UPDATED EDITION

# Diagnostic & Treatment Algorithms for Ocular Surface Disease States

# Allergy

*Part one of an ongoing series*

New paradigms in the understanding and management of ocular allergy.

Supported by an Unrestricted Grant from BAUSCH + LOMB

*Dear Colleagues:*

*Every one of us is all too familiar with the various ocular surface disease states with which our patients routinely present. Whether it be allergy, conjunctivitis, dry eye or keratitis, eyecare practitioners are constantly faced with the task of sifting through the available literature and data in an effort to find the best approaches to treating and managing these conditions.*

*The four of us agreed to come together to talk about our experiences, cases and pearls for several different ocular disease states, starting with allergy, in an attempt to reach a consensus on the most effective ways to address these conditions in the typical optometric practice. Our discussion regarding new paradigms in the understanding and management of ocular allergy, summarized here and updated since the original release of this series in 2008, is heavily evidence-based with the thought that it may serve as a useful reference for the busy clinician.*

*We had the greater good of the profession in mind while compiling this information and we hope you find the end result to be beneficial. Finally, we would like to thank Bausch + Lomb for providing the support needed to put this project together.*

*— The Authors*

## About the Authors

**Jimmy D. Bartlett, O.D., D.O.S., Sc.D.,** is Professor and Chairman of the Department of Optometry at the University of Alabama at Birmingham.

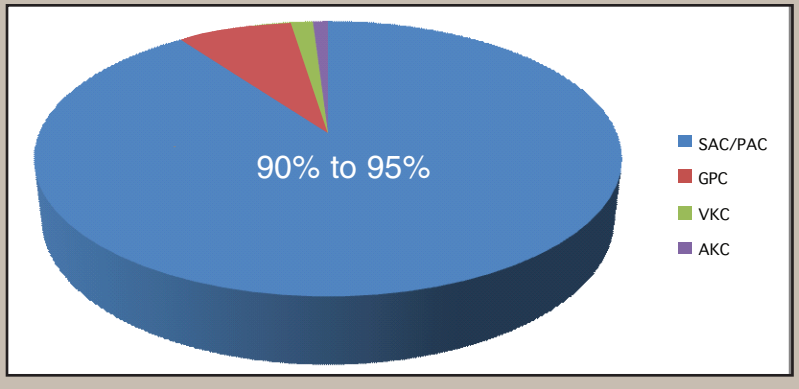
**Paul M. Karpecki, O.D.,** practices at the Koffler Vision Group in Lexington, Ky. in Cornea Services and External Disease. He is also Director of Research.

**Ron Melton, O.D., F.A.A.O.,** is in private group practice in Charlotte, N.C., an adjunct faculty member at the Salus University College of Optometry and Indiana University School of Optometry, and co-founder of Educators in Primary Eye Care, LLC.

**Randall K. Thomas, O.D., M.P.H., F.A.A.O.,** is in private group practice in Concord, N.C., and co-founder of Educators in Primary Eye Care, LLC.

# PART 1: Epidemiology and Etiology of Ocular Allergy

Allergy is an important and growing health problem. Approximately 30% of the U.S. population suffers from some form of allergy, including at least 15% to 20% with ocular allergies, primarily seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC).[1,2] In many parts of the country, a thorough history will reveal an even higher percentage of patients with allergy-related complaints. The National Health and Nutrition Examination Survey, which collected data from 1988 to 1994, recently reported that up



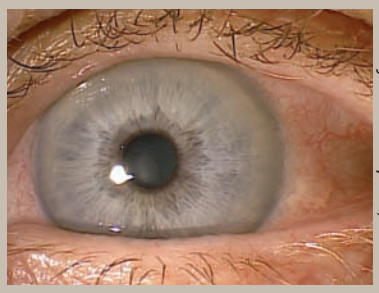

Prevalence of ocular allergies in the United States.

to 40% of the U.S. population had experienced ocular allergy symptoms, with a peak of symptoms in the months of June and July.[3] Isolated ocular symptoms (without concomitant nasal symptoms) were most likely in people over age 50, and in those with allergies to animals, household dust and pollen.

The hallmark symptom of ocular allergy is itching. This is a necessary, but not sufficient complaint to make the differential diagnosis of allergy. A thorough patient history that includes medications, timing, and recurrence of symptoms, as well as personal and family history of allergic or atopic conditions is also critical.

To understand the various forms of ocular allergy and their management it is very important to review the four categories of immunologic responses, as categorized by Gell and Coombs.[4] Most ocular allergies are Type I, IgE/mast cell reactions, but Type IV delayed hypersensitivity reactions may also be involved in some forms of allergy expression.[5,6]

In Part 1 of this monograph, we review the etiology of ocular allergy. In Part 2, we discuss key steps in diagnosis, the range of available treatments, and pearls for the clinical management of each type of ocular allergy. Much of the text is devoted to SAC and PAC, as these conditions account for the vast majority of ocular allergy cases. However, clinicians should also be aware of less common, but potentially more serious forms of allergy.



Courtesy of Paul Karpecki, O.D.

Typical ocular injection in the case of a patient with seasonal or perennial ocular allergies.

## Seasonal Allergic Conjunctivitis

SAC is caused by a hypersensitivity reaction to airborne allergens such as tree, grass or ragweed pollen, and frequently occurs in conjunction with nasal symptoms of rhinitis or hay fever.

The incidence of SAC, like other chronic allergies, has been rising in developed countries. Various hypotheses exist as to the reasons for this increase, including genetic factors; the lack of exposure to dirt and allergens in modern, overly clean societies, especially during early childhood; increases in environmental pollution; and exposure to chemicals and food additives.

