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Allergic conjunctivitis. How to alleviate symptoms. The perspective of an allergist and ophthalmologist

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HIGHLIGHTS

Treatment of allergic eye diseases initially involving allergen avoidance and artificial tears, preparations containing ectoine and hyaluronic acid, and secondarily, topical antihistamines, such as azelastine. In severe cases, topical corticosteroids are used under the supervision of an ophthalmologist.

ABSTRACT

Allergic ocular diseases, such as seasonal (SAC) and perennial (PAC), are common, estimated to affect 14–45% of the general population, yet are often underdiagnosed and inadequately treated. Diagnosis is based on the history and the presence of symptoms such as itching, tearing, congestion, watery discharge, and discomfort, as well as a physical examination. Infections, especially viral infections, should be considered in the differential diagnosis. Skin prick testing and/or specific IgE testing are helpful in diagnosing the allergen and potentially initiating specific immunotherapy, the sole causal treatment. Symptomatic treatment of alergic ocular diseases is gradual, with the goal of symptom control and improved quality of life. The first step is allergen avoidance and non-pharmacological interventions (cold compresses, artificial tears – preferably preservative-free). In mild cases, a preparation combining ectoine and hyaluronic acid can be effective, stabilizing the tear film and reducing inflammation, while being safe for children and pregnant women. The second step includes topical medications (H_1 receptor blockers and mast cell stabilizers) and oral second-generation antihistamines (LH_1). Azelastine (topical) deserves consideration due to its strong affinity for H_1 receptors and dual antiallergic mechanism (rapid relief, convenient dosing). Oral LH_1 is recommended to be initiated two weeks before the pollen season in the SAC. In more severe cases (third step), topical glucocorticosteroids (GCs) are used, always under the supervision of an ophthalmologist. Fludrocortisone acetate ointment is the only GC in this form approved for the treatment of allergic conjunctivitis and blepharitis. Intranasal GCs can alleviate ocular symptoms via the nasal-ocular reflex, especially in concomitant allergic rhinitis. In SAC and PAC, ophthalmological consultation is not usually required, but in other forms of allergic ocular diseases, cooperation is essential.

Key words: allergic eye diseases, itching, tearing, congestion, watery discharge, discomfort, artificial tears, preparations containing ectoine and hyaluronic acid, topical antihistamines, topical corticosteroids

INTRODUCTION

Allergic eye diseases represent one of the most common manifestations of hypersensitivity and are frequently encountered in clinical practice. At the same time, allergic inflammation is among the most prevalent ocular disorders, occurring most commonly in late childhood and early adulthood.

Allergic inflammation is triggered by exposure to allergens (primarily airborne) and typically involves the conjunctiva (the membrane lining the inner surface of the eyelids and the outer surface of the eyeball), as well as the cornea. Less frequently, it may also affect the eyelid skin, uveal tract, sclera, and optic nerve. The prevalence of allergic diseases is estimated at 15–20% in developed countries; however, some studies suggest that in European populations it may affect up to 50% of individuals.

The prevalence of allergic eye diseases has been increasing worldwide over the past several decades [1]. Seasonal and perennial allergic conjunctivitis (PAC) (the most common forms of allergic eye diseases) may affect between 14% and as many as 45% of the general population, depending on the geographic region. In Europe, allergic eye diseases are estimated to affect approximately 25% of children [2, 3]. Seasonal allergic conjunctivitis (SAC) is the most common form, accounting for 25–50% of all allergic eye diseases. At the same time, allergic eye diseases are considered an underdiagnosed and consequently undertreated health problem. It is estimated that only about 10% of patients with allergic ocular symptoms seek medical attention; the majority rely on over-the-counter (OTC) medications and adjunctive non-pharmacological measures.

Like other forms of allergic disease, allergic ocular conditions significantly affect quality of life in children, including academic performance and examination outcomes. In addition, they may contribute to behavioral disturbances such as irritability, fatigue, and reduced concentration.

