to fetus, in a small number of women or in a small number of animals
- **Category B3** – no observed increase in harm to fetus, in a small number of women; however, some fetal damage has been observed in animals and its significance in humans is uncertain
- **Category C** – observed harm to fetus in humans, though without malformation and where effects may be reversible
- **Category D** – observed harm to fetus in humans, including malformation or irreversible damage
- **Category X** – high risk of harm to fetus in humans, not to be used in pregnancy or where there is a possibility of pregnancy

Olopatadine and ketotifen alleviate acute itch and prevent mast-cell degranulation as a delayed effect after one to two weeks of use.⁶ The symptoms of seasonal allergic conjunctivitis and perennial allergic conjunctivitis are often controlled with these agents alone. Olopatadine and ketotifen can be used safely throughout the year in patients with perennial allergic conjunctivitis or AKC and can be discontinued over autumn and winter in patients with seasonal allergic conjunctivitis and VKC.

There are no conclusive data in randomised controlled trials to suggest clinical superiority of olopatadine over ketotifen, or vice versa. Alcaftadine, a newer topical antihistamine that is not yet available in Australia, has shown superiority to olopatadine in reducing ocular itch.¹³

Topical NSAIDs

Topical NSAIDs may be useful when the patient's symptoms are inadequately controlled despite the use of dual-activity

agents or when the prescription of topical corticosteroids is not suitable. Topical NSAIDs inhibit the production of prostaglandins by blocking the cyclo-oxygenase pathway in IgE-mediated allergic responses. The main benefit is the temporary relief of severe symptoms of discomfort. Examples of topical NSAIDs used in ocular allergies include ketorolac trometamol, diclofenac sodium and nepafenac. These drugs can reduce histamine-invoked pruritus, ocular itch and hyperaemia associated with seasonal allergic conjunctivitis.⁶ Unlike corticosteroid agents, they do not mask ocular infection, affect wound healing or increase intraocular pressure. They may have an analgesic effect but can cause significant irritation due to toxicity and superficial keratitis, particularly in patients with a compromised ocular surface.¹⁴ Corneal melting, leading to corneal perforation and vision loss, is rare with the use of topical NSAIDs.¹⁵

Topical corticosteroids

Corticosteroids can treat allergic conjunctivitis by reducing cytokine production, mast-cell proliferation, and cell-mediated immune responses. Although effective, they are recommended for short-term treatment only due to the risk of cataract development, elevated intraocular pressure, ocular infection, corneal stromal melting and delayed healing.³ Their use should be restricted to short periods of two to three weeks and only when the diagnosis is certain. Topical corticosteroids should be prescribed under the supervision of administration by an ophthalmologist for the monitoring of potential side effects and the patient's response to therapy.

Topical corticosteroids (e.g. fluorometholone, dexamethasone and prednisolone) are prescribed in conjunction with dual-activity agents when symptoms and signs are severe or unresponsive to conventional treatment. They are most useful for the control of VKC and AKC and are rarely indicated in the treatment of acute seasonal or perennial allergic conjunctivitis.²

Corticosteroids may also be administered

systemically or as a local, subconjunctival depot injection in cases of uncontrolled VKC or AKC that require administration by ophthalmologist. Intranasal corticosteroids used for allergic rhinitis (e.g. fluticasone) have been shown to have positive effects on some ocular allergic symptoms compared with placebo.³

Other immunomodulating agents

Severe and chronic cases of allergic ocular disease that do not respond to conventional therapies may require other immunomodulating agents. The WHO recommends allergen-specific immunotherapy as an effective approach in patients with allergic diseases, such as rhinoconjunctivitis and asthma.^{2,5} Specialist supervision is imperative. Topical ciclosporin 0.05% or newer high-dose formulations (e.g. ciclosporin 0.09% or ciclosporin 0.1%) are potent steroid-sparing agents and may be useful for AKC and VKC as they are T-cell-driven, chronic inflammatory processes.⁶ Controlled trials of topical 0.05% topical ciclosporin A have demonstrated clinical safety and improvement in signs and symptoms of AKC and VKC.^{16,17} These medications are PBS listed for chronic severe dry eye disease with keratitis in patients aged 18 years and older and can only be prescribed by an ophthalmologist or optometrist. Dosages can be increased if the patient becomes resistant to lower doses. Systemic ciclosporin has a significant side effect profile, but can be used as a steroid-sparing agent in selected patients.

Monoclonal antibodies

Although not approved for allergic eye disease, monoclonal antibodies for other systemic allergic disorders (e.g. omalizumab) can provide significant relief of ocular symptoms in some patients with allergic conjunctivitis.^{3,18} Research into newer monoclonal antibodies for allergic conjunctivitis is promising, with several Phase 1b studies showing favourable outcomes. However, various adverse ocular symptoms have also been observed in clinical trials and off-label use studies.¹⁹

Ocular allergies in pregnancy

There are no adequate well-controlled studies in pregnant and breastfeeding women for the use of most ophthalmic antihistamines; however, olopatadine and ketotifen are listed under pregnancy category B1 and both can be used during breastfeeding. The topical corticosteroid fluorometholone is listed under pregnancy category B3, but stronger topical corticosteroids are pregnancy category C. TGA categories for prescribing in pregnancy are outlined in Box 6.²⁰

When to refer

Patients should be referred urgently to an ophthalmologist in the following scenarios:

- the patient experiences any reduction in vision
- the diagnosis of a red eye is uncertain
- there is a poor response to recommended supportive measures, such as artificial tears or lubricants and antihistamines or vasoconstrictors, or mast-cell stabilisers
- the severity of allergic disease is significant enough to warrant the consideration of topical corticosteroids
- the patient has a vision-threatening diagnosis, such as AKC, VKC or giant papillary conjunctivitis.

An allergist should be involved early to assess for systemic atopic conditions, identify offending allergens (with or without patch testing) and consider immunotherapy in severe cases of perennial allergic conjunctivitis and seasonal allergic conjunctivitis that are unresponsive to conservative measures.

Conclusion

Allergic eye diseases are highly prevalent in Australia but continue to remain underdiagnosed and undertreated with patients presenting late after failing conservative measures. There are many pharmacological options available and the choice of therapy should be tailored to the individual patient. Potent topical mast-cell stabilisers have greatly improved the

management of allergic conjunctivitis. GPs, ocular specialists and allergists can work collaboratively to optimise patient management and prevent vision-threatening complications from more severe forms of allergic disease and from the inappropriate use of corticosteroids. **MT**

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