

An algorithm for the management of allergic conjunctivitis

Leonard Bielory, M.D., Eli O. Meltzer, M.D., Kelly K. Nichols, O.D., Ph.D.,
Ron Melton, O.D., Randall K. Thomas, O.D., M.P.H., and Jimmy D. Bartlett, O.D., D.Sc.

ABSTRACT

Allergic conjunctivitis has been reported to be increasing in prevalence in the United States. It significantly impacts patient quality of life and reduces their productivity. It has been noted that nasal and ocular symptoms are equally bothersome in the majority of patients. Despite the development of new therapeutic interventions, ocular allergy is often underdiagnosed and undertreated. This article outlines current best practices regarding diagnosis and treatment of allergic conjunctivitis; suggests criteria for referral to a colleague with different expertise; and provides an algorithm for step recommendations including treatment with antihistamines, mast cell stabilizers, corticosteroids, nonsteroidal anti-inflammatory drugs, and immunotherapy.

(Allergy Asthma Proc 34:408–420, 2013; doi: 10.2500/aap.2013.34.3695)

The ocular conjunctiva is among the mucosal surfaces most accessible to airborne allergens and is a very common site of allergic inflammation.¹ Millions of Americans—at least 30% of the population—are affected by allergies, often at a significant detriment to their quality of life and productivity at school and work.¹ Although the importance of allergic conjunctivitis is often linked more to its frequency than its severity, symptoms of ocular pruritus, redness, and tearing can cause significant distress in moderate-to-severe cases.² Multiple surveys have shown who, in patients with seasonal allergic conjunctivitis, ocular symptoms are at least as bothersome as nasal symptoms in the majority of patients that experience both.^{3,4}

Despite its high prevalence and potential to diminish patient wellbeing, ocular allergy may be overlooked or undertreated by patients and health care practitioners.³ When patients present with an array of allergy-related manifestations, practitioners may fail to appreciate the extent of ocular involvement. Patients who self-diagnose commonly fail to seek medical attention, even when relief from over-the-counter (OTC) remedies is inadequate.³ Those who do seek medical care may incur significant out-of-pocket and insurance costs, and some remain unsatisfied with their care.⁴

Progress in the management of ocular allergy has continued, and family practice specialists, eye care spe-

cialists, and allergists are now familiar and equipped with topical medications—including dual-acting antihistamine/mast cell stabilizers and ester-based corticosteroids options.⁵ Substantial relief from allergic conjunctivitis symptoms—whether mild or severe—has become a feasible goal for nearly all patients.

INTRODUCTION

Allergies are widespread in the United States, affecting $\geq 30\%$ of the population.¹ According to an analysis from 1993 to 2008, prescribing for allergic conditions has accelerated by $\sim 20\%$.⁸ This likely reflects an increasing prevalence of allergic disease in developed countries. Although the exact reason for this is not known, multiple factors are thought to play a role, including industrialization, urbanization, air pollution, climate change, and the “hygiene hypothesis,” which attributes immune hypersensitivity among city dwellers to low microbial exposure during childhood.^{1,9,10} In addition, the epidemic of dry eye syndrome may be contributing to a rising incidence of conjunctival allergies, because a robust tear film is necessary to wash away allergens and irritants from the ocular surface.^{11,12}

Presentation

Typically, ocular allergy presents as one of many clinical manifestations and in conjunction with other systemic atopic manifestations, including rhinoconjunctivitis (or hay fever), rhinosinusitis, asthma, urticaria, and/or atopic dermatitis (eczema).¹ Allergic rhinitis, the most common allergic disorder, is complicated by ocular symptoms in 50–75% of patients, according to multiple studies; and this may be increasing.^{3,13} On the other hand, patients with systemic allergic inflammation may experience ocular symptoms as an isolated or predominant complaint; in the United States this phenomenon is particularly common during spring/late

From Department of Medicine, Rutgers University, Robert Wood Johnson University Hospital, New Brunswick, New Jersey

L Bielory is a consultant for Allergan and Bausch & Lomb; is on the committees for Merck and GlaxoSmithKline, and has received grants from Allergan. EO Meltzer is a consultant for Alcon, Meda, Merck, Mylan, SanofiAventis, Sunovion, and Teva; speaker for Alcon, Meda, Merck, Mylan, Sunovion, and Teva; and received grants from Alcon, Merck, Sunovion and Teva. The remaining authors have no conflicts of interest to declare pertaining to this article

Address correspondence to Leonard Bielory, M.D., Rutgers University, 400 Mountain Avenue, Springfield, NJ 07081

E-mail address: bielory@Rutgers.edu

Copyright © 2013, OceanSide Publications, Inc., U.S.A.

summer months.³ Among patients with a predominance of ocular symptoms in addition to nasal symptoms, the term allergic conjunctivorhinitis may be more descriptive.¹

Seasonal versus Perennial Allergy

The two most common forms of ocular allergy are seasonal and perennial allergic conjunctivitis, and, of the two, seasonal is the more common.² Seasonal allergies are triggered by aeroallergens that have a botanical periodicity, such as tree, grass, and weed pollens that abound in spring and late summer/fall.¹ Patients sensitive to those allergens tend to present most frequently during one or more of those seasons. Perennial allergies, by contrast, are triggered by environmental allergens commonly found in the home, such as dust mites, mold spores, or animal dander, and which are problematic for patients all year long.¹

To a limited extent, distinguishing between seasonal and perennial allergies is useful. Perennial allergies may be more likely than seasonal to cause chronic inflammation due to the prolonged nature of the exposure. Patients may require *in vivo* skin testing or *in vitro* IgE serum testing to determine which category and specific type of allergen is causing their distress, if history alone is insufficient for diagnosing the allergens.¹⁴ Identifying specific allergen sensitivities provides patients the information to minimize allergen exposure and enables appropriate targeted immunotherapy.¹⁴

In both conditions, the body's pathophysiological response to the allergen depends on the phase of exposure rather than the nature of the triggering allergen. Thus, treatment is best devised according to the duration and severity of signs and symptoms regardless of whether the exposure is classically "seasonal" or "perennial."

DIAGNOSIS

Signs and Symptoms

Symptoms of allergic conjunctivitis may fluctuate throughout the year, with exacerbations most likely during times of highest allergen exposure and in weather that is warm, windy, and dry. Patients with allergic conjunctivitis present with one or more signs and symptoms including itching, burning, stinging, redness (Figs. 1 and 2), swelling (chemosis; Fig. 3), and tearing, redness and itching are the most common symptoms. The *sine qua non* of allergic conjunctivitis is itching, and a diagnosis of allergic conjunctivitis should be called into question if a patient does not complain of ocular itch.^{15,16}

Itching may be particularly aggravating in the nasal quadrant of the eye and may range from mild to severe. Itching is less common in other ocular conditions,

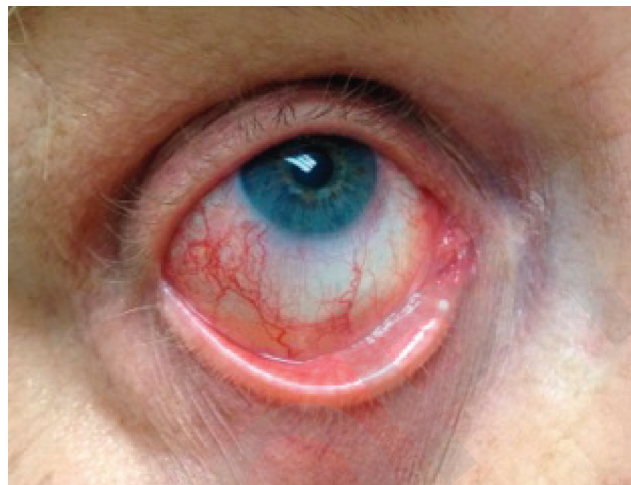


Figure 1. Conjunctival injection involving the bulbar and palpebral conjunctiva characteristic of an ocular allergic response in a mild form of allergic conjunctivitis. (Photograph courtesy of L. Bielory.)



