A Scientific Review and Expert Case Debate

TARGET AUDIENCE
- Allergists
- Ophthalmologists

ACTIVITY PURPOSE
Educate physicians on the various forms of ocular allergies as well as current management options and emerging treatment.

STATEMENT OF NEED
Allergic conjunctivitis is one of the most common conditions seen by ophthalmologists, optometrists, and allergists. During the past 40 years, both the incidence and prevalence of allergic conjunctivitis have risen exponentially, and they continue to rise. Numerous treatment strategies abound without any clear consensus from various clinical studies, creating a challenge for healthcare providers.

Current ocular allergy treatment options are effective only at mediating the symptoms, and these options have many different methods of action and modes of delivery. Allergists, ophthalmologists, and optometrists must become better versed in the classification, severity indices, and various options available for treatment of ocular allergy and they must also become cognizant of the differences between the various subtypes of dry eye disease and ocular allergy. In addition, they must be able to recognize the severity of dry eye disease and ocular allergy.

LEARNING OBJECTIVES
After completing this enduring activity, participants should be able to:
- Differentiate between the various types of ocular allergies based on clinical presentation
- Individualize management options for ocular allergy based on disease severity, patient factors, and associated risks and benefits
- Describe the newer studies on the diagnosis and treatment of ocular allergy that are rapidly changing potential treatment algorithms

DESIRED RESULT/OUTCOME:
Ophthalmologists know and apply current treatment strategies through an individualized stepwise approach to optimize treatment outcomes in patients with ocular allergy.

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Introduction

Allergies are said to affect up to 50 million Americans, and up to 40% of the global population has signs of allergies. 1-3 Ocular allergies involve the conjunctiva and often coexist with allergic rhinitis, atopic dermatitis, and/or asthma. 4 In the pediatric population, one study found that 32% of children with allergies had ocular symptoms as their sole manifestation. 5 About 15% of the worldwide population is affected by ocular allergies, with increasing numbers in industrialized nations. 6, 7 In addition, the economic impact of allergies is significant—about $5.9 billion is spent yearly on ocular allergy treatments. 8 Most allergies treated by eye care specialists involve seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC), with chronic vernal keratoconjunctivitis (VKC), atopic keratoconjunctivitis (AKC), and giant papillary conjunctivitis (GPC) comprising a much smaller percentage. 9 The chronic forms may involve the lid, conjunctiva, and cornea and may necessitate comanagement with eye care specialists, allergists, dermatologists, and pediatricians. Chronic cases may also induce ocular surface tissue remodeling: safe, long-term treatment regimens for severe cases are lacking. 10

SAC and PAC are localized type 1 hypersensitivity reactions with fewer eosinophils than the more chronic forms. Typical presentation includes hyperemia, chemosis, watery discharge, tearing, and itching (the hallmark symptom). Patients with SAC will often have few, if any, findings upon ophthalmic examination, and thus the patient’s history leads to the diagnosis. Papillae—a somewhat common finding in the more-severe forms of ocular allergy—are also commonly found in children and teenagers and are not considered a hallmark for the diagnosis of SAC or PAC. 11

Left untreated, ocular allergies can have a negative impact on a patient’s quality of life and ability to work; chronic forms can lead to ocular surface damage. Although treatment of ocular allergies can improve functionality and from arachidonic acid by the action of cyclooxygenase and lipooxygenase, respectively. The net effect of the release of these mediators is to cause vasodilation and fluid transudation, resulting in swelling and pruritus. The acute response is often augmented by a delayed response that occurs several hours later. Although it is still regulated and initiated by IgE, the delayed response depends on upregulation of adhesion molecules and increased production of mast cells, neutrophils, eosinophils, macrophages, and basophils. 15-17

From a clinical perspective, swelling and itch are the hallmark signs of an allergic response, and within the spectrum of ocular allergy, itching remains the pathognomonic symptom. This mast cell–driven inflammation caused by exposure to an ocular allergen results in transient itching, tearing, and conjunctival edema. 18 Clinical examination may confirm vasoconstriction and reveal that chemosis is present.