Currently, the following hypersensitivity-related ocular surface disorders are distinguished:

1. Allergic hypersensitivity disorders:
   a. type I hypersensitivity mediated by IgE, Th2 cells, and ILC2 – seasonal, perennial, and acute allergic conjunctivitis
   b. combined type I hypersensitivity and cell-mediated hypersensitivity (types IVa and IVb, less commonly IVc) – vernal keratoconjunctivitis and atopic keratoconjunctivitis
   c. type IVc and type V hypersensitivity – contact conjunctivitis and blepharitis.
2. Epithelial barrier dysfunction with mixed Th2/Th17 responses: giant papillary conjunctivitis, ocular surface disease associated with dupilumab, urban eye allergy syndrome.
3. Non-allergic hypersensitivity: irritative conjunctivitis (and blepharitis).

Allergic conjunctivitis accounts for approximately 98% of all allergic eye diseases. The following clinical entities are distinguished:

1. **Acute allergic conjunctivitis (AAC)** – a conjunctival hypersensitivity reaction following exposure to a high concentration of an allergen (e.g., animal dander, pollen, medications, or preservatives); symptoms typically persist for 24–48 h.
2. **Intermittent allergic conjunctivitis (IAC), also referred to as seasonal allergic conjunctivitis (SAC)** – a conjunctival hypersensitivity reaction occurring seasonally in individuals sensitized to airborne allergens such as grass, tree, or weed pollens.
3. **Persistent (perennial) allergic conjunctivitis (PAC)** – a chronic conjunctival hypersensitivity reaction occurring throughout the year in individuals sensitized to perennial allergens (e.g., house dust mites, molds, domestic animals).
4. **Occupational allergic conjunctivitis (OAC)** – clinically similar to PAC; symptoms occur or are exacerbated following exposure to workplace allergens.

ALLERGIST'S PERSPECTIVE

In clinical practice, allergists most frequently encounter two forms of allergic eye diseases, accounting for up to 95% of all cases [4]:

1. **Seasonal allergic conjunctivitis (SAC)** – an IgE-mediated conjunctival hypersensitivity reaction, most commonly associated with sensitization to tree and grass pollens. It is characterized by typical allergic symptoms and is often accompanied by seasonal allergic rhinitis (SAR). In cases of exposure to a high concentration of

allergens within the conjunctival sac or as a result of a toxic reaction to irritants, acute allergic conjunctivitis (AAC) may develop, with rapid onset (within minutes) and severe symptoms.

2. **Perennial allergic conjunctivitis (PAC)** – characterized by chronic symptoms that are generally less severe than those observed in SAC. PAC is associated with sensitization to perennial allergens such as house dust mites, animal dander, fungi, and occasionally latex. Symptoms are typically mild but may worsen with prolonged or intense allergen exposure. Pruritus – the most characteristic symptom – may vary in intensity and localization, ranging from generalized itching of the eyelid skin and conjunctiva to localized itching, particularly at the medial and lateral canthi.

Diagnostics

As patients are often referred to an allergist without a definitive diagnosis, the first step is to confirm the preliminary clinical suspicion.

The diagnosis of allergic eye diseases, as with other manifestations of allergic conditions, is based on medical history and physical examination. The history should focus on identifying typical symptoms of allergic conjunctivitis, including conjunctival hyperemia, intense pruritus, tearing, discharge (most commonly watery), ocular discomfort, and occasionally pain. In rare cases, allergic inflammation may occur without pruritus, which is otherwise considered a sine qua non symptom of allergic conjunctivitis.

Visual acuity is usually unaffected, although impairment may occur in more severe forms. A detailed clinical history is essential, as symptoms may be seasonal (SAC), intermittently exacerbated (PAC), or associated with exposure to allergens or irritants (AAC). The presence or suspicion of other allergic conditions – particularly allergic rhinitis, asthma, or atopic dermatitis (often manifesting in infancy or early childhood) – supports the diagnosis of allergic eye diseases.

Attention should also be given to risk factors, including exposure to high concentrations of aeroallergens and occupational allergens.

Physical examination and additional diagnostic tests

The physical examination should focus on identifying typical signs of allergic conjunctivitis (AC) and is best performed during periods of symptom exacerbation (particularly important in SAC and AAC). Evaluation should include the eyelids, conjunctiva, cornea, and the nature of ocular discharge. Assessment of ocular motility and visual acuity may also aid in differential diagnosis. Findings such as eyelid edema, conjunctival injection and hyperemia, and watery discharge support the diagnosis of AC. In the presence of atypical findings or diagnostic uncertainty, referral to an ophthalmologist is recommended.