Figure 2. Allergic conjunctivitis with moderate-to-severe injection and chemosis noted clearly in nasal and lateral portions (light reflection). (Photograph courtesy of J. Bartlett.)

although patients with blepharitis, dry eye, or other conditions may complain of itching as well.¹⁵

Discharge associated with allergic conjunctivitis is usually watery (and is frequently referred to simply as tearing). The discharge may contain a small amount of mucus, making it stringy or ropey, which can occasionally lead to the erroneous diagnosis of bacterial conjunctivitis.

Because the nasal and ocular mucosal tissues react to allergens in a similar way, most patients with ocular complaints also have nasal symptoms. Among patients with seemingly isolated ocular symptoms, mild nasal or even lower respiratory symptoms can often be uncovered with further questioning.¹⁵

Medical History and Exposures

Additional aspects of the patient history may be useful in ruling out conditions that are unrelated to

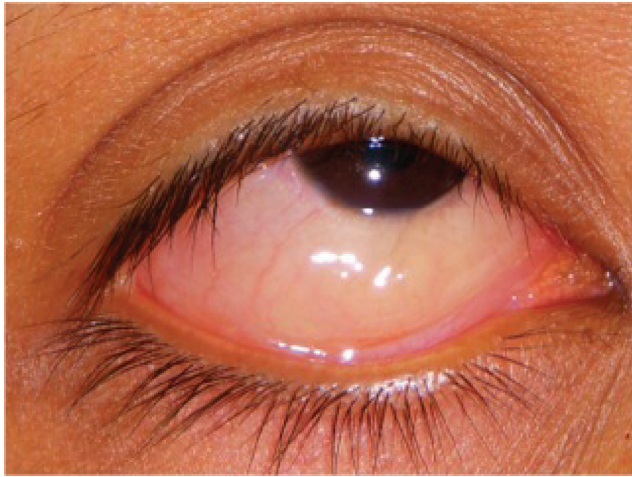


Figure 3. Chemosis involving the bulbar conjunctiva in mild allergic conjunctivitis. (Photograph courtesy of R. Thomas.)

allergic conjunctivitis. Recent exposure to infectious conjunctivitis or respiratory tract infections in home, school, or workplace may point toward an infectious cause. Topical ocular medications, including preserved artificial tears or decongestants, may occasionally irritate or inflame the ocular surface tissues.^{17–20}

A history of allergic rhinitis, hay fever, asthma, or atopic dermatitis may commonly be noted in the patient and/or family members. A medical history that is remarkable for systemic autoimmune disease (e.g., rheumatoid arthritis and Sjögren's syndrome) may suggest comorbidity with keratoconjunctivitis sicca or dry eye.

Physical Examination

Physical examination of patients suspected of having ocular allergy involves inspection of periocular and ocular tissues.¹⁶ Eyelids should be examined for abnormalities, including evidence of blepharitis, dermatitis, meibomian gland dysfunction, swelling, crab lice infestation, discoloration, or spasm. Periorbital edema (eyelid swelling) that results from allergies may be more marked in the lower lid because of the effects of gravity. A dull bluish skin discoloration below the eye (an "allergic shiner") results from venous congestion and is present in some patients with allergies.

The conjunctiva (palpebral and bulbar) should be inspected for abnormalities, such as chemosis, hyperemia, papillae, and the presence of secretions, although patients with allergic conjunctivitis frequently have unremarkable physical examinations. Conjunctival injection (redness) may be mild to moderate. Swelling or chemosis may seem out of proportion to the amount of redness present and may be most noticeable at the plica semilunaris, the relatively loose area of bulbar conjunctiva at the nasal canthus (Fig. 3). The palpebral conjunctiva in patients with allergic conjunctivitis

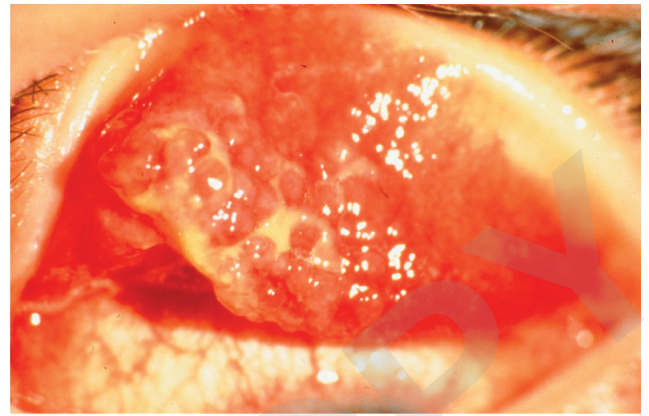


Figure 4. Everting the upper eyelid reveals giant papillae on the upper tarsal with fibrinous discharge. (Photograph courtesy of J. Bartlett.)

tends to have a milky or pale pink appearance, related to allergy-associated edema; by contrast, bacterial infections tend to produce a velvety, beef-red palpebral conjunctiva. Small, vascularized nodules (papillae) may be seen on the palpebral conjunctiva.¹

Differential Diagnosis and Comorbidities

Seasonal and perennial allergic conjunctivitis must be distinguished from other more severe conditions—both allergic and nonallergic—with similar clinical characteristics. With careful history and examination, these conditions are unlikely to be misdiagnosed as acute allergic conjunctivitis.

Vernal keratoconjunctivitis (VKC) and atopic keratoconjunctivitis (AKC) are advanced forms of allergic conjunctivitis with unique characteristics and presentations. VKC is named for its seasonal recurrence in spring and is characterized by chronic lymphocyte and mast cell infiltration of the conjunctiva. Symptoms, including itching, are characteristically severe and can be triggered by dust, bright light, hot weather, and other nonspecific stimuli.¹ Inflammation of the palpebral conjunctiva can lead to the development of giant papillae on the superior tarsal conjunctiva, yellow-white points on the limbus (Horner's points) or conjunctiva (Trantas dots), lower eyelid creasing (Dennie's lines), pseudomembrane formation on the upper lid, and copious fibrinous discharge (Fig. 4).^{1,15}

AKC, like VKC, is a chronic mast cell-mediated allergic condition; a patient or family history of atopy (e.g., eczema, asthma, or allergic rhinoconjunctivitis) is nearly always present and is central to making the diagnosis.³ Symptoms of itching, tearing, and swelling in atopic patients tend to be much more severe than in patients with allergic conjunctivitis (Fig. 5).^{21,22} As evident from their names, both VKC and AKC may involve the cornea and in severe, uncontrolled cases can cause significant visual impairment.²³

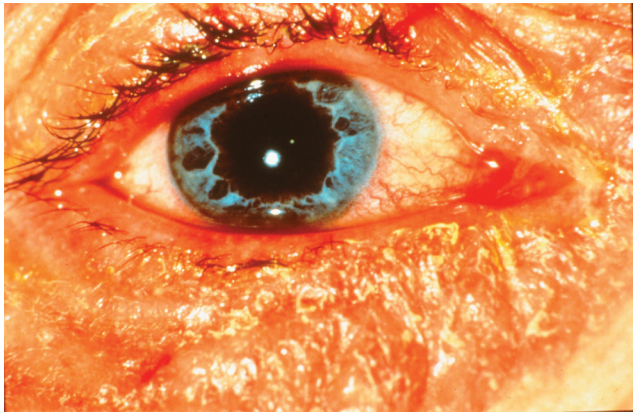


Figure 5. Atopic keratoconjunctivitis (AKC) with severe redness, eyelid edema, and scaling. (Photograph courtesy of J. Bartlett.)