Pathophysiology of ocular allergy

At its most simplistic, an ocular allergic reaction follows the same pathophysiologic pathway as an allergic reaction in any other location: a type 1 hypersensitivity reaction is mediated by highly directed subsets of immunological mechanisms that predominantly involve mast cells and immunoglobulin E (IgE). When patients are exposed to an allergen, the antigen binds to the IgE molecules, crosslinking the molecules on the mast cell surface. Mast cells respond by releasing a large number of mediators of an allergic response that are preformed or synthesized de novo. Histamine and eosinophil chemotactic factor are the predominant preformed mediators stored in mast cell granules. Prostaglandins and leukotrienes are synthesized by allergists, dermatologists, and pediatricians. Chronic cases of ocular allergy are prevalent in 15% of the worldwide population, with increasing numbers in industrialized nations. 6 In addition, the economic impact of allergies is significant—about $5.9 billion is spent yearly on ocular allergy treatments. 8 Most allergies treated by eye care specialists involve seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC), with chronic vernal keratoconjunctivitis (VKC), atopic keratoconjunctivitis (AKC), and giant papillary conjunctivitis (GPC) comprising a much smaller percentage. 9 The chronic forms may involve the lid, conjunctiva, and cornea and may necessitate comanagement with eye care specialists, allergists, dermatologists, and pediatricians. Chronic cases of ocular allergy may also induce ocular surface tissue remodeling: safe, long-term treatment regimens for severe cases are lacking. 10

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As in other allergic responses, in SAC and PAC an IgE-mediated mast cell response leads to the production of histamine, leukotrienes, and prostaglandins. This initial reaction is rapid, generally within 30 minutes of the initial allergen exposure. During the subsequent several hours, upregulation of adhesion molecules occurs, with increased infiltration of mast cells, neutrophils, eosinophils, macrophages, and basophils into the conjunctival epithelium.10 The delayed phase results in additional mast cell activation within the conjunctiva, increasing the severity of the reaction.10 No single gene has been identified as the genetic basis for allergies. Rather, the inheritance pattern of allergies implies a polygenic mode. Interleukins (ILs), especially IL-5, IL-4, IL-10, and IL-13, are the most prominent of the genes associated with allergy. IL-10 has been identified as the switch cytokine, regulating which immunoglobulin B cells will alter one isotype to another (IgM to IgG, for example). Other cytokines that can have a prominent role in allergy immunology models.

Allergy immunology models

There is a large body of literature that explores the problem of why there is a switch to production of IgE instead of IgG in patients who express allergies, including ocular allergies. (See “For further reading”). It seems clear that some patients have a genetic predisposition toward developing an IgE response, and these patients develop allergies. What is not clear is what acts on the presynthesizing T-cells to induce a class switch to IgE and an allergic response. The most prominent among the paradigms is the “hygiene hypothesis.”

“Hygiene hypothesis”

Studies from Southern Germany and Sweden have shown that children who grow up on working animal farms are and exposed to higher levels of endotoxin have a lower incidence of allergies and asthma than control children who grow up in the city. The interpretation of these data has led to the hypothesis surmising that children are exposed to fewer antigens and develop asthma and allergy more frequently. By this theory, the infancy is born with T cells set at 0, termed Th0. Under the influence of genetics and environmental exposure, these cells become either Th1 or Th2 cells. Th2 cells are distinguished by IL-4, IL-5, and IL-13 that drive the B cells toward making IgE. It is not clear what antigens would drive Th1 cells to develop to Th12 cells, but viruses, allergens (cockroaches, dust mites, and animal dander), and reduced exposure to endotoxin have postulated. There are concerns about the “hygiene hypothesis” because studies supporting it do not account for the complexity of immune maturation, and this maturation probably depends on multiple factors that have yet to be delineated. In addition, most of these studies have been done in homogeneous populations and may not be applicable to the general population. Clinically, the “hygiene hypothesis” theory that both atopy and asthma are Th2 driven and that the imbalance between Th1 and Th2 immunity is the primary causative factor. Atopic people have increased IL-4, IL-5, IL-13, and IgE antibody responses; increased immediate skin test reactivity; and decreased interferon-gamma (Custovic A, von Mutius E. The Hygiene Hypothesis Revisited: Pros and Cons. Presented at the 60th Anniversary Meeting of the American Academy of Allergy, Asthma, and Immunology, March 7-12, 2003; Denver, CO). What role, if any, the “hygiene hypothesis” plays in ocular allergies has not been addressed.