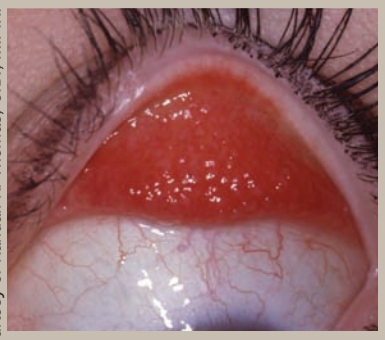
### Seasonal Allergic Conjunctivitis

- Caused by a hypersensitivity reaction to airborne allergens.
- Frequently occurs in conjunction with nasal symptoms of rhinitis or hay fever.
- Type I, IgE-mediated allergic reaction.
- Symptoms treated with over-the-counter or prescribed systemic allergy medication.
- Hypersensitivity response and symptoms are identical to those of perennial allergic conjunctivitis.

SAC is a Type I, IgE-mediated allergic reaction. Following initial exposure to the allergen, the eye begins producing IgE antibodies that bind to the surface of ocular mast cells. During subsequent contact between the airborne allergen and the tear film, IgE antibodies cause an immediate hypersensitivity reaction. The mast cells degranulate, releasing a host of inflammatory and allergic mediators, most notably, histamine, which binds to receptors on endothelial vascular cells, stimulating hyperemia and edema, and activates the nerve cells that cause itching.

New research shows that changes in tear protein components and concentration in SAC and PAC may contribute to tear film instability in allergy sufferers.[7]

In two recent European studies, only 11% to 19% of individuals suffering from allergy symptoms first consulted an eye-care professional.[8,9] One consequence is that, particularly in allergic rhinoconjunctivitis, patients may treat their symptoms with over-the-counter (OTC) or prescribed systemic allergy medications. These medications can have a drying effect on the eye and may worsen ocular discomfort and contact lens tolerance even while relieving nasal symptoms.



Courtesy of Randall K. Thomas, O.D., M.P.H.

This example of GPC shows a patient with both grade 2 giant papillae and grade 2 injection to the superior tarsal palpebral conjunctival plate of the upper lid. This patient was moderately symptomatic with moderate itching and a scant mucous discharge.

## Perennial Allergic Conjunctivitis

In PAC, the offending allergens (including pet hair and dander, dust mites, and molds) are ubiquitous and present year-round. Otherwise, the hypersensitivity response and symptoms are identical to SAC. In our experience, perennial allergies are on the rise, perhaps because of some combination of changes in home construction, sedentary habits, and environmental factors.

## Contact Allergy

Allergic conjunctivitis can also be caused by contact with ingredients in eye drops, contact lens solutions, ocular ointments, or facial creams. This is a Type IV reaction. Clinicians should be suspicious of a non-atmospheric (i.e., contact) cause if the lower lid and inferior conjunctiva are most affected and there is no history of allergy. Remember, though, that mild to moderate bacterial infection may also show a similar pattern. The distinguishing feature of bacterial etiology would be mucopurulent discharge.

## Giant Papillary Conjunctivitis

Giant papillary conjunctivitis (GPC) is characterized by relatively large papillae on the upper tarsal conjunctiva that develop over time in response to contact lens wear or some other foreign body, such as sutures or an ocular prosthesis. Causation is likely multifactorial. The presence of the contact lens or foreign body creates mechanical irritation that recruits lymphocytes, mast cells, basophils, and eosinophils and stimulates mucus production. The mucus- and antigen-coated lens then triggers a hypersensitivity immune reaction. Giant papillae occur from structural changes associated with the release into the tears of inflammatory mediators such as IgE, IgG, and C3 anaphylatoxin. The pathophysiology involves mainly Type I, but likely some Type IV hypersensitivity reaction as well.

### Giant Papillary Conjunctivitis

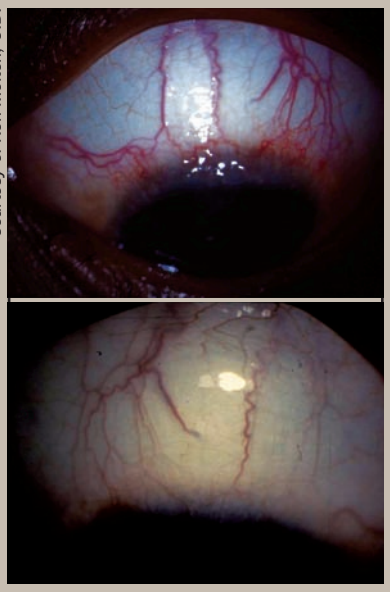
- Characterized by relatively large papillae on the upper tarsal conjunctiva
- Causation likely multifactorial
- Contact lens deposits, increased wearing time, infrequent lens replacement and a genetic predisposition in individual with a history of atopy contribute to the condition
- Reversible with temporary discontinuation of lens wear or foreign body removal.

Major factors contributing to GPC include contact lens deposits; increased wearing time (greater antigen exposure); infrequent lens replacement; individual reaction to lens type; larger lenses with a greater area for antigenic deposits; and a genetic predisposition among individuals with a history of atopy. Although contact lens material likely plays a role in GPC, the condition still occurs even with modern, high-Dk silicone hydrogel lenses.[10]

Giant papillae may not be evident in the early stages, but patients will experience increasing contact lens intolerance and increasing amounts of mucus production as the condition progresses. It is reversible with temporary discontinuation of contact lens wear or removal of the foreign body.

## Vernal Keratoconjunctivitis

Vernal keratoconjunctivitis (VKC) is a severe form of ocular allergy seen mostly in children (especially black males) and young adults. A clinician in a typical practice might see one case of VKC per year, although it is more common in warm, dry climates. Onset usually occurs before puberty and reaches a peak between 11 to 13 years of age. We have seen this condition in children ages 7 and older; rarely in any-



Courtesy of Ron Melton, O.D.