As noted, the diagnosis is primarily based on medical history and physical examination; however, additional investigations may be helpful in selected cases. Skin prick testing and/or measurement of allergen-specific IgE (using allergen extracts or molecular components) to suspected aeroallergens fall within the scope of the allergist's expertise. These tests aim to identify the causative allergen and may guide the initiation of allergen-specific immunotherapy.

Differential diagnosis

In the differential diagnosis, infectious conjunctivitis (viral and bacterial) should be primarily considered due to the distinct therapeutic approaches required. Viral infections, in particular, may be especially challenging to differentiate (tab. 1) [5].

Therapeutic management

The primary goal of treatment in allergic eye diseases is to alleviate and control symptoms and improve quality of life. Allergic conjunctivitis should not interfere with normal functioning, behaviour, or academic and professional performance, particularly in children [4–8].

An additional objective is the prevention and suppression of inflammation, especially in patients with prolonged or continuous allergen exposure. Multiple therapeutic options are available for the management of allergic eye diseases, and the choice of treatment depends on several factors [4]:

TABLE 1

Differential diagnosis of the most common ocular conditions.

Disease	History	Pruritus	Pain	Discharge	Conjunctiva	Laterality
SAC, PAC	Allergic history	+++	–	Watery	Superficial hyperemia	Bilateral
Bacterial conjunctivitis	Contact with infected individuals; upper respiratory tract infection	+/-	+	Purulent	Superficial or ciliary injection	Initially unilateral
Viral conjunctivitis	Contact with infected individuals; upper respiratory tract infection	–	+	Watery, mucoid	Superficial or ciliary injection	Predominantly unilateral
Blepharitis	–	–	–	Foamy discharge at eyelid margins	No significant changes	Bilateral

SAC – seasonal allergic conjunctivitis; PAC – perennial allergic conjunctivitis.

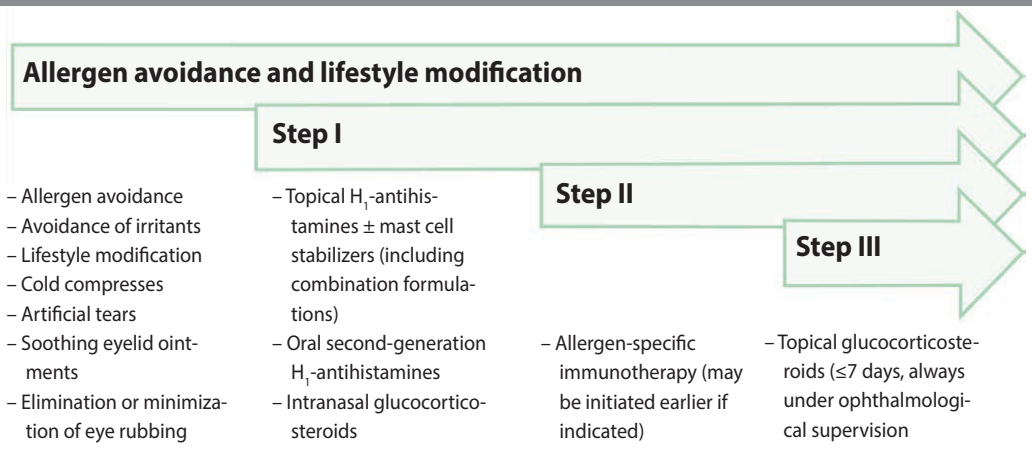
1. Severity of allergic symptoms – the presence or absence of corneal involvement is a key determinant.
2. Disease pattern – SAC: intermittent with complete remissions or chronic with seasonal exacerbations; PAC: chronic, often severe.
3. Nature of inflammation – acute onset, chronic continuous, or acute-on-chronic course.
4. Type of allergic manifestation – SAC, PAC, vernal keratoconjunctivitis (VKC), atopic keratoconjunctivitis (AKC), as well as coexisting allergic conditions.
5. Patient age and expected disease duration.
6. Adverse effects of previous treatments – such as corticosteroid response or cataract formation.
7. Comorbid conditions – including glaucoma, cataract, keratoconus, and corneal scarring.
8. Impact of the disease on daily functioning and quality of life.

