Managing the Red Eye in Primary Care
Part 2 – Allergic Conjunctivitis

Learning Objectives
After participating in this educational activity, participants should be better able to

1. Diagnose red eye patients including common allergic conjunctivitis problems and rarer emergent causes that may need referral based on a patient’s history, signs, and symptoms
2. Manage allergic conjunctivitis based on an understanding of its pathophysiology and the appropriate pharmacological and non-pharmacological treatments
3. Recognize those patients with allergic conjunctivitis and other allergy-related eye conditions that need to be referred to an ophthalmologist and/or an allergy specialist

Overview of Allergic Conjunctivitis
Allergic conjunctivitis is a general term that encompasses a variety of conditions that affect the eye and its external surrounding tissues. As our world continues to become industrialized, overcrowding and pollution will cause an increased prevalence in allergy-related eye conditions. Primary care clinicians are often the first to encounter these patients. This activity is designed to assist clinicians in differentiating the various clinical entities of allergic eye disease and to identify those patients that can be safely treated from those that should be referred to
an ophthalmologist. An overview of the pharmacological treatments for allergic conjunctivitis will also be discussed as well as non-pharmacological strategies to help prevent future flare-ups.

Background

Allergic conjunctivitis is a common, multifaceted condition that has a variety of etiologies and clinical features, and requires a variety of treatments. Allergic conjunctivitis encompasses a wide spectrum of allergy-related conditions that predominantly affect the eyes. These conditions include the following:

- Seasonal allergic conjunctivitis
- Perennial allergic conjunctivitis
- Vernal keratoconjunctivitis
- Atopic keratoconjunctivitis
- Giant papillary conjunctivitis secondary to contact lenses or ocular prosthesis
- Drug-related allergies and complications

The underlying pathology in all cases of conjunctivitis is an immune hypersensitivity to an allergen, an otherwise harmless substance to most individuals. Allergic conjunctivitis is often part of a systemic allergy condition that may induce rhinitis and/or asthma. The common manifestations of allergic conjunctivitis include ocular itching, tearing, chemosis, and redness.

Conjunctivitis has a worldwide distribution - affecting persons of all ages, races, social strata, and genders. Allergic conjunctivitis alone is estimated to affect over 30 to 60 million US patients each year, or approximately 15% of the population.[1,2] The prevalence of allergic conjunctivitis ranges worldwide from 9% to 42%.[3,4] The overall economic impact of allergic conjunctivitis is difficult to assess but it is estimated to be at least $6 billion/year.[3] As our world becomes increasingly populated and industrialized, more individuals will develop allergy-related eye problems because of exposure to air pollutants and environmental antigens.

Primary care clinicians are often the first to encounter patients with allergy-related eye disease. Accurate diagnosis and appropriate treatment can minimize the societal costs of allergic conjunctivitis and alleviate patient suffering. It is important for clinicians to distinguish the various entities of this disease as some conditions can threaten eyesight. Seasonal allergic conjunctivitis comprises up to 90% of all ocular eye allergy-related conditions with perennial allergic conjunctivitis at 5% of all cases.[5] Less common, but important, entities to rule out include vernal and atopic keratoconjunctivitis, - both of which can affect the cornea and contribute to vision loss. These patients must be referred to an ophthalmologist.

The management of allergic conjunctivitis is highly variable among clinicians. A recent systemic review on all clinical trials of allergic conjunctivitis in the literature revealed that the majority of studies were poorly designed and lacked useful outcome parameters.[6] There is no clear consensus on the optimal clinical management of allergic conjunctivitis. In this module, we will attempt to highlight key concepts essential in managing allergy-related eye disease through clinical case scenarios that primary care clinicians may encounter in their everyday practice.
Initial History and Workup

A key symptom for allergic conjunctivitis is ocular itching. This symptom is rarely seen in patients with infectious conjunctivitis and can help clinicians identify patients with allergy-related eye disease. As discussed in part 1 (Infectious Conjunctivitis), the physical eye exam is usually the most important part of the workup. However, asking some key questions during the initial patient history can help narrow the differential diagnosis for allergy-related eye disease. These questions include:

- How long has the eye(s) been red, tearing, and itching?
- Is there any rhinitis?
- Is this the first episode or a recurrent problem?
- Are the symptoms seasonal or perennial?
- Is this unilateral or bilateral involvement?
- Is the vision affected?
- Does the patient have hay fever or systemic allergies?
- Is there a history of atopy? (eczema, dermatitis, asthma)
- Does the patient wear contact lenses?
- Does the patient use any eye medications? (vasoconstrictors, glaucoma medications)
- Is the patient exposed to any animals or plants?
- Is there any occupational or residential exposure to pollutants?
- How long has the patient lived in the area?

Eye Exam

Primary care clinicians should develop a routine checklist for the eye exam. (Table 1) The most important aspects of the eye exam in patients with allergy-related eye disease include inspection of the conjunctiva and the cornea. The upper and lower conjunctival sac must be inspected for papillary reactions (giant papillae) that can be indicative of more serious disease (atopic or vernal conjunctivitis). This may require eversion of the upper eyelid to view the tarsal conjunctiva (Figure 5). This skill requires practice and a cotton swab can help the clinician evert the upper eyelid. The cornea must be stained with fluorescein to rule out ulcerations that can be seen in atopic or vernal conjunctivitis.

Table 1

<table>
<thead>
<tr>
<th>Eye Exam Checklist for Primary Care</th>
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<tr>
<td>• Visual acuity (measure each eye with patient wearing glasses if available)</td>
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<td>• Confrontational visual fields</td>
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<tr>
<td>• Pupils (size, symmetry, reactivity, Marcus Gunn pupil)</td>
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<td>• Eye motility</td>
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<td>• External exam (for proptosis especially)</td>
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<td>• Magnifying glass with penlight and cobalt filter (or Wood’s lamp) to examine the</td>
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<tr>
<td>o Lids</td>
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<td>o Conjunctiva</td>
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<td>o Cornea (fluorescein staining)</td>
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<td>o Anterior chamber</td>
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<td>o Iris</td>
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<td>o Lens</td>
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<tr>
<td>• Eye pressure</td>
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<tr>
<td>o Digital palpation</td>
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<tr>
<td>• Direct ophthalmoscope</td>
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<tr>
<td>o Optic nerve</td>
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<td>o Central retina (fovea)</td>
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Case Study 1:
It is springtime, and a 33-year-old emergency room nurse presents with bilateral ocular itching, tearing, and redness for the past 4 weeks. She recently moved from Hawaii to the north Texas region. This is her first time in her life that she has ever lived outside the Hawaiian Islands. The patient has tried a variety of over-the-counter vasoconstrictors and artificial tears which offer no relief (Figure 1). She is tired of rubbing her eyes constantly because of the itching. The nurse is very self-conscious about her appearance. She is really tired of co-workers and patients inquiring about her constantly “red eyes.”

Figure 1. Itchy red eyes for 4 weeks

1. What is the patient’s most likely diagnosis?
   A. Seasonal allergic conjunctivitis
   B. Adenovirus conjunctivitis
   C. Vernal conjunctivitis
   D. Vasoconstrictor abuse
   E. Narcotic abuse

2. Which of the following medications has been shown to NOT offer any benefit for allergic conjunctivitis?
   A. Topical antihistamine
   B. Topical mast cell stabilizer
   C. Topical antihistamine-mast cell stabilizer
   D. Topical steroids
   E. Intranasal steroids

Discussion – Seasonal Allergic Conjunctivitis
The patient’s symptoms and presentation are classic for seasonal allergic conjunctivitis. The ocular itching and the social stigma of having red eyes caused by allergic conjunctivitis can be troubling for any healthcare personnel. Non-pharmacological remedies to help the patient include using cold compresses and instilling chilled preservative-free artificial tears to help dilute antigen exposure. The patient should be encouraged to use an air filter at home or work. When driving, she should use her air conditioner (with a new cabin filter) and keep her car windows closed. Frequent bathing, especially before sleeping, and frequent clothes washing have also been recommended to help symptoms.[7]