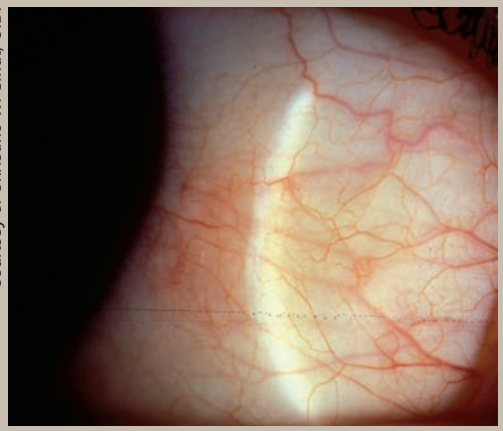
An example of VKC in an 8-year-old black male (top image). Marked injection to superior limbus OU was present. A topical, ester-based corticosteroid successfully treated the condition (bottom image).

one over the age of 20. Young males are affected at twice the rate of females, although the gender distribution is more even among older teens.

As might be expected from its name, VKC is most severe between April and August; however, many patients experience recurrences year-round. VKC is often hereditary and frequently occurs in conjunction with other atopic disorders. The pathophysiology is not well understood, but likely involves a combination of Type I and Type IV hypersensitivity reactions with hormonal and neuroendocrine influences.

The tarsal form of the disease is characterized by giant papillae on the upper tarsal conjunctiva, which consist of dense fibrous tissue and a variety of inflammatory cells; the limbal form is characterized by yellow-gray gelatinous limbal infiltrates. Trantas dots containing eosinophils and epithelial cells define the limbal form of VKC. Corneal changes are common due to mechanical irritation from the giant papillae, conjunctival inflammation, concomitant dry eye, and inflammatory mediators released from mast cells and eosinophils. Occasionally, there can be corneal epithelial compromise resulting in a shield-shaped defect.

Although VKC is a self-limiting disorder with a mean duration of approximately five years, untreated corneal complications may lead to permanent impairment of vision. Bonini reported that 6% of cases suffered loss of visual acuity from corneal scarring and in 2%, ketone steroid-induced glaucoma was observed.[11]



Courtesy of Christine W. Sindt, O.D.

Chemosis secondary to allergic conjunctivitis.

## *Clinical Pearl*

*Avoidance of eye rubbing is an effective, but often neglected piece of advice for allergy patients. We explain to patients that rubbing actually contributes to the breakdown of the mast cell and floods their eye with more of the inflammatory mediators that cause the itching.*[13]

## Atopic Keratoconjunctivitis

Atopic keratoconjunctivitis (AKC) is a severe, chronic form of ocular allergy. The incidence is about 2% to 8% of the population, but may be rising.[5] As with VKC, AKC is often hereditary and occurs more frequently in males. However, the typical onset is later, in the late teens or 20s, and symptoms persist longer than in VKC, usually peaking between 30 to 50 years of age. There is a close association between AKC and other atopic disorders. Most (95%) patients with AKC have also had eczema and 87% have a history of asthma.[12]

The pathophysiology of AKC is not entirely clear. The condition may involve both a Type I and Type IV allergic reaction that is both antibody- and cell-mediated. In eyes with AKC, the conjunctiva contains increased concentrations of several allergic and inflammatory mediators, including mast cells, eosinophils, lymphocytes, and basophils that contribute to chronic damage.[1]

This condition can become severe, debilitating, and sight-threatening.

Persistent epithelial defects are painful and leave the eye prone to corneal infection. Corneal scarring and vascularization secondary to chronic inflammation of the ocular surface can result in vision loss. Cataracts and keratoconus are also associated with AKC.

# PART 2: Diagnosis and Management of Ocular Allergies

Each year, allergies (of all types) are responsible for about 4 million lost work days and more than $6 billion spent on prescription drugs.[14] A recent survey found that more than 50% of people with ocular allergies report difficulty sleeping and concentrating because of their allergies.[15] More than 60% have trouble driving and 70% or more report difficulty with reading or outdoor activities. In another study, nearly half of patients with ocular allergy rated their quality of life during an acute episode as significantly impaired (≥6 on a 10-point scale).[9]

We believe optometrists often miss the opportunity to address this important health issue with patients. The key to treating allergy effectively, of course, is diagnosing it in the first place. We recommend that clinicians routinely ask patients about itching and other allergy symptoms.

> ***Clinical Pearl***
>
> *Always ask patients if they are using any OTC eye drops now or have tried any allergy therapies in the past that were not successful. You want to avoid either doubling up on medications or prescribing a medication that has been previously ineffective.*

Below, we discuss key factors in the diagnosis of each form of ocular allergy, as well as strategies for managing each condition. In the past five to 10 years, we have seen a paradigm shift toward much more targeted therapy that specifically addresses the underlying inflammation and offers more rapid relief of symptoms.

## SAC/PAC: Diagnosis

Allergic conjunctivitis of either the perennial or seasonal type can be distinguished from viral or bacterial conjunctivitis by itching, recurrence, personal/family history of atopic disorders and also the appearance of the conjunctiva and ocular discharge. In the eye with ocular allergy, the conjunctiva will typically have a pink or milky appearance, rather than the vibrant red color seen in infectious conditions. Also, the SAC/PAC mucoid discharge is

Courtesy of Paul Karpecki, O.D.

In this eye with routine allergic conjunctivitis, one can see the classic level of injection (pink/milky) and papillae of the lower fornix (left). By contrast, these eyes have the vibrant red injection more commonly associated with an infectious (bacterial or viral) conjunctivitis (right).