Other conditions to consider in the differential diagnosis of allergic conjunctivitis include giant papillary conjunctivitis (GPC), dry eye disease, anterior blepharitis, meibomian gland dysfunction, infectious conjunctivitis, conjunctivitis medicamentosa, and contact lens-related pathology. These conditions may also be comorbid in patients with allergic conjunctivitis.

GPC is a moderate-to-severe reaction to a contact lens or other stable ocular foreign body (*e.g.*, a suture or ocular prosthetic). Patients present with moderate-to-severe itching, blurred vision, inability to tolerate contact lens wear, conjunctival injection, and white stringy discharge most noticeable in the morning. The condition derives its name from a characteristic finding on physical examination: large papillae (“cobblestoning”) on the upper tarsal conjunctiva.^{1,15}

Dry eye disease is the result of decreased aqueous tear production, increased tear evaporation, or abnormalities in tear composition.²⁴ Dry eye patients may complain of itching; burning; gritty feeling in the eye; sensitivity to light; ocular fatigue; and lowered tolerance for reading, night driving, or wearing contact lenses. Symptoms tend to progress throughout the day. The relationship between dry eye disease and allergic conjunctivitis is not entirely clear, and the two conditions often coexist. In these patients, dry eye may contribute to the pathogenesis, prevalence, and severity of the allergic conjunctivitis. A properly functioning tear film dilutes and removes many environmental allergens that deposit on the ocular surface, reducing their chance of attaining a concentration sufficient to elicit an allergic response. However, as the tear film becomes more viscous or sticky, allergens become better able to collect on the ocular surface and can more easily reach the threshold for causing symptoms, both in contact lens wearers and nonwearers as well.^{11,12,25}

Itching is a classic presenting symptom in both allergic conjunctivitis and dry eye disease. A recent survey of optometry outpatients ($n = 689$) found that a ma-

jority of patients who had itchy eyes had clinically significant ocular dryness.²⁶ The same survey found a high degree of overlap in self-reported symptoms of itching, dryness, and redness among patients with allergic conjunctivitis, dry eye, or both.²⁶

Because symptoms of dry eye and allergic conjunctivitis can be similar, it is important to assess whether a patient has isolated dry eye, isolated allergic conjunctivitis, or both. The diagnosis of dry eye is based primarily on history and clinical examination, tear film osmolarity, tear film breakup time, or other tests.²⁷ Treatment depends on the extent and severity of the disease and may include preventive measures or topical treatments such as lubricating tear substitutes, corticosteroids, or cyclosporine.⁸

Blepharoconjunctivitis

Blepharitis describes inflammation of the eyelid due to chronic, low-grade infection or seborrhea, which can lead to secondary conjunctivitis (“blepharoconjunctivitis”) in some instances. Patients complain of burning, itching, tearing, and a dry feeling in the eye. They may awaken with their eyes heavily crusted and notice debris and swelling of the lids.^{25,28,29} When attributable to staphylococcal infection, examination reveals crusting around the base of the lashes; in severe cases, fine eyelid ulcerations at the base of the lashes may also be present.^{25,28–30}

Infectious Conjunctivitis

Many infectious agents can cause conjunctivitis, including viral, bacterial, and fungal pathogens. Infectious conjunctivitis may be distinguished from allergic conjunctivitis by conducting a thorough history and physical examination because this process typically causes ocular burning, foreign body sensation, stinging, and discomfort, rather than itching. Bacterial conjunctivitis is most commonly unilateral; viral conjunctivitis tends to start unilaterally, becoming bilateral within a few days; and allergic conjunctivitis is nearly always bilateral. In bacterial conjunctivitis, the discharge is thick and more purulent (Fig. 6); in viral conjunctivitis, it is serous or watery; and in allergic conjunctivitis or dry eye, the discharge is typically scant and clear or mucoid.

Patient Referral

Most patients with acute allergic conjunctivitis do not present diagnostic challenges. Some patients, however, may have comorbidities, symptoms that overlap with other conditions, or a constellation of signs and symptoms that are either more severe than the average allergic conjunctivitis patient or otherwise warrant a team approach to care (Fig. 7).



Figure 6. Bacterial conjunctivitis with thick purulent discharge that can adhere to corneal surfaces and has a “glue eye” effect seen in the morning. (Photograph courtesy of J. Bartlett.)

Patients who have ocular involvement warranting examination by slit lamp biomicroscopy—such as those with photophobia, those wearing contact lenses or having a corneal abnormality, or those on long-term corticosteroids—should be referred to an optometrist or ophthalmologist for a comprehensive workup and care plan. Patients suspected of having dry eye and those with an advanced allergic ocular condition (e.g., VKC, AKC, or GPC) who have been treated with long-term oral or inhaled steroids rendering them at increased risk of intraocular pressure (IOP) increases and cataract formation, as well as those who have unilateral red eye with pain, should be seen in concert with an eye care specialist.

Patients who suffer from multisystem disease, including rhinitis or asthma, may benefit from referral to a specialist in allergy and immunology; and patients with allergies whose ocular manifestations are not well controlled may also benefit from referral to an allergist-immunologist. Allergen identification by skin-prick or *in vitro* testing allows for more effective avoidance of allergens. To date, immunotherapy for decreasing reactivity to offending allergens is the only disease-modifying treatment available.

TREATMENT: AVAILABLE MODALITIES

Goals of Treatment

The principal goals of treatment in allergic conjunctivitis is to minimize and control signs and symptoms and improve quality of life (Fig. 8; Table 1). These include reducing itching and lessening redness, tearing, swelling of the conjunctiva and/or eyelids, and other associated symptoms. An additional goal of treatment is the interruption and prevention of the cycle of inflammation for patients with prolonged exposures to allergens and/or long duration of symptoms.

Nonpharmaceutical Measures

Allergen avoidance when practical is a reasonable approach but may be difficult because of the unavoidable presence of the allergen source (e.g., a family fur-bearing pet) or the number of allergens to which the patient is sensitive. This may include the use of various environmental exposure reduction methods including dust mite, mold and animal dander control measures, proper ventilation of home and office environments, air filtration systems (e.g., air conditioners), awareness of the distribution, and density of common allergens (i.e., pollen and mold counts). Washing the hair prior to going to bed can also help reduce allergen exposure.³¹ Application of a cold compress to the eyelids (for 5–10 minutes once or twice daily) may relieve symptoms—especially itching—for a small group of patients. The instillation of OTC lubricating drops (“artificial tears”) can also provide a soothing sensation and dilute allergens and the mediators of allergic inflammation in the tear film.