Depending on the nature and severity of the allergy, a stepwise therapeutic approach is recommended (fig. 1).

1. **Non-pharmacological therapy** – aimed at symptom relief. This may include: cold compresses applied to the eyes (water or saline may alleviate pruritus), artificial tears (to rinse out allergens, inflammatory mediators, and irritants).
   A crucial component of management is the avoidance of allergens and irritants through modification of lifestyle and daily habits. Some authors recommend washing the hair before bedtime to reduce exposure to accumulated allergens and irritants. It is particularly important to eliminate or minimize eye rubbing, especially in children (soothing ointments applied to the eyelids may be helpful).
   Patient education remains an essential element of therapy. A therapeutic option worth considering in this context is the use of ophthalmic solutions that alleviate irritation and provide symptomatic relief in daily life. These products contain ectoine – a natural molecule with cytoprotective properties that stabilizes cell membranes and reduces inflammation. Hyaluronic acid, an additional component, has a high water-binding capacity, ensuring prolonged hydration of the ocular surface, thereby improving visual comfort and protecting against irritation. Moreover, these formulations stabilize the natural tear film through a dual mechanism: hyaluronic acid enhances the aqueous layer, while ectoine supports the lipid layer. This complementary mode of action may protect against the harmful effects of allergens and other environmental factors and support the regeneration of the irritated and sensitive conjunctiva.
   It is important that such ophthalmic preparations are preservative-free, as preservatives may induce or exacerbate allergic reactions. These formulations may be administered once or twice daily, or more frequently as needed, without strict dosing limitations. They are generally considered safe for use across all age groups, as well as in pregnant and breastfeeding women. This dual mechanism of action–providing both hydration and protective effects – represents a valuable adjunct to pharmacological therapy.
2. **Pharmacological therapy** – targeting the underlying inflammatory process. The following options are available to the allergist:
   a. Topical (conjunctival) medications [4, 7]:
      – Antihistamines (H_1-receptor antagonists) and mast cell stabilizers (often available as combination formulations) – these represent the mainstay of therapy. Among the available agents, azelastine has been shown to exhibit high affinity for H_1 receptors and a rapid onset of action. In addition, it exerts a dual antiallergic mechanism by inhib-

FIGURE 1

Stepwise management algorithm for allergic conjunctivitis [5].



iting histamine release as well as the synthesis and release of other inflammatory mediators. It provides rapid symptom relief – within minutes after administration – and its convenient dosing regimen (one drop twice daily) may improve patient adherence.
- Topical glucocorticosteroids – reserved for more severe forms of allergic eye diseases and should be prescribed under ophthalmological supervision.
- Nonsteroidal anti-inflammatory drugs (NSAIDs) – recommended particularly in atopic keratoconjunctivitis (AKC) and vernal keratoconjunctivitis (VKC); they reduce conjunctival hyperreactivity and may contribute to mast cell stabilization. They are typically used under ophthalmological supervision.

b. Systemic medications: second-generation antihistamines (first-line agents in allergic diseases – recommended by allergists, particularly in SAC and PAC) and immunosuppressive agents (used in VKC and AKC, prescribed under ophthalmological supervision). In addition, intranasal glucocorticosteroids may be used. Through the naso-ocular reflex, they may exert beneficial effects on ocular symptoms of allergy; examples include fluticasone furoate, mometasone furoate, and triamcinolone acetonide.

3. **Allergen-specific immunotherapy** – the only causal treatment modality. This approach is highly effective and, in Poland, may be initiated, administered, and monitored exclusively by allergists. In the most common forms of allergic eye diseases (SAC, PAC, AAC), ophthalmological consultation is not usually required. In other forms, coordinated management and close collaboration between the allergist and ophthalmologist are essential.

Prevention

Regular follow-up is recommended in patients with chronic allergic eye diseases (every 2–3 months or more frequently if required), while in patients with intermittent forms, visits should be scheduled before and during the pollen season. The visual analogue scale (VAS) may be used to monitor disease severity and treatment response.