# Case: Allergic Blepharoconjunctivitis

*Randall K. Thomas, O.D., M.P.H.*

**Presentation:** An 18-year-old male presented with a 2-week history of red, itchy, scratchy eyes and photophobia.

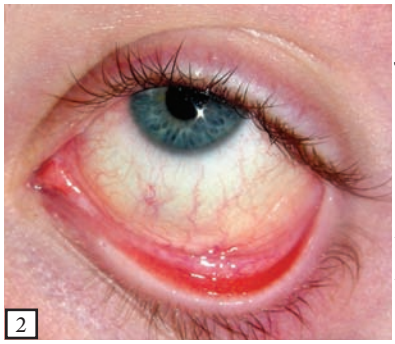
**History:** He had tried OTC Visine drops without relief and was also using OTC Claritin episodically without relief. He wore silicone hydrogel contact lenses on a daily-wear basis, but had worn the lenses on a very limited basis for the past two weeks. The patient was not aware of any triggering exposure to known allergens.

**Clinical findings:** Vision with glasses was 20/20 OU. The slit lamp exam revealed clear, nonstaining corneas, 1+ conjunctival injection, and 1+ puffiness of all four eyelids (Figure 1). Upon eversion, the lids were normal. The tear film meniscus was low, with thin, stringy mucus excess (Figure 2). Tear break-up time was approximately 5 to 7 seconds. Facial acne rosacea was noted.

This patient was diagnosed with allergic blepharoconjunctivitis with concomitant ocular surface dryness.

**Management and follow up:** The patient was instructed to discontinue contact lens wear for 1 week. I prescribed Alrex ophthalmic suspension q.i.d. for 1 week, then b.i.d. for 1 month, along with Soothe XP, 2 to 4 times per day as needed to relieve other symptoms. A follow-up visit was scheduled for 1 week later.

At that visit, the patient reported that his eyes were much improved within 3 to 4 days of initiating treatment and that he had been successfully wearing his contact lenses for the past couple of days. His vision was still 20/20 OU with well-fitting silicone hydrogel lenses. Both eyes were minimally injected. The tear film was low, without mucus excess. Tear break-up time had improved to 8 to 10 seconds. The patient had no more itching, and only needed to use the Soothe XP b.i.d. to enable 10 to 12 hours of comfortable contact lens wear. He was instructed to continue this regimen. Oral doxycycline and/or punctal plugs could be considered if comfort of contact lens wearing time becomes compromised in the future.



Courtesy of Randall K. Thomas, O.D., M.P.H.

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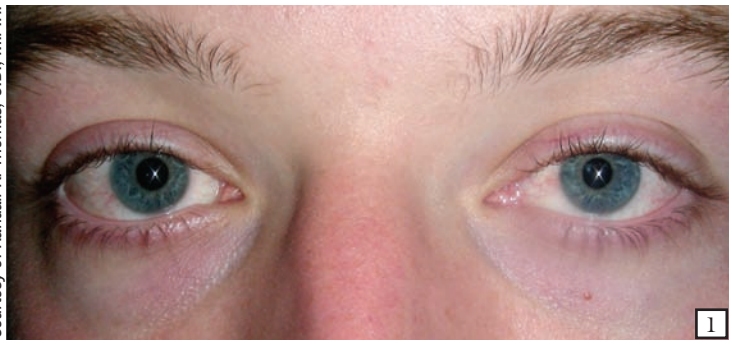
**Commentary:**

This soon-to-be college freshman developed allergic blepharoconjunctivitis from some unknown trigger. He also had subnormal tear film function, which may have contributed to his allergy expression.

While a topical antihistamine would have suppressed his symptomatic itching, it would have left the initial conjunctival injection and photophobia untreated. Therefore, an ester-based topical corticosteroid was selected, as this would also suppress any baseline inflammation that could be an aggravating component to his dry eyes. A state-of-the-art, lipid-based artificial tear was chosen because of its ability to maximally enhance the ocular surface.

The patient does have some oculodermal and facial acne rosacea; as evidenced by the telangiectatic microvasculature, and he may need oral doxycycline therapy in the future.



Courtesy of Randall K. Thomas, O.D., M.P.H.

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## Ocular Allergy Medicine Profile

| Brand Name | Generic Name | Manufacturer | Pediatric Use | Bottle Size(s) | Dosing |
|---|---|---|---|---|---|
| **CONTEMPORARY AGENTS** | | | | | |
| Acular LS | ketorolac tromethamine 0.4% | Allergan | 3 years | 5ml, 10ml | q.i.d. |
| Alaway (OTC) | ketotifen fumarate 0.025% | Bausch + Lomb | 3 years | 10ml | b.i.d. |
| Alrex | loteprednol etabonate 0.2% | Bausch + Lomb | 12 years | 5ml, 10ml | q.i.d. |
| Bepreve | bepotastine besilate 1.5% | ISTA | 2 years | 5ml, 10ml | b.i.d. |
| Claritin Eye (OTC) | ketotifen fumarate 0.025% | Schering-Plough | 3 years | 5ml | b.i.d. |
| Elestat | epinastine HCl 0.05% | Allergan | 3 years | 5ml | b.i.d. |
| Emadine | emedastine difumarate 0.05% | Alcon | 3 years | 5ml | q.i.d. |
| Lastacaft | alcaftadine 0.25% | Allergan | 2 years | 3ml | q.d. |
| Optivar | azelastine hydrochloride 0.05% | Meda | 3 years | 6ml | b.i.d. |
| Pataday | olopatadine hydrochloride 0.2% | Alcon | 3 years | 2.5ml | q.d. |
| Patanol | olopatadine hydrochloride 0.1% | Alcon | 3 years | 5ml | b.i.d. |
| Zaditor (OTC) | ketotifen fumarate 0.025% | Novartis | 3 years | 5ml | b.i.d. |
| **HISTORICAL AGENTS** | | | | | |
| Alamast | pemirolast potassium 0.1% | Vistakon Pharm. | 3 years | 10ml | q.i.d./ b.i.d. |
| Alocril | nedocromil sodium 2% | Allergan | 3 years | 5ml | b.i.d. |
| Alomide | lodoxamide tromethamine 0.1% | Alcon | 2 years | 10ml | q.i.d. |
| Crolom | cromolyn sodium 4% | Bausch + Lomb | 4 years | 10ml | q.i.d. |
| Opticrom | cromolyn sodium 4% | Allergan | 4 years | 10ml | q.i.d. |

typically stringy or ropey compared to the purulent discharge of bacterial conjunctivitis or the watery discharge common to viral etiologies.