Histamine

Histamine, a common mediator released during mast cell degranulation along with eosin, is stored prefomed in mast cell granules. Histamine is one of the most important of the mediators and is predominant in SAC.22 In the pure IgE-mediated mast cell response associated with SAC, histamine is the definitive cause of most of the typical signs and symptoms of ocular allergy, and, therefore, antihistamine therapy remains a prime treatment regimen.10

When histamine is released into the conjunctiva, clinical responses include itching, vasodilation, and swelling. The conjunctiva hosts numerous histamine receptors; H1, H2, and H3/H4 are thought to have a role in ocular allergies. There is some evidence of H4 receptors in the conjunctiva.22

The release of histamine is a controlled process. A pinocytic vacuole forms on the outside of the mast cell, attaches to the granule, and then partially dissolves and releases a small amount of histamine. Uncontrolled or massive release of histamine causes anaphylaxis and shock and can be fatal.

Leukotrienes and prostanoids are synthesized for each reaction by the mast cells, and thus histamines, leukotriene antagonists, cyclooxygenase inhibitors, and mast cell stabilizers are used to treat the symptoms and prevent the more chronic disorders.

Role of IgE

During SAC and PAC the localized reaction begins with specific IgE bound to mast cells; few eosinophils or eosinophil mediators are generally present. The IgE-mediated response depends on the immunoglobulin being produced and being bound to mast cells before a clinical reaction can occur. It is thus a two-stage process: 1) exposure to the antigen causes the production of IgE specifically directed against the antigen. The specific antibody then binds to mast cells in several sites, including the conjunctiva. No reaction takes place in this phase. 2) on reexposure, the antigen binds to IgE on mast cells, causing them to degranulate and release histamine. An allergic reaction occurs. Because of this mechanism, monoclonal anti-IgE directed against the IgE receptor is used in asthma treatment to displace IgE off the mast cells, preventing them from disintegrating and essentially rendering IgE harmless.

Prostaglandins/leukotrienes

Both prostaglandins and leukotrienes are newly formed mediators. Leukotrienes are considered more potent than histamine. LT4 (leukotriene D4), a prominent leukotriene by-product, is considered potent at vasodilation and fluid transudation, whereas histamine has a small effect. Prostaglandins, however, are known to induce vasodilation and are responsible for the clinical findings of redness. Both prostaglandins and leukotrienes overlap in this manner, and most targeted therapeutics are directed specifically at these mediators. Both prostaglandins and leukotrienes can be blocked by nonsteroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase-2 inhibitors, and/or leukotriene modifiers. In rat conjunctiva, direct application of leukotriene B4 increased the number of eosinophils and neutrophils.24
Seasonal/perennial allergies

SAC is the most common form of ocular allergy, affecting about 90% of those afflicted with allergic conjunctivitis. Bilateral presentation is common, although severity may differ slightly between the eyes. Although SAC can include photophobia and blurred vision on rare occasions, it is generally not a cause of permanent visual impairment. PAC is more likely to be associated with perennial rhinitis than SAC, but otherwise the demographics of patients who have PAC versus SAC is similar. In PAC, seasonal spikes have been noted in up to 80% of those afflicted.5

Patients with PAC and SAC have elevated IgE levels in both tears and serum as well as aerosol allergen sensitivity. About one-quarter of those with SAC have eosinophilic infiltration in the conjunctiva, but almost 80% have elevated IgE levels. Tear-fluid IgE has been reported in 96% of samples from patients with SAC.2 Clinically, about twice as many patients with PAC than with SAC have specific serum IgE for house dust, and the percentage of patients with SAC who test positive for IgE in tear serum is negligible. Neutrophils, basophils, and eosinophils have been found in late-phase allergic reactions.

Vernal/atopic allergies

Although patients with VKC or AKC should be closely monitored because VKC and AKC and SAC can affect only a small number of patients (estimated at up to 2% of those with ocular allergies), VKC has a higher prevalence in males than females, occurs more often in those who have atopic dermatitis, and has usually run its course by early adulthood. However, in a study of 509 patients with VKC, the incidence of VKC was higher in females than males over the age of 16.2 A histologic analysis of patients with VKC and SAC shows the deposit of proteins and glycoproteins in patients with VKC, and intense itching, tearing, and severe photophobia are characteristic of this inflammation. Local lymphocyte phenotypes are found in patients with VKC, and it is unknown whether the same number of cytokines (rather than the quality) will differentiate it from SAC or PAC.

AKC also occurs more frequently in men (usually between the ages of 30 and 50 years) and is associated with atopic dermatitis. Other patients with AKC have a family history of systemic diseases (such as eczema), allergies, asthma, urticaria, or hay fever (or some combination). Atopic blepharitis, meibomian gland dysfunction, and associated dry eye symptoms commonly coexist, and the conjunctiva may be hyperemic and edematous. The periciliar skin involvement can be debilitating to some patients.