The underlying pathophysiology is due to an IgE mediated type I hypersensitivity reaction to an environmental antigen. In this patient’s case, hypersensitivity is likely due to exposure to a pollen
(grass, tree, weed) or mold not previously encountered. The mast cell is the key instigator of the allergy inflammation cascade. The degranulation of the mast cell triggered by antigen exposure leads to the release of histamine that causes ocular redness, tearing and itching. Mast cell degranulation also leads to the release of other chemotactic factors such as prostaglandins and leukotrienes that contribute to a cycle of prolonged mast cell activity and persistent allergic ocular symptoms. Antihistamines and steroids provide immediate relief of symptoms such as itching and redness. Mast cell stabilizers do not offer immediate relief, as they have no antihistamine activity. The purpose of the mast cell stabilizer is to prevent degranulation of the cell and release of chemotactic factors that prolong the inflammatory cascade. Mast cell stabilizers help prevent further inflammation but do not offer relief for symptoms caused by the presence of histamine. For this reason, topical combination antihistamine-mast cell stabilizer agents have gained popularity among ophthalmologists for the treatment and prevention of allergic conjunctivitis because of their dual-action mechanism.

There are several topical antihistamine-mast cell stabilizer eye drops on the market, some available over the counter. Most are used twice daily with the exception of olopatadine 0.2% which can be used once daily because of a higher concentration.[8] There are several topical antihistamine-mast cell stabilizers available that vary in cost, side effect profile, and formulary coverage. There is no clear consensus on which agent is superior because of the lack of well-designed comparative studies[6] above but most topical antihistamine-mast cell stabilizers are generally effective. Intranasal steroids have been shown to not be effective for allergic conjunctivitis as topical antihistamine-mast cell stabilizers.[9] If the patient continues to have symptoms despite all these measures, she should be referred to an ophthalmologist for topical steroid use (see Part 1 – Dangers of topical steroids).

As with any allergy-related condition, the issue of antigen exposure must be addressed to prevent the problem. Simply treating the patient’s symptoms is not enough. The patient should be referred to an allergist for further advice and management. The possibility of moving to another geographic location should also be considered in this patient to avoid seasonal exposure to offending outdoor pollen.

Case Study 2:
A 28-year-old computer engineer has met the perfect companion after being set up on a blind date. Unfortunately, the partner has a pet cat. Since they met, the patient has developed episodic tearing and ocular itching when in close proximity with the cat. After 2 years of dating and constant ocular allergy symptoms, the patient is getting frustrated (Figure 2). The patient has tried virtually every topical and systemic allergy medication and none offers relief. The engineer is convinced that the cat is the source of his problem and asks for your advice before he makes a decision.
Figure 2. Frustrated patient with itchy red eyes for 2 years. There are periocular skin color changes and scaling from chronic inflammation and constant eye rubbing.

3. What should you recommend?
   A. Tell the partner – "it's me or the cat"
   B. Prescribe a topical antihistamine-mast cell stabilizer
   C. Prescribe a topical steroid
   D. Refer the patient to an allergist
   E. Refer the patient to an ophthalmologist

4. Which of the following allergens can cause perennial (chronic) allergic conjunctivitis?
   A. Cat dander
   B. Dog dander
   C. Dust mite debris and feces
   D. Cockroach debris and feces
   E. Molds
   F. All of the above

Discussion - Perennial Allergic Conjunctivitis - Indoor Antigens
Perennial allergic conjunctivitis occurs when the patient’s allergy symptoms are persistent year round. It is important to make this distinction from seasonal allergic conjunctivitis because the antigens that cause the allergies are completely different. Outdoor antigens such as those from grass, weed, and tree pollen are seasonal. Indoor antigens, on the other hand, threaten to cause patient allergies year-round. The most common indoor antigen is the dust mite.[10,11] It is estimated that at least 5 to 10 million dust mites occupy a bed in the average home.[10] Another common source of perennial allergies is from the skin dander of cats and dogs. Other sources of indoor antigens include cockroaches and indoor molds that can be present year round (Alternaria, Cladosporium, Aspergillus). Chronic exposure to any of these indoor antigens can create a vicious cycle of inflammation that leads to persistent red, itchy eyes.