Symptoms, which always include itching, can range from mild to quite severe during periods of peak allergen exposure. Itching may be accompanied by burning, stinging, conjunctival redness, and/or mucoid discharge, as noted above. SAC and PAC are almost always bilateral.

Clinical signs include hyperemia and/or chemosis of the bulbar conjunctiva, palpebral micro- or macro-papillary changes, and possibly lid involvement, including swelling, a very subtle Dennie's line, or allergic "shiner." The cornea is rarely involved and vision is typically unaffected. It is important to note that there may

### *Clinical Pearl*

*When treating a new allergy patient with topical steroid therapy, schedule a follow-up appointment 3 to 4 weeks after beginning treatment. Follow-up goals:*

- *Confirm compliance with regimen*
- *Confirm efficacy and symptom relief*
- *Evaluate IOP*
- *Educate about long-term management.*

be no obvious indication of allergic involvement other than ocular itching.

Because symptoms can exist without obvious clinical signs, it is important to routinely ask patients about itching, even if they don't spontaneously mention it during an exam. When there is a complaint of itching, we try to determine whether the eyelids or the eye itself that itches. Itching can also be a symptom of dry eye, blepharitis, and even psoriasis and should not be presumed to always be allergy. Marked itching is the hallmark symptom of crab lice infestation of the eyelid margins. Conversely, chemosis without itching would cause one to consider orbital inflammatory disease in the differential.

In determining the severity of the allergy, remember that the redness of the eye almost always correlates with the severity of itching. It is also helpful to ask specific questions about the effect of the symptoms on the patient's lifestyle. For example:

- Do they keep you from working or affect your work performance?
- Do they keep you awake at night?
- Do they bother you when you are driving or reading, or keep you from going outdoors?

The answers to these questions are important in determining the aggressiveness of treatment.

## SAC/PAC: Management

The first step in managing seasonal allergies is to avoid exposure to the allergen to whatever degree possible. Remind patients to stay inside during peak pollen days, keep car windows rolled up, avoid eye rubbing, wash hair before sleeping, and take other simple measures to minimize ocular exposure. Of course, it may not be practical or possible to completely avoid the allergen, particularly for those who suffer from perennial allergies.

### *Clinical Pearl*

*For contact lens wearers who need topical steroids, the timing of drops can be a challenge. One might consider either b.i.d. use or using the steroid before applying lenses in the morning, limiting contact lens wear and instilling another drop immediately after removal, then a third drop before bedtime.*

Medical therapy for SAC/PAC depends on the severity of clinical signs and especially, in our opinion, on the degree of symptoms experienced by the patient. We use the simple principle that the more the allergy bothers the patient, the more emphasis should be placed on an aggressive therapeutic course. With this in mind, we can think of seasonal and perennial allergies in three categories:

1. Mild
2. Mild to Moderate
3. Moderate to Severe.

• ***Mild.*** The patient with a truly mild case typically doesn't come in for a visit because of allergy symptoms, but perhaps mentions them during a regular eye exam when queried about itching. This patient is only mildly concerned about symptoms and is functioning well in day-to-day activities. Artificial tears can dilute the allergen on the ocular surface and, along with cold compresses, may sufficiently relieve symptoms. Such palliative measures are an inexpensive, simple, and accessible approach to mild allergies.

Educate mild allergy sufferers about avoiding eye rubbing and use of OTC vasoconstrictors without medical oversight.

• ***Mild to moderate.*** The mild-to-moderate allergy patient is the one who presents for a consultation because of allergy symptoms that are affecting daily life. There may or may not be any clinical signs. For many clinicians, this is the most challenging group to treat because of the plethora of categories from which to choose.

Historically, the first line of treatment for these patients was a topical antihistamine, with or without a decongestant. The older literature supported using drugs such as Vasocon-A (antazoline-naphazoline), Opcon-A (pheniramine maleate 0.315%) or Emadine (emedastine difumarate) for relief from allergy symptoms.[16] However, these drugs are typically dosed on an

## Management Protocol: Seasonal and Perennial Allergies

| | Symptoms | Signs | Treatment |
|---|---|---|---|
| **Mild** | Mentions allergy symptoms only incidentally; not the primary complaint | Minimal or no signs | Palliative measures; Possibly an antihistamine/mast cell stabilizer |
| **Mild to Moderate** | Primary reason for visit is itching/other symptoms; Lifestyle is affected | Minimal or no signs | Topical steroid q.i.d. for 2 weeks, then b.i.d. for 1 to 2 months, then switch to an antihistamine/mast cell stabilizer if symptoms persist |
| **Moderate to Severe** | Primary reason for visit is itching/other symptoms; Lifestyle is greatly affected | Red eyes; conjunctival congestion or chemosis above normal baseline | Topical loteprednol 0.2% or 0.5%, q.i.d. for 2 weeks, then b.i.d. for 1-2 months, then move to a combination antihistamine/mast cell stabilizer |

inconvenient t.i.d. or q.i.d. dosing schedule. Moreover, rebound hyperemia may occur with long-term use of decongestants.[17]

In our opinion, these older, first-generation products have been displaced in the contemporary management of ocular allergy by eyecare providers. Likewise, there is almost no role anymore for a pure mast cell stabilizer. Practically speaking, a mast cell stabilizer alone, while it may offer effective long-term therapy, does little to relieve acute symptoms and is less attractive to patients for that reason. Newer multimechanism products combine the long-term effects of a mast cell stabilizer with immediate antihistamine relief and are a better choice in almost all cases.