Eosinophils are characteristic of both VKC and AKC. After the initial release of mast cell mediators, other cells are recruited (specifically eosinophils), which are present within hours of exposure to an allergen. Lymphocytes are

Current and future treatment modalities

When both allergic rhinitis and allergic conjunctivitis are present, comanagement with allergists, pediatricians, and eye care professionals is usually recommended. Dermatologists may also be helpful in comanaging AKC. A stepwise approach is common when treating patients with SAC and PAC. Educating patients about the environment may help, but it may not be easily avoided (ie, allergens, cigarette smoke, pets) or modified (ie, keeping windows closed, cleaning ducts, replacing pillows frequently, installing hardwood floors, washing hair and pulling it back [pocket collector], and avoiding peak outdoor times when pollen counts are high) should be the first step. Although rubbing the eye may exacerbate the symptoms and perpetuate the conjunctivitis, it is important not to have been discussed in the first few patient visits. Cold compresses can be helpful if patients are unable to avoid the airborne allergens but do not exhibit more moderate allergy signs.

Adding over-the-counter (OTC) artificial tears (ATs) helps alleviate the itch and may also help wash away the antigens. Many SAC and PAC patients also have dry eye, and preservative-free ATs are safe to use in patients who wear CLs. ATs can provide symptomatic relief but will not address the underlying allergy. Antihistamines (emedastine 0.05%, levocabastine 0.05%) can provide rapid relief of ocular symptoms when applied topically. Benefits include excellent antihistamine activity plus the ability to stabilize the mast cells. Most antihistamines also inhibit leukotriene formation and migration. However, most have a limited duration of action and require up to four daily doses. CL wearers may need to discontinue use during more-severe outbreak periods. Oral antihistamines are effective in controlling some of the symptoms of allergic conjunctivitis but may contribute to drying of the ocular surface. Some patients benefit from the addition of topical antihistamines while they are using oral antihistamines.

Decongestants (oxymetazoline, tetrahydrozoline, and naphazoline) in combination with antihistamines act as vasoconstrictors but are known to sting or burn on instillation. Other adverse events include mydriasis and rebound hyperemia, and they are not suitable for use over the long term. Oral antihistamines are effective in controlling some symptoms of allergic conjunctivitis but may contribute to drying of the ocular surface. Some patients benefit from the addition of topical antihistamines while they are using oral antihistamines.

Mast cell stabilizers (cromoglycate 2% or 4%, lodoxamide 0.1%, nedocromil 2%) can be used for long-term therapy and require up to four daily doses. CL wearers may need to discontinue use during more-severe outbreak periods. Oral antihistamines are effective in controlling some of the symptoms of allergic conjunctivitis but may contribute to drying of the ocular surface. Some patients benefit from the addition of topical antihistamines while they are using oral antihistamines.

Alcaftadine, “a potent histamine H1, H2, and H4 receptor antagonist that has also demonstrated anti-inflammatory properties,” is the newest antihistamine/mast cell stabilizer to market. Alcaftadine 0.25% and alcaftadine 0.25% are the longest-acting antihistamine/mast cell stabilizers, allowing once-daily dosing. NSAIDs help reduce itching in patients with allergic conjunctivitis, but to date only one (ketorolac 0.5%) has been approved for use in the U.S. The NSAIWS works on the arachidonic cascade, but the specific mode of action is unknown. Lower doses of ketorolac are currently being marketed for postoperative pain after cataract surgery but are not approved for treatment of ocular allergy. In general, nonsteroidal medications are no longer used for treating ocular allergy.

Topical steroids can be useful for VKC and AKC, but long-term use may be associated with serious adverse events, including cataract formation, glaucoma, and localized suppression of immune responses. (The following statement refers to off-label or investigational use). Off-label use of steroids via topical or intraocular injection has anecdotally shown promising results in severe VKC. Low-dose topical steroids (flurometholone or lopetredon) are mostly recommended for patients presenting with highly inflamed eyes but should not be considered a primary therapy. Systemic steroids (prednisone) can be helpful in severe cases with debilitating itching. Steroid creams have shown some benefit for patients with eyelid eczema. (The following statements refer to off-label or investigational use). Topical pimecrolimus or tacrolimus may be used off-label on the eyelid skin. Topical cyclosporine 0.05% drops applied to the conjunctiva off-label can also provide relief as a steroid-sparing agent for patients with AKC or VKC. Matrix metalloproteinase 9 (MMP-9) activity is elevated in patients with allergic conjunctivitis and dry eye.20–22 Developing therapies that specifically target MMP-9 may be warranted.