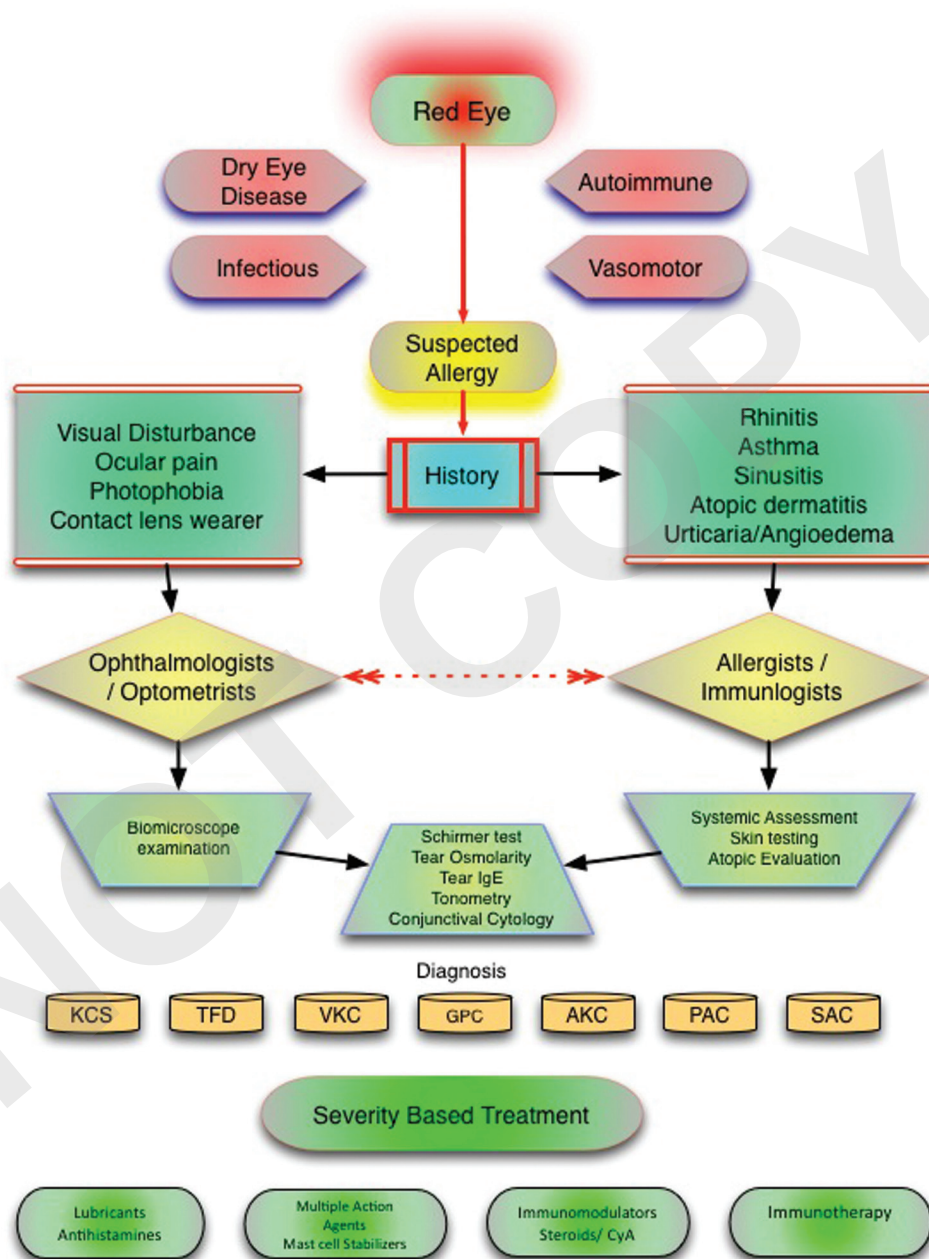
Topical Ocular Decongestants

Topical ocular decongestants are synthetic adrenergic agonists that cause constriction of ocular blood vessels to reduce redness but are generally not recommended for the treatment of allergic conjunctivitis: they are effective in the short-term acute management of redness but have little effect on itching.^{32,33} Intensive use of ocular decongestants (e.g., excessive daily use for ≥ 1 week) causes down-regulation of conjunctival α -1 receptors, resulting in “rebound hyperemia” once the medication is stopped.³² A brief regimen of low-dose ocular decongestant use (e.g., up to 4 times/day for 1–2 days) is a reasonable recommendation (Table 1). Ocular decongestants are contraindicated for patients with angle-closure glaucoma, and caution is advised for patients with cardiovascular disease, hyperthyroidism, and diabetes.^{32,34}

Oral Antihistamines

Antihistamines act principally as inverse H_1 -receptor agonists and competitively block the physiological effects of histamine molecules that have not yet bound to a receptor. Oral first-generation antihistamines are problematic and, therefore, are best used adjunctively,³⁵ because they may bind histamine receptors in unaffected tissues, leading to side effects of sedation, and, because of anticholinergic activities, dry mouth, dry eye, and tachycardia.³⁶ Patients with peptic ulcer disease, prostate hypertrophy, genitourinary or intestinal obstruction, or risk for acute angle-closure glaucoma should exercise caution with first-generation antihistamines with strong anticholinergic properties (clemastine, diphenhydramine, and promethazine).³⁶ Second-generation agents have lower lipid solubility, which reduces their ability to penetrate the blood–brain barrier, improving their side effect profile particularly with regard to sedation.^{37–39}

Figure 7. Proper evaluation of the “red eye” involves the assessment of a wide spectrum of disorders affecting the ocular surface as well as some intraocular and periocular disorders. The suspicion of an allergic-based condition based on history may lead one to consult with allergists depending on the systemic features of asthma, allergic rhinitis, sinusitis, atopic dermatitis, urticaria, or eye specialists (e.g., optometrists and ophthalmologists) with localized complaints of visual disturbances, photophobia, contact lens irritation, and/or ocular pain. Slit lamp examination by an eye care professional can further facilitate the identification of conditions that may confound the diagnosis of acute allergic conjunctivitis. Skin or in vitro testing can better define the offending allergen for the assistance in environmental control measures and the development of immunotherapy regimens. An integrated approach and collaboration of allergists and eye care specialties including ophthalmologists and optometrists will maximize the diagnosis and managements of patients with allergic conjunctivitis.



Because a significant proportion of patients with ocular allergy complain of dryness related to their allergies or have comorbid dry eye symptoms, these individuals may benefit from discontinuing therapy with first-generation oral antihistamines.

Topical Ocular Antihistamines (Single Acting)

Topical ophthalmic agents for the treatment of ocular allergy have a more rapid onset of action compared with oral antihistamines and are generally better tolerated. Topical antihistamines do not cause significant systemic side effects and generally do not contribute to ocular dryness.³⁵ The topical antihistamine pheniramine is available OTC in combination with the decongestant

naphazoline (Table 1). Compared with placebo, topical antihistamines have been shown to significantly reduce signs and symptoms of conjunctivitis induced by allergen challenge in clinical trials. These agents possess a single mechanism of action and therefore primarily affect the early phase response of allergic conjunctivitis. Like all antihistamine agents, topical antihistamines are contraindicated in patients at risk for angle-closure glaucoma.

Topical Ocular Nonsteroidal Anti-Inflammatory Drugs

Topical ophthalmic nonsteroidal anti-inflammatory drugs (NSAIDs) were initially used in perioperative