Antihistamine/mast cell stabilizers such as Zaditor and Alaway (ketotifen 0.025%, Novartis and Bausch + Lomb, respectively), Patanol (olopatadine hydrochloride 0.1%, Alcon), Pataday (olopatadine hydrochloride, 0.2%, Alcon), Optivar (azelastine hydrochloride 0.05%, Meda Pharmaceuticals), Elestat (epinastine hydrochloride 0.05%, Allergan), Lastacaft (alcaftadine ophthalmic solution 0.25%, Allergan) and Bepreve (bepotastine besilate ophthalmic solution 1.5%, ISTA Pharmaceuticals) all provide both long-term management as well as rapid initial relief of acute symptoms.[18] They are FDA-approved for twice-daily use in patients three years of age and older, except for Pataday, which has a once-daily dosing indication. Lastacaft is approved for once-daily dosing in those age two and older.

Clinicians may wish to begin treatment with these agents a few weeks prior to the beginning of the anticipated allergy season to better suppress symptoms associated with SAC.[19]

A conservative eye-care practitioner may want to start with a multimechanism product and reserve topical steroid treatment for later, in case the initial therapy does not bring relief.

If patients are significantly bothered by their symptoms and/or there is even low grade redness, a more aggressive approach is to opt for a short course of an ester steroid at the outset. After dosing the steroid q.i.d. for two weeks, many doctors taper to b.i.d. for another month or two. Then, the steroid can be replaced with a combination antihistamine/mast cell stabilizer for long-term management. In a contact lens wearer whose symptoms are closer to the mild end of the spectrum, steroid drops could be used b.i.d., before and after lens wear.

This paradigm has certainly evolved. Ten years ago, the

side effects of older ketone corticosteroid options were undesirable and therefore topical steroid therapy was considered a last resort. Today, however, we have Alrex (loteprednol etabonate 0.2%, Bausch + Lomb), a site-active steroid approved for the treatment of ocular allergy that has much less potential for unwanted side effects. Ilyas and colleagues reported several years ago that patients using Alrex for more than 12 months—including some who instilled nearly 4,000 drops per eye over the study period—had no adverse effects.[20]

• ***Moderate to severe.*** In moderate to severe cases of SAC/PAC, the patient has intense itching that significantly affects daily life and has usually been bothered by the symptoms for days or weeks. The eyes are typically very red, and the clinician will see increased conjunctival chemosis. For these patients, topical steroid therapy is certainly indicated, with treatment eventually being replaced with an antihistamine/mast cell stabilizer, as described above. More frequent dosing of an ester (not ketone) steroid (e.g., every two hours for 2 to 3 days) can really increase the anti-inflammatory efficacy. When there is itching, chemosis, and significant lid involvement at initial presentation, a short-course oral steroid such as prednisone may be needed as an adjunct to topical steroid therapy.

A follow-up appointment should be scheduled whenever a steroid is prescribed, particularly if the patient has glaucoma or other medical issues. Even with loteprednol, it is possible to see pressure spikes, so we recommend seeing patients back after 3 to 4 weeks to check IOP and to assess the therapeutic response.

Oral antihistamines may augment topical agents for treatment of allergic rhinoconjunctivitis. First-generation antihistamines, such as Benadryl (diphenhydramine hydrochloride, McNeill, PPC), are sedating. Second-generation drugs such as Allegra (fexofenadine hydrochloride, Sanofi Aventis), Claritin (loratadine, Schering-Plough), Clarinex (desloratadine, Schering-Plough), Zyrtec (cetirizine hydrochloride, McNeill-PPC) and Xyzal (levocetirizine dihydrochloride, Sanofi Aventis) are less sedating, but can still can cause ocular surface drying. (*Note: Allegra, Claritin and Zyrtec are now available OTC.*) Although they may be appropriate for atopic disease, we consider them to be only rarely appropriate for seasonal allergies. An inhaler or nasal spray would be preferable for control of nasal/sinus symptoms. Keep in mind that inhaled corticosteroids, when combined with oral corticosteroid use, increase the risk of posterior subcapsular cataract formation.[21]

## GPC: Diagnosis

GPC is bilateral in 90% of contact lens-related cases. The onset of symptoms may occur weeks or years after beginning contact lens wear. Diagnosis of the condition is generally fairly straightforward. However, it can easily be missed if the clinician neglects to evert the lids and stain with sodium fluorescein.