Adjunctive therapy

Allergy immunotherapy is useful in reducing the response to allergens, but its role in allergic conjunctivitis has not been proven. The therapy is administered subcutaneously in progressively increasing doses to subsequently recruited and are believed to play a crucial role in the more-chronic disease states. Pathologic examination of the conjunctiva in these conditions will show an escalation of eosinophils being recruited. Although patients develop an ocular infiltrate or cicatrized ocular surface similar to a pemphigoid presentation. Systemically, the true atopic individual will have extreme rhin and eczematoid changes on the skin, may have severe asthma, and may be introducing allergens into the eye from the additional rubbing. The patient may also develop lid skin changes from using tissues to wipe the eyes for excessive tearing. The lid margin is more involved in AKC than in the other forms of allergic conjunctivitis.

GPs is caused by repeated mechanical irritation (such as occurs with contact lens [CL] use, limbal sutures, glue, scleral buckle, and prosthetic devices). It is not considered a true allergic reaction but can be aggravated substantially by allergens. AKC and VKC can produce sight-threatening complications. The most characteristic sign of patients with tarsal VKC is giant cobblestone papillae, which are filled with eosinophils. These papillae can easily be seen by blinking the eyelids of these patients. Shield ulcers— an immunologic response to the eosinophils may form on the conjunctiva in direct apposition to the cobblestone papillae and are generally difficult to treat, have difficulty healing, and often heal with corneal scarring and irregularities of corneal shape. In the worst cases, these ulcers can produce permanent visual loss. Limbal VKC differs not only in geographic location but also in the gelatinous infiltrates that mark the limbus. People with darker pigmentation are more likely to have limbal VKC.

Patients with AKC not only have immediate allergy considerations but also have needs that should be considered when planning for future opthalmic surgery. The chronicity of AKC can have significant implications for the health of the ocular surface, and therapy for AKC can be more arduous and have longer-term implications than for patients with AKC. The CLEK (Collaborative Longitudinal Evaluation of Keratoconus) study did not find a strong association between keratoconus and AKC, but the increased eye rubbing has been suggested as a driving force for the progression of keratoconus.20

Diagnostics

IgE levels alone may not be sufficient to determine the presence of allergy. Skin testing is more useful for demonstrating a particular sensitivity to a specific IgE. A downside to using skin tests is that they assume the most relevant allergens are those in the nose or eye, which may not be accurate. A general correlation between the environmental allergens and reaction is usually more accurate. Direct conjunctival and nasal challenge studies are practical but do show much higher specificity and sensitivity.
Avoidance, cold compresses, tears, over-the-counter medications might do almost as well just using the topical antihistamine/mast cell stabilizer. DR. RAIZMAN: Some patients will describe rhinorrhea, but antihistamine/mast cell stabilizer would help his nasal parasympathetic influence as a “noise cancelling” effect before we place plugs. This is somebody that you will need to manage with preservative-free artificial tears and topical ocular therapy and lubrication. The third is to stop oral antihistamines and use a nasal spray and a topical. DR. WOLF: There’s no reason not to stop his oral antihistamine. DR. RAIZMAN: All oral antihistamines can dry the eyes, even the so-called nonsedating oral antihistamines. DR. SHOVLIN: Unfortunately, I hate to add additional drops, but I probably would cover him at least initially prophylactically if we’re using other medications. DR. RAIZMAN: I think that complicates things. Once the epithelial defect is there, you should absolutely use an antibiotic. Maybe an ointment would be helpful. DR. LUCHS: You need steroids on board right away because of the ominous corneal finding. The confluent staining of the cornea suggests that we have an area of the cornea that’s ripe to become a shield ulcer. I would start the steroid right away, and I’d immediately add a topical antihistamine/mast cell stabilizer and a systemic antihistamine. DR. SHOVLIN: If I’m trying to control their asthma with a lot of steroids, I want someone to look in their eyes for complications.

Case study 3: A 44-year-old woman with known allergy to cat dander, dust, and mold presents in January with itching of both eyes and inability to tolerate her CLs. She cannot wear makeup because her eyes are tearing and she has to rub them. Her eyelashes have crust, mostly in the morning. An eye examination reveals debris on the lashes, obstructed meibomian glands, conjunctival hyperemia with minimal papilla, decreased tear volume, and punctate staining of the inferior cornea.