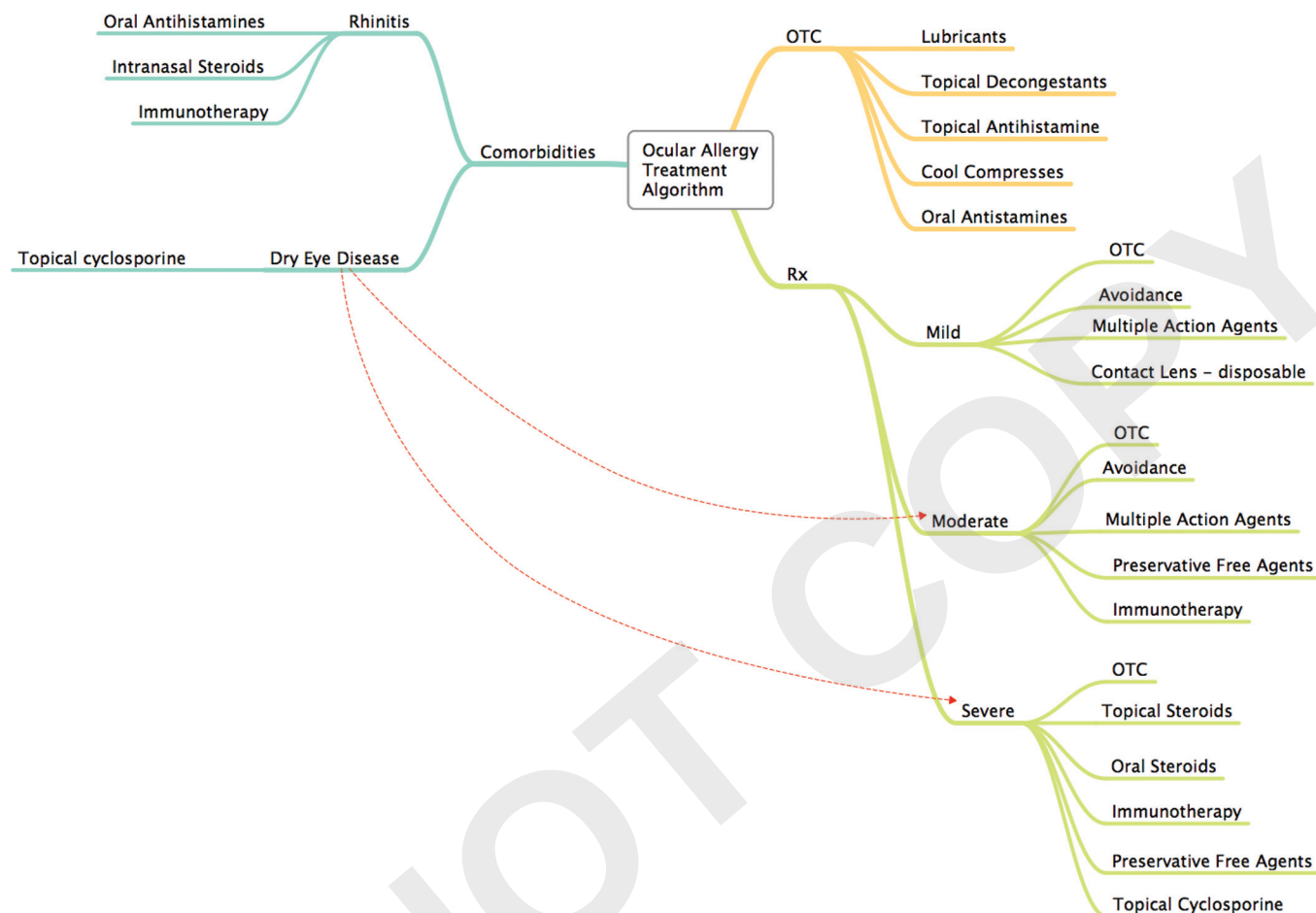


Figure 8. The algorithm presented outlines current best practices regarding diagnosis and treatment of allergic conjunctivitis based on recent medical findings and expert opinion similar to those provided for asthma and allergic rhinitis.^{6,7} Greater awareness of the allergic conjunctivitis disease state and knowledge of treatment options for symptom relief can improve patient management and encourage health care providers to further collaborate in assisting patients to reach closer to their objective of ameliorating the symptoms of ocular allergy. The ocular allergy treatment algorithm includes over-the-counter (OTC) agents and then progresses to include a stepwise approach using prescription medications that build on the various complementary mechanisms of action of therapeutic agents including topical lubricants, cool compresses, decongestants, antihistamines, nonsteroidal anti-inflammatory drug (NSAID), mast cell stabilizers, corticosteroids, and subcutaneous (and potentially sublingual*) immunotherapy, but also include the treatment of comorbid conditions such as allergic rhinitis and tear film dysfunction (dry eye disease). (*Not FDA approved.)

cataract care and found serendipitously to reduce symptoms associated with allergic conjunctivitis.^{40,41} Ketorolac is the only NSAID approved for the topical treatment of seasonal allergic conjunctivitis (Table 1).⁴² NSAIDs interfere with mediators of the late-phase response, prostaglandin production. In the experience of the authors, because of the availability of other classes of agents with established efficacy and proven greater comfort profiles, ophthalmic ketorolac is recommended for only occasional use in the treatment of acute allergic conjunctivitis not responsive to other agents.

Topical Mast Cell Stabilizers (Single Acting)

These ophthalmic agents work by stabilizing mast cell membranes and preventing degranulation and reducing the influx of various inflammatory cells, includ-

ing eosinophils, neutrophils, and monocytes.⁴³ Mast cell stabilizers have been shown to decrease itching, tearing, and overall disease in clinical trials in comparison with placebo.^{44–48} In the experience of the authors, single-acting mast cell stabilizers are now rarely used in the treatment of acute allergic conjunctivitis because they are slow to act; it may take 3–5 days before symptoms abate⁴³ (Table 1).

Topical Dual-Acting Antihistamine/Mast Cell Stabilizers

Dual-acting antihistamine/mast cell stabilizers are the most recently developed class of agents for the treatment of allergy-associated ocular itching. In a single molecule, they combine the mechanisms of two established classes: antihistamines and mast cell stabi-

Table 1 Topical (ophthalmic) agents for allergic conjunctivitis

Topical Ophthalmic Agents Generic (Trade) Name	OTC/Rx (Conc)	Mechanism of Action	Dosage	Most Common Side Effects	Pregnancy Category
Ketotifen (Alaway, Zaditor Zyrtec itchy eye, Claritin Eye; previously Rx Zaditor)	OTC 0.01–0.035%	Noncompetitive H ₁ -receptor antagonist and mast cell stabilizer	≥3 yr: 1 drop up to 3 times daily	Conjunctival injection, headache, and rhinitis (10–25%)	C
Cromolyn (Opticrom and Crolom)	OTC 4%	Mast cell stabilizer	≥2 yr: 1–2 drops up to 4 times daily	<4% Irritation, burning, stinging eye redness, and eye pruritus	C
Pheniramine maleate/naphazoline (multiple names)	OTC 0.315%/ 0.02675%	Combination H ₁ -receptor and decongestant	1 or 2 drops up to 4 times daily	Conjunctival injection and chemosis	C
Alcaftadine (Lastacraft)	Rx 0.25%	Noncompetitive H ₁ -receptor antagonist and mast cell stabilizer	≥3 yr: 1–2 drops once daily	< 4% Irritation, burning, stinging eye redness, and eye pruritus	B
Bepotastine (Bepreve)	Rx 1.5%	Selective H ₁ -receptor antagonist and mast cell stabilizer	≥3 yr: 1 drop twice daily	Taste (~25%) headache, eye irritation, and nasopharyngitis in 2–5%	C
Olopatadine (Pataday)	Rx 2%	Selective H ₁ -receptor antagonist and mast cell stabilizer	≥3 yr: 1–2 drops once a day	Headache (7%)	C
Epinastine (Elestat)	Rx 0.05%	Direct H ₁ -receptor antagonis; does not penetrate the blood– brain barrier and therefore should not induce CNS side effects	≥3 yr: 1 drop twice daily	Upper respiratory infection/cold symptoms (10%)	C
Olopatadine (Patanol)	Rx 1%	Selective H ₁ -receptor antagonist and mast cell stabilizer	≥3 yr: 1–2 drops up to four times daily	Headache (7%)	C
Azelastine (Optivar)	Rx 0.15%	Competes with H ₁ -receptor sites on effector cells and mast cell stabilizer	≥3 yr: 1 drop twice daily	Ocular burning (~30%), headache (~15%), and bitter taste (~10%)	C
Emedastine difumarate (Emadine)	Rx 0.05%	Relatively selective histamine receptor antagonist	≥3 yr: 1 drop up to four times daily	Headache (11%)	C