Similar to seasonal allergic conjunctivitis, the patient’s symptoms can be treated with a topical antihistamine-mast cell stabilizer to provide immediate relief. If the patient continues to have ocular problems, the patient should be referred to an ophthalmologist for more intensive, topical steroid therapy. However, simply treating the patient’s symptoms does not solve the problem. The exacerbating antigen should be identified. In this case, although it appears the partner’s cat may be the offending antigen source, it is important to rule out other causes such as dust mites. The patient should be referred to an allergist who can help identify the offending antigens before the patient alters his social life.
It should be noted that a recent systemic review of the literature found that the use of impermeable bedding to prevent dust mite colonization, as an isolated intervention event, was not likely to offer any benefit for allergic conjunctivitis-rhinitis.[12] Minimizing exposure to dust mites and other indoor antigens will therefore require a multi-interventional strategy that includes:

- keeping household pets outdoors and away from the bed and bedroom
- frequently cleaning and vacuuming indoor carpet, draperies, and comforters
- cleaning or replacing old pillows and mattresses
- using a protective, non-allergic barrier cover over pillows and mattresses
- maintaining low indoor humidity with a de-humidifier to prevent dust mite proliferation
- using an indoor HEPA air filter
- replacing all home air conditioner filters
- replacing all car cabin filters
- treating any cockroach infestation
- testing for indoor molds and removing their source

**Case Study 3**
A 50-year-old executive assistant with seasonal allergic conjunctivitis presents with chronic red eyes. (Figure 3) Her symptoms are usually worse in the spring. She is usually able to control her ocular symptoms with over-the-counter medications. For this most recent flare-up, she has found that her favorite topical remedy is no longer effective. Normally, she uses this medication once or twice daily to relieve symptoms. She now finds that she has to use it up to 8 to 10 times a day to barely achieve the same effect. In fact, when she stops the medication, her eyes become even more red and bothersome.

**Figure 3. Frustrated patient with chronic red eyes – “I’M tired of what people are saying about my eyes”**

5. **Which of the following medications has she been using?**
   A. Topical antihistamine – mast cell stabilizer
   B. Topical naphazoline or tetrahydrozoline
   C. Topical artificial tears with preservatives
   D. Topical steroids
   E. Topical antihistamine

**Discussion - Vasoconstrictor Abuse**
Conjunctivitis caused by indiscriminate use of topical vasoconstrictors (naphazoline, tetrahydrozoline, or phenylephrine) is a well-known phenomenon among ophthalmologists.[13] These are often seen in patients who self-treat their ocular allergies or who seek to eliminate conjunctival redness from their eyes before a public appearance. Topical vasoconstrictors limit the blood flow to external eye surface in an effect to reduce swelling from histamine release.
and antigen exposure. When used long term, topical vasoconstrictors do not treat the underlying cause of allergic conjunctivitis. In fact, when used repeatedly, a phenomenon known as tachyphylaxis occurs that results in drug tolerance. The topical vasoconstrictor has to be used more often to achieve the same effect of eliminating the ocular redness. As a result, patients develop an even more inflamed eye that can take several weeks to resolve once the topical vasoconstrictor has been discontinued.[13] Topical vasoconstrictor agents are thus not preferred first-line agents for allergic conjunctivitis among ophthalmologists.[7] Topical antihistamine-mast cell stabilizers achieve better results than topical vasoconstrictors.[14] When offering strategies to whiten the eye, primary care clinicians should recommend the use of preservative-free OTC artificial tears that do not contain vasoconstrictors or other agents that can exacerbate the eye. These artificial tears can be refrigerated and used chilled to provide comfort and a cosmetic benefit.