DR. SHOVLIN: She needs a hiatus from CL wear. She has at least a secondary dry eye (maybe from CLs or aqueous deficiency or obstructed meibomian glands), so you need to address the ocular surface as well. Before we can even think about returning her to CL wear, we have to address the lid disease and the secondary dry eye as well as the allergy. I’d start with an antihistamine/mast cell stabilizer, maybe concomitant use of ester-based steroids. This is a great patient even for daily disposable CLs.

DR. WOLF: There may be an extra wrinkle—she might have contact dermatitis that is aggravating her condition (in addition to her eye makeup).

DR. RAIZMAN: How do you decide if patients have sensitivity to their makeup?

DR. WOLF: Pattern, first of all. If there are local reactions, particularly reactions that are more on the epithelium, and if there is the initial itchiness. These are not IgE-mediated reactions. There remain below the threshold of a clinical reaction. Immunotherapy works best in situations with severe symptoms, poor control with conventional pharmacotherapy, and good correlation of symptoms with a few specific antigens.

Sublingual immunotherapy (SLIT) is considered an alternative to subcutaneous allergy immunotherapy and is administered orally under the tongue, but long-term results with SLIT are not yet available. Most of the trials with this form of therapy have been for allergic rhinitis.

Clinical challenges in ocular allergies: case examples

On the following pages, you will find several case studies examining specific diagnostic and treatment challenges of allergic conjunctivitis. These case studies have been designed to address challenging issues that often confound allergists and eye care professionals.

Case study 1: A 30-year-old man presents during spring tree pollen season with itching and irritation of the eyes. These symptoms occur every year, but they are especially bad this year. After taking oral antihistamines, his nasal itching and rhinorrhea have decreased, but his eyes are still bothering him. He cannot play golf or mow his lawn, and he has trouble reading and using the computer at work. He tried over-the-counter antihistamine/vasoconstrictor eyedrops, but these did not provide much relief and his eyes are now red. An eye examination reveals mild conjunctival hyperemia, trace papillae, decreased tear volume, rapid tear breakup time, and no staining.

DR. LUCHS: I would approach it a little differently. This is a great case history that illustrates the real functional impact of ocular allergies on someone’s daily life. If he happened to be a CL wearer, the significance of all of these factors may be elevated. The OTC antihistamine vasoconstrictor drops are not providing relief. He clearly has some signs of dry eye based on the decreased tear volume and the tear breakup time, although there is no staining. I’d keep him on the oral antihistamine because clearly he’s getting some relief from his nasal symptoms and we don’t want to necessarily withdraw that benefit from the patient. We need to add ATs and to treat his ocular surface. Punctal plugs won’t work just yet because they could make his allergies worse by allowing us to retain antigen on the ocular surface, so we want to initiate treatment of both his allergies and dry eye before we place plugs. This is somebody that you will need to manage with preservative-free artificial tears and maybe some ointment at night, you should advise lifestyle changes and use topical antihistamines.

DR. RAIZMAN: All oral antihistamines can dry the eyes, even the so-called non-sedating oral antihistamines. DR. WOLF: There’s no reason not to stop his oral antihistamines. I would switch him to a topical nasal antihistamine.

DR. RAIZMAN: We have three different approaches here. The first is to just stop the oral antihistamines. The second is to continue the oral antihistamines but add topical ocular therapy and lubrication. The third is to stop oral antihistamines and use a nasal spray and a topical.

DR. SHOVLIN: The naso-ocular lavage can help with the parasympathetic influence as a “noise cancelling” effect with allergic rhinitis. I believe just using the topical antihistamine/mast cell stabilizer would help his nasal itching as well.

DR. RAIZMAN: Some patients will describe rhinorrhea, but he also has nasal itching, which is a bit different. Pure ocular allergies do not involve nasal itch.

DR. SHOVLIN: I bet you would find therapeutically that he would do almost as well just using the topical antihistamine/mast cell stabilizer.

DR. WOLF: What tends to get lost with the non-sedating oral antihistamines is the anticholinergic effect. It depends how much the anticholinergic properties are playing a part in drying the eye as to whether these sedating antihistamines will also work. That might be a factor.

Case study 2: A 13-year-old boy with no known allergies, no asthma or allergic rhinitis, and negative skin and RAST test results has severe ocular itching in the spring with lid swelling, red eyes, and uncontrollable rubbing. The boy has not been able to go to school for the past few days. Findings of an eye examination include lid edema and giant papillae in both eyes. The right cornea shows heavy punctate staining with fluorescein but no defect.