Table 1 Continued

Topical Ophthalmic Agents Generic (Trade) Name	OTC/Rx (Conc)	Mechanism of Action	Dosage	Most Common Side Effects	Pregnancy Category
Levocabastine (Livostin)	Rx 0.1%	Selective H ₁ -receptor antagonist	≥12 yr: 1 drop up to four times daily	Ocular burning, stinging, and itching (10%)	C
Lodoxamide tromethamine (Alomide)	Rx 0.1%	Mast cell stabilizer	≥2 yr: 1–2 drops up to four times daily	Ocular burning, stinging, and itching (10%)	C
Nedocromil (Alocril)	Rx 2%	Mast cell stabilizer	≥3 yr: 1–2 drops twice daily	Headache (10%), bitter taste (10%), ocular burning (10%), and nasal congestion (10%)	C
Loteprednol etabonate (Alrex)	Rx 0.2%	Decreases inflammation by suppressing migration of polymorphonuclear leukocytes and reversing capillary permeability	≥3 yr: 1–2 drops twice up to four times daily	Headache (10%), pharyngitis (10%), and rhinitis (10%)	C
(Lotemax) Ointment gel suspension	Rx 0.5%				
Ketorolac tromethamine (Acular)	Rx 0.5%	Pyrrolo-pyrrole NSAIDs, and inhibits prostaglandin synthesis	≥12 yr: 1 drop up to four times daily	Ocular burning, stinging, and itching (10%)	C

The array of topical agents used in the therapeutic approach to the treatment of allergic conjunctivitis includes a spectrum of OTC and Rx agents including decongestants, antihistamines, dual-acting agents, NSAID, and corticosteroids. The doses, concentrations, mechanisms of action, pregnancy categories, and common side effects are important considerations in choice of agents.

H₁ = histamine 1; CNS = central nervous system; PC = Pregnancy category; OTC = over-the-counter; Rx = prescription; NSAIDs = nonsteroidal anti-inflammatory drugs.

lizing agents. These dual-acting agents reduce allergic inflammation by preventing mast cell release of inflammatory mediators and by selectively blocking the H₁-receptor, thus countering the effects of histamine that has already been released—and enabling a relatively rapid onset of action and an effect on the late-phase response.^{32,46} Selectivity for the H₁-receptor decreases rates of adverse events such as drowsiness and dryness associated with binding to other receptors.³⁵

In clinical trials, dual-acting agents have been shown to effectively reduce itching associated with allergic conjunctivitis with longer duration of effect and better tolerability than single-action antihistamines (Table 1).^{46,49} With the exception of sensitivity to any of the formulation components, there are no contraindications to the use of these topical antihistamine/mast cell stabilizing agents.^{5,32} Contact lens wearers may experience up to a 2-hour increase in comfortable wearing time with the use of topical dual-acting antihistamine/mast cell stabilizers when applied before and/or after removing contact lenses.⁵⁰

Topical Ophthalmic Corticosteroids

As a class, corticosteroids have multiple sites and mechanisms of action, affecting both early and late-phase allergic response; they suppress mast cell proliferation, reduce inflammatory cell influx, inhibit cell-mediated immune responses, and block the production of all of the inflammatory chemical mediators, including prostaglandins, leukotrienes, and platelet activating factor.^{51,52} Patients with moderate-to-severe manifestations of seasonal allergic conjunctivitis, prolonged or repeated allergen exposures, and those with persistent symptoms are likely to experience both early and late-phase inflammatory processes that would respond to an appropriate topical ophthalmic corticosteroid.⁵³ In the past, this class of compounds was reserved for patients with advanced or recalcitrant forms of ocular allergy because of their adverse effect profile. However, that paradigm changed when a key modification in the chemical structure, an ester group at carbon-20 in place of a ketone group at that location (Table 1), was found to provide unique pharmacokinetic properties that resulted in rapid metabolism, lowering the risk of steroid-induced side effects, compared with steroids that have a ketone group at carbon-20.^{51,52,54–58}

Immunotherapy

Allergen immunotherapy has shown improvement in ocular signs and symptoms with subcutaneous immunotherapy⁵⁹ and the investigational forms of sublingual immunotherapy^{60–62} with duration of effect persisting for up to 5 years after termination of treatment. Using visual analog scale, ocular symptom

scores showed a two- to threefold improvement whereas the conjunctival surface challenge required 10–100 more allergens to provoke a response.⁶³ Sublingual immunotherapy that has also shown some improvement in ocular allergy scores.^{64,65} Sublingual immunotherapy is not currently Food and Drug Administration approved in the United States.

ALGORITHM FOR THE MANAGEMENT OF ALLERGIC CONJUNCTIVITIS

Comprehensive clinical guidelines that have been developed for the management of allergic rhinitis and asthma categorize patients according to duration and severity of illness and other factors.^{66,67} Based on those models, the following algorithm represents a synthesis of the clinical expertise of the authors and the relevant aspects of the literature.

Patient Assessment

Appropriate management of allergic conjunctivitis should result in prompt relief and control of patients' symptoms.

Assessment begins with a careful patient history and clinical examination evaluating for severity of itching (mild, moderate, or severe) and whether the itch is intermittent or persistent. Severe itching should lead the clinician to consider the possibility of a serious ocular allergic condition (*e.g.*, VKC and AKC) or crab lice infestation.^{1,68} Other ocular symptoms, such as foreign body sensation, tearing, and burning, and the presence and severity of conjunctival redness should be addressed. Severe unilateral redness may indicate the presence of infectious conjunctivitis.

Patient characteristics may be sorted into one of three steps of involvement. In step 1, itching is mild and either intermittent or of short duration. In step 2, itching may be mild, moderate, or severe, and either intermittent or chronic. Redness is absent and symptom duration is moderate (from a few days to 2 weeks). In step 3, itching may be moderate to severe and chronic and redness may be present.

In addition to these criteria, the presence of additional symptoms, including foreign body sensation, tearing, and burning, may contribute to the overall severity of the presentation. Use of prior treatments should be considered. Patients with significant complaints of dryness that are worse in the afternoon or evening (or related symptoms such as foreign body sensation) may have dry eye disease in addition to (or instead of) allergic conjunctivitis. Some OTC or prescription medications (*e.g.*, first-generation oral antihistamines) may contribute to symptoms of ocular dryness and patients may benefit from cessation of that therapy.

Table 2 Algorithm for the management of allergic conjunctivitis

	Level 1	Level 2	Level 3	Notes
Main factors				
Itching	Mild	Mild to severe	Moderate to severe	If severe, consider alternative diagnosis (e.g., vernal, atopic, or GPC)
	Intermittent	Intermittent to persistent	Persistent	
Redness	Absent	Absent	Moderate to severe	If severe, consider alternative diagnosis (e.g., infectious conjunctivitis)
Supportive factors				
Foreign body sensation, tearing, burning, and/or other symptoms	Absent	Absent	Moderate to severe	For dryness, inquire about oral antihistamines (may contribute to ocular dryness); consider diagnosis of comorbid dry eye disease
Symptom duration	Days	Days to weeks	Weeks to months	
Prior treatments	None	None or OTC medications not tolerated or not effective	Previous therapy tried	
Treatment				
First line	Cold compress and artificial tears	Antihistamine/mast cell stabilizer	Topical steroid	
Alternatives	(a) Short-term topical OTC treatment or (b) Antihistamine/mast cell stabilizer	Immunotherapy	Immunotherapy	
Follow-up				
Clinic visit/IOP assessment	As needed	As needed	At 10–14 days Then every 2–4 wk through week 6 Then every 3–6 mo while using steroid	
Complete ophthalmic exam with dilation	Yearly or as needed	Yearly or as needed	Yearly	

Contact lenses should be removed when using ophthalmic administration and may be replaced after at least 10 min to a nonred eye. Patients using ophthalmic steroids for >10 days should have IOP monitored.

GPC = giant papillary conjunctivitis; OTC = over-the-counter; IOP = intraocular pressure.

Patients with ocular allergies should be asked about extraocular symptoms including nasal congestion, nasal itch, rhinorrhea, sneezing, coughing, wheezing,

shortness of breath, and skin rash. Signs or symptoms of systemic allergies should prompt referral to an allergist for a comprehensive allergy assessment (Fig. 7).