Clinical findings of large papillae on the upper tarsal conjunctiva and a history of contact lens wear, ocular prosthesis or presence of exposed sutures point to the condition. Note that in an asymptomatic patient, a micro-papillary response can be perfectly normal and may not in fact indicate GPC. Recent literature suggests that the clinical papillary presentation can be generalized, which is more common with low-Dk hydrogel lenses, or more localized, which seems to be more common with gas permeable lenses and high-Dk silicone hydrogel lenses.[22]

Symptoms are also important in diagnosing GPC. Often, complaints of fluctuating vision and mucoid discharge will override itching as the patient's primary complaint. Recent-onset contact lens intolerance,

### *Clinical Pearl*

*In contact lens wearers, do not skip eversion of the lids and fluorescein staining, as these steps are critical for diagnosing GPC. Contact lenses can be re-inserted 10 to 15 minutes after staining or sooner with lavage.*

## Management Protocol: GPC

(If concurrent tear film dysfunction is present, use of an artificial tear can be helpful adjunctive therapy.)

| Presentation | Therapy | Long-term Management |
|---|---|---|
| **Mild** | Lotemax q.i.d. for 1 to 2 weeks, then resume CL wear with Lotemax b.i.d. for 2 to 4 more weeks (or substitute a 3/4-inch strip of Lotemax ointment at night). | Move to more frequent replacement of CLs or daily disposable lenses. Educate patient on compliance and proper lens hygiene. |
| **Moderate to Severe** | Lotemax q.i.d for 2 to 4 weeks, then resume CL wear with Lotemax b.i.d. for 2 to 4 more weeks (or substitute a 3/4-inch strip of Lotemax ointment at night). | |

particularly at the end of the day, is also to be expected.

### GPC: Management

There are two steps in the management of GPC. First, one must treat the acute inflammation and symptoms. Once the inflammation is resolved and symptoms are under control, patient education, changes in contact lens brand, and wear patterns become critical to avoiding a recurrence.

The appropriate treatment for the acute signs and symptoms is a topical steroid. Specifically, Lotemax (loteprednol 0.5%, Bausch + Lomb) is the only steroid that has been shown to be an effective and safe treatment for this condition.[23] GPC is a conjunctival inflammation, and it may be that ester steroids are more effective than ketone steroids at resolving conjunctival inflammation.

The degree of tarsal hyperemia and extent of papillary response dictate whether we consider the condition to be mild or moderate to severe. The difference in treatment between these two categories is the length of time the patient should abstain from contact lens wear (1 to 4 weeks) and use the steroid drops q.i.d., as seen in the accompanying treatment protocol. Tapering is not required, but many clinicians like to go down to b.i.d. as the patient transitions back into contact lenses. If this is the case, the patient should be instructed to use the drops before inserting lenses in the morning and after removing them in the evening. In milder cases, patients may continue to wear contact lenses and start with a b.i.d. steroid schedule from the beginning. Improvement in itching, lens tolerance, and papillae appearance can be noted as early as one week into therapy.

We do not use mast cell stabilizers after the course of steroid therapy. It is important, however, to address the modality of contact lens wear, tear film function, and compliance with care recommendations. The incidence of GPC has been shown to be as high as 36% in patients who replace their contact lenses every 4 weeks or longer, compared to 4.5% in patients on a daily to every 3 weeks replacement

### *Clinical Pearl*

*In the past, we had limited choices in steroid ointments with good clinical efficacy, but a new ointment slated for release soon may be an excellent option for many allergic conditions. When treating contact allergic conjunctivitis, GPC, VKC or AKC, the clinician may wish to consider prescribing topical loteprednol ointment (Lotemax, Bausch + Lomb) at bedtime, instead of or in addition to the last eyedrop dosing of the day, depending on the clinical need.*

schedule.[24] We always stress better lens hygiene and generally move GPC patients into a more frequent replacement regimen than that being followed when the condition developed.

## VKC: Diagnosis

As discussed in section 1, one should be suspicious of VKC in children, particularly boys of African descent, with a history of atopic disorders. Although the symptoms commonly flare up at the same time as seasonal allergies (in the spring and summer), these are more severe.[25]

Again, fluorescein staining of the everted upper lid is necessary for correct diagnosis. Two forms of VKC actually exist:

1. Palpebral
2. Limbal.

In the palpebral form, one will see giant papillae > 1 mm on the superior palpebral conjunctiva in a distinctive cobblestone pattern. In fact, the papillae make the lids so heavy that it is not unusual to see bilateral pseudo-ptosis. There may also be significant photosensitivity due to the corneal changes.

The limbal form of VKC usually has no associated giant papillae or corneal plaque formation, no corneal complications, and a shorter clinical course than palpebral VKC.[12]

## VKC: Management

Classically, mast cell stabilizers have been used to treat VKC.[26–28] Mast cell stabilizers inhibit release of cytokines from the mast cells, decreasing the papillary formation, and interrupt recruitment of eosinophils, diminishing the opportunity for corneal changes and formation of Trantas dots.

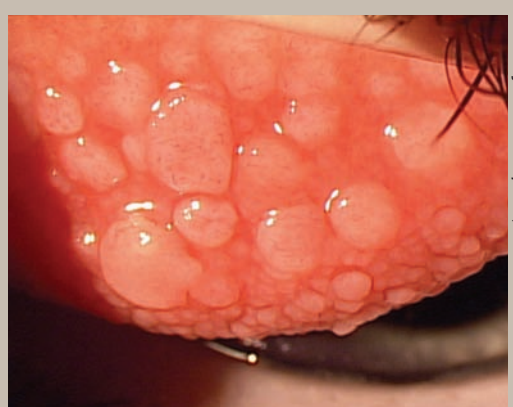
In our opinion, however, modern management of VKC requires long-term aggressive therapy (q.i.d. for 6 to 9 months) with topical steroids to prevent potentially sight-threatening consequences. Given that long-term therapy is required, the ester steroid, loteprednol is the wisest option.

If, after six to nine months, the eyes are quiet and almost totally free of symptoms, one could transition the patient to once- or twice-daily steroid maintenance, or potentially move to an antihistamine/mast cell stabilizer.

One study found that olopatadine 0.1% effectively relieved signs and symptoms of VKC, including reducing the number of goblet cells in the conjunctiva, which decreased the amount of mucous discharge.[29] While olopatadine should not be relied on for primary therapy of VKC, it could be considered an option after the eye is quiet.