DR. RAIZMAN: This is a classic presentation of VKC. What are the special issues with a child with allergy as opposed to an adult in terms of drug administration, compliance, and issues with the parents?

DR. WOLF: Clinically, there are not many differences. Children need help administering the eyedrops, so parents need to take greater responsibility. It’s likely this patient wouldn’t initially present to an allergist. I’d recommend topical antihistamines in the eye, possibly topical therapy in addition to treating any concomitant skin involvement in blepharitis. I usually tell parents to put the drops into the inner angle of the eye and let the child blink to get the drop into the eye. That’s usually easier. I’d refer this child, but first I’d try topical therapy, more topical antihistamines, and combination drugs. If necessary, I’d use a systemic steroid antihistamine and see him in 1-2 weeks.

DR. RAIZMAN: These kids who come in the spring need a high-dose topical steroid. I wouldn’t wait 2 weeks before bringing him back for these presentations; an immediate referral is appropriate.

DR. LUCHS: You need steroids on board right away because of the ominous corneal finding. The confluent staining of the cornea suggests that we have an area of the cornea that’s ripe to become a shield ulcer. I would start the steroid right away, and I’d immediately add a topical antihistamine/mast cell stabilizer and a systemic antihistamine.

DR. SHOVLIN: Unfortunately, I hate to add additional drops, but I probably would cover him at least initially prophylactically if we’re using other medications. DR. RAIZMAN: I think that complicates things. Once the epithelial defect is there, you should absolutely use an antibiotic. Maybe an ointment would be helpful. DR. LUCHS: Maybe even a steroid ointment at night. DR. WOLF: From an allergist’s point of view, we don’t have the eye findings at that point because this child is presenting with a red eye and itching that is fairly severe. In this case, we’ve had a full eye exam already, which is not going to happen in an allergist’s office.

DR. RAIZMAN: Let’s say this is a child coming for the first time in the spring with swollen eyes and allergy. It would be absolutely appropriate to do what you said initially. Treat for a week or two. But if a child with known VKC who has been fine for a year comes into your office in the spring, he or she should get an immediate referral and steroids.

DR. WOLF: By that point, the child is already seeing an eye care specialist. If I’m trying to control their asthma with a lot of steroids, I want someone to look in their eyes for complications.

DR. SHOVLIN: If they’re on oral steroids, then the pediatrician or allergist needs to be involved. You have to find that balance. In states where optometrists can’t prescribe oral steroids, they should be referred to an ophthalmologist.

DR. RAIZMAN: All the above, plus additional therapy as mentioned. The eye rarely stands alone—comorbidities include rhinitis, rhinosinusitis, and asthma.


topical antihistamines/mast cell stabilizers

Topical anabolic agents (tacrolimus, cyclosporine)

Topical immunomodulating agents (tacrolimus, cyclosporine)

oral steroids

Mild

Avoidance, cold compresses, tears, over-the-counter medications

Topical antihistamines/mast cell stabilizers

Oral antihistamines (allergists may already have patients on oral, as well as topical treatments in mind)

Moderate

+ Mast cell stabilizers (treats allergy before mediator is released)

+ Combination antihistamine/mast cell stabilizers

Severe

Topical corticosteroids (most beneficial for severe outbreaks)

Maximal tolerated dose

Topical immunomodulating agents (tacrolimus, cyclosporine)

Stepwise Treatment Strategies for Allergic Conjunctivitis

What to refer to?

Refer patient to an eye care specialist if:

• Changes in vision
• Persistent ocular complaints
• Ocular steroid use for more than 2 weeks
• Persistent conjunctivitis
• Complaints of ocular pain

Refer patient to an allergist if:

• Systemic evaluation is warranted
• Immunotherapy is being considered
• Significant persistent allergic complaints
• Predominance of nonocular allergic complaints

Refer patient to a dermatologist if:

• Severe atopic keratoconjunctivitis and persistent contact dermatitis remain uncontrolled
DR. WOLF: Probably the touching. Eyelids are much more susceptible and less resilient than the skin around the eye.

DR. WOLF: Rhinitis or nasal allergy is a common problem, although it certainly raises it to the top of the list. Is there a CL problem? Fitting issue? Hygiene issue? None of these is present.