Treatment

Note that treatment should follow a stepwise approach (Table 2).

Step 1. Patients with mild, intermittent itching may use nonpharmaceutical measures such as cold compresses and lubricating ophthalmic drops. Alternatively, OTC medication or an ocular antihistamine/mast cell stabilizer may be prescribed.

Step 2. This group includes patients with itching (ranging from mild to severe and from intermittent to prolonged) who do not have significant redness or concurrent ocular conditions. Treatment with a topical ocular antihistamine/mast cell stabilizer is recommended. However, steroids are commonly used by eye care specialists.

Step 3. For seasonal allergy patients with moderate-to-severe symptoms of allergic conjunctivitis and redness, treatment with a topical ocular antihistamine/mast cell stabilizer and/or a topical ocular corticosteroid indicated for allergic conjunctivitis can be recommended.

Patients placed on a topical ocular steroid should receive careful follow-up to assess efficacy and rule out adverse effects, such as drug-induced IOP elevation. IOP should be assessed before initiation of treatment. If steroid therapy continues beyond 10 days, IOP should be monitored beginning at approximately day 14. A slit lamp examination of the ocular surface can rule out opportunistic infections (e.g., with herpes simplex virus or fungi).⁵²

A visit 2–4 weeks after the initial follow-up is recommended. Most steroid responders will have shown evidence of increased IOP by 4–6 weeks after initiation of therapy; so once that window has passed, it is safe to follow patients at longer intervals.⁵⁷ While using any corticosteroid, patients should be followed at 3- to 6-month intervals. It is important to refrain from allowing refills during that time so that compliance with the follow-up schedule is enforced and adverse effects can be detected.

Studies have not found even long-term therapy with loteprednol etabonate 0.2% to be associated with the development of cataracts.⁵² However, it is good practice for every patient to annually undergo a complete ophthalmic examination.

It is always best to use the shortest course of therapy that effectively suppresses signs and symptoms. In addition, stepping down to step 2 treatment should be considered when a patient's symptoms and signs are well controlled.

ACKNOWLEDGMENTS

The authors acknowledge Ethis Communications, Inc., for its editorial assistance in the preparation of this article.

REFERENCES

1. Bielory L. Ocular allergy overview. *Immunol Allergy Clin North Am* 28:1–23, v, 2008.
2. Bielory L, and Friedlaender M. H. Allergic conjunctivitis. *Immunol Allergy Clin North Am* 28:43–58, 2008.
3. Rosario N, and Bielory L. Epidemiology of allergic conjunctivitis. *Curr Opin Allergy Clin Immunol* 11:471–476, 2011.
4. Pitt AD, Smith AF, Lindsell L, et al. Economic and quality-of-life impact of seasonal allergic conjunctivitis in Oxfordshire. *Ophthalmic Epidemiol* 11:17–33, 2004.
5. Bartlett JD (ed.) Antiallergy and decongestant agents. In *Ophthalmic Drug Facts*. St. Louis, MO: Wolters Kluwer Health, 2012.
6. Meltzer E. Pharmacotherapeutic strategies for allergic rhinitis: Matching treatment to symptoms, disease progression, and associated conditions. *Allergy Asthma Proc* 34:301–311, 2013.
7. National Institutes of Health (NIH). Guidelines for the diagnosis and management of asthma (EPR-3). National Institutes of Health (NIH), National Heart, Lung and Blood Institute, Bethesda, MD, 2007.
8. Origlieri C, and Bielory L. Emerging drugs for conjunctivitis. *Expert Opin Emerg Drugs* 14:523–536, 2009.
9. Liu AH. Hygiene theory and allergy and asthma prevention. *Paediatr Perinat Epidemiol* 21(suppl 3):2–7, 2007.
10. Bielory L, Lyons K, and Goldberg R. Climate change and allergic disease. *Curr Allergy Asthma Rep* 12:485–494, 2012.
11. Fujishima H, Toda I, Shimazaki J, and Tsubota K. Allergic conjunctivitis and dry eye. *Br J Ophthalmol* 80:994–997, 1996.
12. Bielory L. Ocular allergy and dry eye syndrome. *Curr Opin Allergy Clin Immunol* 4:421–424, 2004.
13. Panagiotis P, and Bielory L. Ocular and nasal allergy in the United States. *Ann Allergy Asthma Immunol* 109:A24, 2012 (Abs).
14. Williams PB, Siegel C, and Portnoy J. Efficacy of a single diagnostic test for sensitization to common inhalant allergens. *Ann Allergy Asthma Immunol* 86:196–202, 2001.
15. Bielory L. Ocular allergy. *Mt Sinai J Med* 78:740–758, 2011.
16. Bielory L, Dinowitz M, and Rescigno R. Ocular allergic diseases: Differential diagnosis, examination techniques and testing. *J Cutan Ocular Toxicol* 21:329–351, 2002.
17. Hong J, and Bielory L. Allergy to ophthalmic preservatives. *Curr Opin Allergy Clin Immunol* 9:447–453, 2009.
18. Rudzki E, Kecik T, Rebandel P, et al. Frequency of contact sensitivity to drugs and preservatives in patients with conjunctivitis. *Contact Dermatitis* 33:270, 1995.
19. Vilaplana J, and Romaguera C. Contact dermatitis from parabens used as preservatives in eyedrops. *Contact Dermatitis* 43:248, 2000.
20. Baudouin C, Labbe A, Liang H, et al. Preservatives in eyedrops: The good, the bad and the ugly. *Prog Retin Eye Res* 29:312–334, 2010.
21. Sy H, and Bielory L. Atopic keratoconjunctivitis. *Allergy Asthma Proc* 34:33–41, 2013.
22. Bielory B, and Bielory L. Atopic dermatitis and keratoconjunctivitis. *Immunol Allergy Clin North Am* 30:323–336, 2010.
23. Bielory L. Allergic diseases of the eye. *Med Clin North Am* 90:129–148, 2006.
24. The epidemiology of dry eye disease: Report of the Epidemiology Subcommittee of the International Dry Eye WorkShop (2007). *Ocul Surf* 5:93–107, 2007.
25. Friedlaender MH. Blepharitis, allergy, and dry eye: Lumpers and splitters. *Ann Ophthalmol* (Skokie) 38:4–5, 2006.
26. Hom MM, Nguyen AL, and Bielory L. Allergic conjunctivitis and dry eye syndrome. *Ann Allergy Asthma Immunol* 108:163–166, 2012.
27. Sullivan BD, Crews LA, Sönmez B, et al. Clinical utility of objective tests for dry eye disease: Variability over time and implications for clinical trials and disease management. *Cornea* 31:1000–1008, 2012.