### Management Protocol: VKC

| Presentation | Short-Term Therapy | Long-Term Management |
|---|---|---|
| **Palpebral** | • Lotemax q.i.d. for 6 to 9 months<br>• Acetylcysteine to control mucous<br>• Add a topical antibiotic if shield ulcer is present | • Continue steroid therapy once or twice daily or transition to antihistamine/mast cell stabilizer |
| **Limbal** | • Lotemax q.2.h. x 4 days, q.i.d. x 2 weeks, b.i.d. x 2 months | •Educate patient on eye rubbing and course of disease<br>•Return to steroids if symptoms break through |
| **Intractable** | All of the above, plus systemic aspirin and/or topical cyclosporine. Consult with corneal specialist. | |



Courtesy of Paul Karpecki, O.D.

In the palpebral form of VKC, one will see giant papillae > 1 mm on the superior palpebral conjunctiva in a distinctive cobblestone pattern.

## *Clinical Pearl*

*The four key locations for eczema are behind the knees, elbows, around the neck, and behind the ear. If you ask patients whether they have skin problems in these areas, you will often get an affirmative answer that no only confirms your suspicion of atopic allergy, but also may lead them to seek treatment for the dermatologic condition.*

If symptoms quickly return during antihistamine/mast cell stabilizer treatment, the patient should resume topical steroid therapy. Patients must also be instructed not to rub their eyes. An excellent potential adjunct is topical acetylcysteine, which works very well to control mucus discharge.

In moderate to severe cases with shield ulcers, a topical antibiotic should be added to the regimen.[11] For the very rare patient who has severe intractable VKC, options include systemic aspirin in conjunction with topical mast cell stabilizers, and topical cyclosporine.[30–33] Consultation with a corneal specialist is recommended in severe or intractable cases.

### AKC: Diagnosis

• ***Diagnosis.*** Distinguishing the truly atopic patient from severe seasonal or perennial allergy can be challenging. Symptoms are similar, but exaggerated and more severe. Patients tend to have significant corneal involvement (with accompanying photophobia), neovascularization, and staining. These patients tend to be truly miserable, with multisystem allergies. Dermatitis or some skin involvement (usually eczema) is essential to the diagnosis of AKC. In fact, virtually 100% of patients with AKC also have eczema. Therefore, a thorough history, including questioning about skin conditions, is important. In these patients, lid eczema can be severely irritating, causing a burning sensation that may be worse than the allergic itching.

### AKC: Management

Topical steroid therapy is warranted in AKC for as long as necessary to control symptoms. One study found Restasis safe and somewhat effective in relieving signs and symptoms in cases of refactory steroid-resistant AKC.[34] In rare cases, oral cyclosporine (3 to 5 mg/Kg/day) may be necessary.[35,36]

Although a dermatologist can treat the lids, there is no reason for the optometrist not

## Case: Atopic Keratoconjunctivitis

*Jimmy D. Bartlett, O.D.*

**Presentation:** A 19-year-old female at the beginning of her second trimester of pregnancy presented for a second opinion about the topical steroids she had been using for ocular allergy.

**History:** The patient was diagnosed elsewhere with severe allergic conjunctivitis. For the past 12 months, she had been using Pred Forte (prednisolone acetate ophthalmic suspension, USP, Allergan) 1% q.i.d. Upon questioning, she said she also suffered from eczema and asthma.

**Clinical findings:** The patient had conjunctivitis and keratitis, corneal pannus and neovascularization. Best-corrected acuity was 20/30. She suffered from severe itching and redness. IOP was normal. Given her other atopic conditions, this patient was a classic case of atopic keratoconjunctivitis.

**Management recommendations:** The clinician has to consider, first of all, whether steroids are indicated for atopic disease. The answer is absolutely yes. But we also have to consider the duration of treatment with steroids, given the possible side effects, and particularly the safety of the medication during pregnancy. I switched this patient to the mast cell stabilizer, Alomide (lodoxamide trometh-amine, Alcon), which is a pregnancy category B drug, so it would be considered somewhat safer during pregnancy. She did well with this alone.

to do so. A good option for lid eczema is Lotemax ointment or 0.1% triamcinolone cream (Kenalog, Cinolar, Triderm). Other options include hydrocortisone and new calcineurin inhibitors such as Protopic (tacrolimus, Astellas Pharma) and Elidel (pimecrolimus, Novartis), although this class of drugs can itself cause irritation. These drugs are considered a second line of therapy due to cost and some animal studies that have suggested a potential link with lymphoma. We have found the Lotemax ointment or triamcinolone cream to be extremely successful.

Over the long term, AKC patients certainly need to be under the care of their primary care doctor, a pediatrician or allergist, in addition to their eyecare provider to ensure that non-ocular aspects of this long-term disease are well controlled.

## Conclusions

Correctly diagnosing and treating ocular allergies is an opportunity for optometrists to have a real impact on their patients' overall health, success with contact lens wear, and quality of life. We believe that eyecare practitioners need to be advocates for their patients in recommending aggressive topical therapy when needed. The safe, ester-based steroid, Alrex, is indicated for the treatment of ocular allergy, but is too often viewed as a last resort, despite the fact that this therapy has been shown to be safe even when used for 12 months or more.

### *Clinical Pearl*

*Neovascularization, along with dermatitis, is a key factor in distinguishing AKC from seasonal or perennial allergies. Examine carefully—even a small amount of peripheral neovascularization should be treated immediately with an ester steroid, as it may begin to affect the visual axis in as little as one month.*

More serious allergic conditions such as VKC and AKC are relatively rare, but the potential for long-term, sight-threatening complications is high; thus, aggressive treatment is warranted. Clinicians should be alert to the signs and symptoms of these serious atopic responses.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