Exacerbations should always be addressed promptly by intensifying treatment and identifying potential triggering factors. In patients with seasonal allergic conjunctivitis (SAC), initiation of oral H_1-antihistamines is recommended approximately 2 weeks prior to the anticipated pollen season [5, 8].

OPHTHALMOLOGIST'S PERSPECTIVE

The first symptoms of allergic conjunctivitis may occur at any age, including in young children and elderly patients; however, they most commonly appear after puberty in girls and before puberty in boys. Allergic inflammation frequently involves the ocular surface and surrounding tissues, largely due to continuous exposure to environmental factors, including allergens. The primary subjective symptom is ocular pruritus. A history of allergic rhinitis, asthma, or other allergic conditions – either in the patient or among family members – is often present.

Objective findings include dilation of superficial vessels of the bulbar conjunctiva, papillary reaction of the palpebral conjunctiva (predominantly the upper eyelid), watery or mucous discharge, and edema of the bulbar conjunctiva or eyelid skin. Periocular skin changes, such as airborne contact dermatitis, may also be observed. Symptoms are typically bilateral, although they may be more pronounced in one eye.

The goal of treatment is rapid symptom resolution with the lowest possible risk of adverse effects, thereby ensuring optimal quality of life.

In the differential diagnosis, the following conditions should be considered:
- other ocular surface diseases associated with allergic or non-allergic hypersensitivity
- conjunctivitis of viral, bacterial, or chlamydial origin
- dry eye disease
- rosacea
- ocular pemphigoid
- blepharitis
- seborrheic skin changes affecting the face and eyelids.

Ectoine

In the management of allergic eye diseases, the initial step – following identification of the causative factor and implementation of preventive measures – is the use of artificial tears. These agents help remove allergens from the ocular surface and stabilize the tear film, which is disrupted in most forms of allergic ocular inflammation. Currently, hyaluronic acid-based formulations are most commonly used. This substance hydrates the ocular surface, enhances the stability of the precorneal tear film, and alleviates irritation. Ectoine is a cyclic amino acid naturally produced by extremophiles – microorganisms that thrive in harsh environmental conditions (e.g., deserts). It enables these organisms to withstand extreme temperatures, high salinity, and ultraviolet radiation. Its biological role involves the protection of proteins and intracellular structures.

Ectoine stabilizes biomolecules and epithelial cells, protecting them from oxidative stress. It may contribute to stabilization of the lipid layer of the ocular surface, enhance epithelial hydration, and reduce inflammation. As a result, it supports cell membrane stability, alleviates symptoms (e.g., in allergic eye diseases), and may provide a protective effect against exacerbations [9].

The combination of these two agents – hyaluronic acid (0.24%) and ectoine (2%) – in a single preservative-free formulation is associated with a favorable safety profile and good tolerability. It may be used in individuals with sensitive eyes and is considered safe for children, pregnant and breastfeeding women, as well as contact lens wearers. This combination may serve as a supportive and preventive option in the management of allergic eye diseases and, in mild to moderate cases, may represent a sufficient therapeutic approach.

In the context of allergic conditions, such formulations may be used both prophylactically and therapeutically in seasonal and perennial allergic conjunctivitis, typically administered twice daily or more frequently as needed. This approach may contribute to reducing the use of conventional antiallergic medications and may also be beneficial in the management of dry eye disease and postoperative ocular surface healing.

Clinical studies have demonstrated a reduction in the overall symptom score of allergic eye diseases, as well as in individual symptoms such as redness, pruritus, and tearing, compared with placebo in patients with seasonal allergic conjunctivitis and rhinitis [10]. Furthermore, the safety and efficacy of ectoine-containing eye drops have been demonstrated in children (>5 years of age) and adolescents in reducing ocular symptoms associated with allergic rhinitis [11].