DR. WOLF: She has lid debris, she has obstructed eyelid glands, she has dry skin (whether it is evaporated tear loss or decreased secretion). Treat the blepharitis with warm compresses +/- lid scrubs, assuming there's no contact dermatitis; treat the meibomian gland disease with either azithromycin or oral doxycycline; get those functioning. And she needs to see an allergist to get her allergy treated. The blepharitis is a treatable condition.

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POSTTEST

Please circle the correct answer for each question.

1. Which condition typically includes hyperemia and chemosis?
   A. Seasonal allergic conjunctivitis  
   B. Vernal keratoconjunctivitis  
   C. Atopic keratoconjunctivitis  
   D. None of the above  
   E. All of the above

2. Vernal keratoconjunctivitis:
   A. Occurs more in females than males  
   B. Is more common in adults than children/teenagers  
   C. Commonly demonstrates giant papillae  
   D. Heavily involves the lid margin

3. Atopic keratoconjunctivitis:
   A. Is not usually associated with atopic dermatitis or atopic eczema  
   B. Rarely involves a family history of allergic diseases  
   C. Occurs more in females than males  
   D. Can include debilitating periocular skin involvement

4. The cell(s) most commonly involved in the early- and late-phase ocular allergic reaction is:
   A. Eosinophil  
   B. Mast cell  
   C. Epithelial cells  
   D. Endothelial cells

5. Allergic conjunctivitis is most commonly associated with:
   A. Asthma  
   B. Urticaria  
   C. Allergic rhinitis  
   D. Contact dermatoconjunctivitis

6. The hallmark symptom of itching in allergic conjunctivitis is primarily caused by:
   A. Tumor necrosis factor  
   B. Immunoglobulin A  
   C. Histamine  
   D. Endothelial cells

7. Late-phase infiltration of eosinophils is most significant in which disorder?
   A. Seasonal allergic conjunctivitis  
   B. Giant papillary conjunctivitis  
   C. Atopic keratoconjunctivitis

8. Which treatment is least often necessary for treating typical seasonal allergic conjunctivitis?
   A. Systemic steroids  
   B. Lubricating eyedrops  
   C. Oral antihistamines  
   D. Combination antihistamine/mast cell stabilizer

9. In SAC and PAC, an IgE-mediated mast cell response typically occurs within _____ minutes of the initial allergen exposure:
   A. 5  
   B. 30  
   C. 60  
   D. 90

10. Contact lens wearers:
    A. Should never be treated with topical lubricating drops  
    B. Should only be treated with topical lubricating drops  
    C. May have to discontinue contact lens wear during severe outbreaks  
    D. May have to discontinue antihistamine drops during severe outbreaks

11. What percentage of the global population has allergies?
    A. 20%  
    B. 40%  
    C. 75%  
    D. 90%

12. Shield ulcers, an immunologic response to eosinophils, are:
    A. Associated with vernal keratoconjunctivitis  
    B. Often difficult to treat and do not heal easily
    C. Can produce permanent visual loss  
    D. All the above

13. One of the typical causes of perennial allergic conjunctivitis is:
    A. Dust mites  
    B. Genetic factors  
    C. Pollen  
    D. Food allergies

14. Giant papillary conjunctivitis is associated with:
    A. Bee stings  
    B. Contact lenses  
    C. Nut allergies  
    D. Aeroallergens

15. Prostaglandins and leukotrienes are synthesized from arachidonic acid by:
    A. Lipoxygenase and cyclooxygenase action, respectively  
    B. Cyclooxygenase and lipoxygenase action, respectively  
    C. Cylooxygenase only  
    D. Lipoxygenase only

16. The “hygiene hypothesis” has been proven in ocular allergies.
    True or False?
    A. True  
    B. False

17. _________ are a primary treatment regimen for most ocular allergies
    A. Corticosteroids  
    B. Topical steroids  
    C. Antihistamines  
    D. Immunotherapy

18. Prostaglandins and leukotrienes:
    A. Are both more potent than histamine at inducing itching
    B. Are both known to increase fluid transudation into the conjunctiva
    C. Cannot be blocked by NSAIDs
    D. Are newly formed mediators after mast cell activation

19. Vernal keratoconjunctivitis affects a small percentage of patients with ocular allergies. True or False?
    A. True  
    B. False

20. Artificial tears:
    A. Should not be recommended for patients with contact lenses  
    B. Can provide symptomatic relief  
    C. Address the underlying allergic response  
    D. Should be used only after antihistamine/mast cell stabilizers fail to provide relief.