28. Bernardes TF, and Bonfioli AA. Blepharitis. *Semin Ophthalmol* 25:79–83, 2010.
29. Jackson WB. Blepharitis: Current strategies for diagnosis and management. *Can J Ophthalmol* 43:170–179, 2008.
30. Lemp MA, and Nichols KK. Blepharitis in the United States 2009: A survey-based perspective on prevalence and treatment. *Ocul Surf* 7(suppl):S1–S14, 2009.
31. Asher I, Baena-Cagnani C, Boner A, et al. World Allergy Organization guidelines for prevention of allergy and allergic asthma. *Int Arch Allergy Immunol* 135:83–92, 2004.
32. Adamczyk DT, and Jaanus SD. Anti-allergy drugs and decongestants. In *Clinical Ocular Pharmacology*, 5th ed. Bartlett JD (Ed). St. Louis, MO: Elsevier, 245–260, 2008.
33. Abelson MB, Sadun AA, Udell JJ, and Weston JH. Alkaline tear pH in ocular rosacea. *Am J Ophthalmol* 90:866–869, 1980.
34. Fraunfelder FT, and Meyer SM. Systemic reactions to ophthalmic drug preparations. *Med Toxicol Adverse Drug Exp* 2:287–293, 1987.
35. Wade L, Bielory L, and Rudner S. Ophthalmic antihistamines and H1–H4 receptors. *Curr Opin Allergy Clin Immunol* 12:510–516, 2012.
36. Simons FE, and Simons KJ. Histamine and H1-antihistamines: Celebrating a century of progress. *J Allergy Clin Immunol* 128:1139–1150, 2011.
37. Bielory L. Allergic and immunologic disorders of the eye. Part I: Immunology of the eye. *J Allergy Clin Immunol* 106:805–816, 2000.
38. Bielory L. Allergic and immunologic disorders of the eye. Part II: Ocular allergy. *J Allergy Clin Immunol* 106:1019–1032, 2000.
39. Bielory L, Buddiga P, and Bigelson S. Ocular allergy treatment comparisons: Azelastine and olopatadine. *Curr Allergy Asthma Rep* 4:320–325, 2004.
40. Donshik PC, Pearlman D, Pinna J, et al. Efficacy and safety of ketorolac tromethamine 0.5% and levocabastine 0.05%: A multicenter comparison in patients with seasonal allergic conjunctivitis. *Adv Ther* 17:94–102, 2000.
41. Ballas Z, Blumenthal M, Tinkelman DG, et al. Clinical evaluation of ketorolac tromethamine 0.5% ophthalmic solution for the treatment of seasonal allergic conjunctivitis. *Surv Ophthalmol* 38(suppl):141–148, 1993.
42. Tinkelman DG, Rupp G, Kaufman H, et al. Double-masked, paired-comparison clinical study of ketorolac tromethamine 0.5% ophthalmic solution compared with placebo eyedrops in the treatment of seasonal allergic conjunctivitis. *Surv Ophthalmol* 38(suppl):133–140, 1993.
43. Allansmith MR, and Ross RN. Ocular allergy and mast cell stabilizers. *Surv Ophthalmol* 30:229–244, 1986.
44. Handelman NI, Friday GA, Schwartz HJ, et al. Cromolyn sodium nasal solution in the prophylactic treatment of pollen-induced seasonal allergic rhinitis. *J Allergy Clin Immunol* 59:237–242, 1977.
45. Friday GA, Biglan AW, Hiles DA, et al. Treatment of ragweed allergic conjunctivitis with cromolyn sodium 4% ophthalmic solution. *Am J Ophthalmol* 95:169–174, 1983.
46. Bielory L. Allergic conjunctivitis: The evolution of therapeutic options. *Allergy Asthma Proc* 33:129–139, 2012.
47. Santos CI, Huang AJ, Abelson MB, et al. Efficacy of lodoxamide 0.1% ophthalmic solution in resolving corneal epitheliopathy associated with vernal keratoconjunctivitis. *Am J Ophthalmol* 117:488–497, 1994.
48. Abelson MB, Berdy GJ, Mundorf T, et al. Pemirolast potassium 0.1% ophthalmic solution is an effective treatment for allergic conjunctivitis: A pooled analysis of two prospective, randomized, double-masked, placebo-controlled, phase III studies. *J Ocul Pharmacol Ther* 18:475–488, 2002.
49. Abelson MB, and Spitalny L. Combined analysis of two studies using the conjunctival allergen challenge model to evaluate olopatadine hydrochloride, a new ophthalmic antiallergic agent with dual activity. *Am J Ophthalmol* 125:797–804, 1998.
50. Nichols KK, Morris S, Gaddie IB, and Evans D. Epinastine 0.05% ophthalmic solution in contact lens-wearing subjects with a history of allergic conjunctivitis. *Eye Contact Lens* 35:26–31, 2009.
51. Bielory BP, Perez VL, and Bielory L. Treatment of seasonal allergic conjunctivitis with ophthalmic corticosteroids: In search of the perfect ocular corticosteroids in the treatment of allergic conjunctivitis. *Curr Opin Allergy Clin Immunol* 10:469–477, 2010.
52. Ilyas H, Slonim CB, Braswell GR, et al. Long-term safety of loteprednol etabonate 0.2% in the treatment of seasonal and perennial allergic conjunctivitis. *Eye Contact Lens* 30:10–13, 2004.
53. Choi SH, and Bielory L. Late-phase reaction in ocular allergy. *Curr Opin Allergy Clin Immunol* 8:438–444, 2008.
54. Dell SJ, Lowry GM, Northcutt JA, et al. A randomized, double-masked, placebo-controlled parallel study of 0.2% loteprednol etabonate in patients with seasonal allergic conjunctivitis. *J Allergy Clin Immunol* 102:251–255, 1998.
55. Shulman DG, Lothringer LL, Rubin JM, et al. A randomized, double-masked, placebo-controlled parallel study of loteprednol etabonate 0.2% in patients with seasonal allergic conjunctivitis. *Ophthalmology* 106:362–369, 1999.
56. Bartlett JD, Howes JF, Ghormley NR, et al. Safety and efficacy of loteprednol etabonate for treatment of papillae in contact lens-associated giant papillary conjunctivitis. *Curr Eye Res* 12:313–321, 1993.
57. Bartlett JD, Horwitz B, Laibovitz R, and Howes JF. Intraocular pressure response to loteprednol etabonate in known steroid responders. *J Ocul Pharmacol* 9:157–165, 1993.
58. Holland EJ, Bartlett JD, Paterno MR, et al. Effects of loteprednol/tobramycin versus dexamethasone/tobramycin on intraocular pressure in healthy volunteers. *Cornea* 27:50–55, 2008.
59. Dreborg S, Agrell B, Foucard T, et al. A double-blind, multicenter immunotherapy trial in children, using a purified and standardized *Cladosporium herbarum* preparation. I. Clinical results. *Allergy* 41:131–140, 1986.
60. Horak F, Stübner P, Berger UE, et al. Immunotherapy with sublingual birch pollen extract. A short-term double-blind placebo study. *J Invest Allergol Clin Immunol* 8:165–171, 1998.
61. Balda BR, Wolf H, Baumgarten C, et al. Tree-pollen allergy is efficiently treated by short-term immunotherapy (STI) with seven preseasonal injections of molecular standardized allergens. *Allergy* 53:740–748, 1998.
62. Didier A, Malling HJ, Worm M, et al. Optimal dose, efficacy, and safety of once-daily sublingual immunotherapy with a 5-grass pollen tablet for seasonal allergic rhinitis. *J Allergy Clin Immunol* 120:1338–1345, 2007.
63. Niggemann B, Jacobsen L, Dreborg S, et al. Five-year follow-up on the PAT study: Specific immunotherapy and long-term prevention of asthma in children. *Allergy* 61:855–859, 2006.
64. Calderon MA, Penagos M, Sheikh A, et al. Sublingual immunotherapy for allergic conjunctivitis: Cochrane systematic review and meta-analysis. *Clin Exp Allergy* 41:1263–1272, 2011.
65. Calderon MA, Penagos M, Sheikh A, et al. Sublingual immunotherapy for treating allergic conjunctivitis. *Cochrane Database Syst Rev* 7:CD007685, 2011.
66. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic Rhinitis and Its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy* 63(suppl 86):8–160, 2008.
67. National Asthma Education and Prevention Program. Expert panel report 3 (EPR-3): Guidelines for the diagnosis and management of asthma-summary report 2007. *J Allergy Clin Immunol* 120(suppl):S94–S138, 2007.
68. Bielory BP, O'Brien TP, and Bielory L. Management of seasonal allergic conjunctivitis: Guide to therapy. *Acta Ophthalmol* 90:399–407, 2012. □

Copyright of Allergy & Asthma Proceedings is the property of OceanSide Publications Inc. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.