Azelastine

The main topical agents used in the treatment of allergic conjunctivitis are antihistamines with a dual mechanism of action. One such agent is azelastine. It exerts its effects by inhibiting mast cell activity and histamine receptors (primarily H_1), reducing eosinophil chemotaxis, and suppressing platelet-activating factor (PAF) as well as intercellular adhesion molecule-1 (ICAM-1). Thus, it acts on both the early and late phases of the allergic response. Its efficacy has been demonstrated in randomized, double-blind trials using conjunctival allergen provocation testing [12]. Dose-dependent efficacy of azelastine in reducing ocular pruritus and redness has also been reported [13].

In another study, reductions in conjunctival hyperemia, itching, tearing, and overall symptom scores were observed within 30 min after administration. A decrease in inflammatory cell counts, including neutrophils, lymphocytes, and monocytes, was also demonstrated [14]. Furthermore, in patients with perennial allergic conjunctivitis (PAC), a reduction in ocular symptoms (itching and redness) was observed in a substantial proportion of patients after 7 and 42 days of treatment compared with placebo [15].

Azelastine has been shown to exhibit high affinity for histamine receptors and inhibitory effects on inflammatory mediators such as interleukin-6 and tryptase [16, 17].

A major advantage of azelastine is its approval for both the prevention and treatment of SAC in patients over 4 years of age, as well as for the symptomatic treatment of PAC in patients over 12 years of age. The standard dosing regimen is twice daily, although it may be increased to up to 4 times daily if necessary. The drug has a prolonged duration of action (up to 12 h) and a rapid onset of action, occurring within minutes after administration. The main contraindication is hypersensitivity to any component of the formulation.

Fludrocortisone acetate

Fludrocortisone acetate is a glucocorticosteroid with approximately tenfold greater anti-inflammatory potency than hydrocortisone. It is available in ointment form for the treatment of allergic conjunctivitis and blepharitis, as well as uveitis and keratitis. Owing to its formulation, it remains on the ocular surface longer than eye drops, which is particularly advantageous in the management of eyelid inflammation.

It should be noted that fludrocortisone acetate is a pure glucocorticosteroid without the addition of an antibiotic. In the absence of a bacterial component, as in allergic inflammation, combination therapy with antibiotics and corticosteroids should be avoided. It should also be emphasized that perennial allergic conditions may be triggered not only by house dust mites, animal dander, molds, or fungi, but also by chemical agents present in cosmetics, eyeglass frames, cosmetic procedures, or ophthalmic medications [18].

Fludrocortisone acetate exhibits anti-inflammatory (including antiallergic), antipruritic, and anti-edematous effects. The recommended dosing involves applying a small amount of ointment 2 to 3 times daily; treatment duration should generally not exceed 2 weeks.

CONCLUSIONS

Allergic diseases are among the most common medical conditions, affecting approximately 40–50% of the population. They are typically associated with manifestations involving the skin, respiratory tract, or gastrointestinal system, while ocular involvement is often underrecognized. Allergy may present exclusively with ocular symptoms (in such cases, diagnostic tests such as skin prick tests may be negative), although it more commonly coexists with other allergic conditions, particularly allergic rhinitis. Allergic eye diseases affect approximately 15–45% of the population, with around 6% of patients presenting with isolated ocular involvement. Symptoms such as pruritus, redness, tearing, edema, and occasionally ocular pain may significantly impair quality of life.

Management of allergic conjunctivitis (SAC, PAC) and eyelid inflammation includes:

1. Avoidance of allergen exposure and minimization of eye rubbing or touching.
2. Maintenance of proper eyelid hygiene.

3. Use of agents that rinse out allergens and protect the ocular surface.
4. Application of cold compresses.
5. Use of mast cell stabilizers (currently less commonly used).
6. Administration of topical antihistamines (with systemic antihistamines in cases of multisystem involvement).
7. In more severe cases, addition of topical glucocorticosteroids (eye drops or ointments).
8. Use of intranasal glucocorticosteroids–particularly in patients with coexisting chronic allergic rhinitis–which may significantly reduce ocular symptoms and can be used long term (e.g., combinations such as azelastine with fluticasone or olopatadine with mometasone).
9. Implementation of allergen-specific immunotherapy, which in patients with seasonal allergic rhinitis and conjunctivitis has been shown to be effective in controlling ocular symptoms, sometimes to a greater extent than nasal symptoms.

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