**Case Study 4:**
A 7-year-old male presents with ocular itching and redness in the right eye. The patient’s mother states these symptoms occur seasonally. The episodes are usually seasonal but have also occurred at sporadic times in some years. Both eyes are usually affected, but sometimes episodes can alternate between the two eyes. On this occasion, the right eye is severely injected and the child has been rubbing his eyes continuously without relief from the topical antihistamine-mast cell stabilizer that was prescribed. The left eye is completely normal. The visual acuity is 20/50 in the right eye and 20/20 in the left eye (Figure 4, 5, and 6).

**Figure 4. Child with an itchy red eye**
Figure 5. Large conjunctival papillae seen on the upper conjunctival tarsal surface. The upper eyelids should always be everted in any patient with chronic allergy-related eye disease.

Figure 6. Limbal and bulbar papillae of the right conjunctiva

6. Based on the appearance of the right eye, the most likely diagnosis is:
   A. Seasonal allergic conjunctivitis
   B. Perennial allergic conjunctivitis
   C. Atopic conjunctivitis
   D. Vernal conjunctivitis
   E. Herpes simplex keratoconjunctivitis

7. What should you do for this patient?
   A. Initiate topical steroids
B. Refer the patient to an ophthalmologist
C. Refer the patient to an allergist
D. Start systemic steroids

Discussion - Vernal Conjunctivitis (VC)

Vernal conjunctivitis is a chronic allergy-related eye condition usually seen in children who live in warmer, temperate climates. Males are 2 to 4 times more likely to be affected than females.\(^1\) VC can affect either eye and exacerbations are often seen in the spring and summer. Patients usually present with an episode of intense ocular itching, redness, and ocular discharge. Large papillae are seen on the lower and upper tarsal conjunctival surface (Figure 5) suggest the diagnosis of VC. Primary care clinicians should always evert the eyelids of pediatric patients to rule out the diagnosis of VC. Large papillae can also be seen surrounding the cornea (Horner-trantas dots) or on the bulbar conjunctival surface (Figure 6).

Patients with VC do not have a history of atopic related conditions (allergy, eczema, dermatitis). Risk factors for VC, however, include a family history of vernal conjunctivitis or atopic disease.\(^{[15]}\) The pathophysiology of VC is more complex than seasonal allergic conjunctivitis. Although VC involves an IgE-mediated response, the pathophysiology is believed to involve T-cell mediated pathways and several interleukins.\(^{[16]}\) This explains why patients with VC cannot be adequately treated and suppressed with topical and oral antihistamines-mast cell stabilizers. Topical steroids are required to treat active flare-ups and keep patients in remission.\(^{[17]}\) However, the long-term of topical steroids, without proper monitoring by an ophthalmologist, can cause cataracts and glaucoma.

VC is an important condition that should be identified by all pediatric and primary care clinicians because it has the potential to affect the cornea and cause vision loss in patients. When the condition affects the cornea, it is referred to as vernal keratoconjunctivitis (VKC). Corneal findings in VKC include punctate keratitis that can cause ocular foreign body sensation and loss of vision. Rarely, corneal shield ulcers can develop which can scar the cornea and cause irreversible vision loss (Figure 7).\(^{[18]}\) Because many patients with VKC are often young and can develop corneal problems\(^{[15]}\), they must be referred to an ophthalmologist to prevent the development of irreversible vision loss caused by amblyopia.
Figure 7. Corneal “shield ulcer” seen in a patient with vernal conjunctivitis. The corneas of any vernal conjunctivitis patient must be stained with fluorescein to rule out the presence of a corneal ulcer.

Figure 8. Long-standing ocular itching and periocular skin folds from prolonged

Case Study 5
A 43 year-old male accounting with a history of long-standing atopic dermatitis presents to you with bilateral ocular itching and redness for the past 3 months.**Figure 8** His wife states that the patient has been constantly rubbing his eyes for years and only recently the symptoms have been worse. He has used topical and oral antihistamine-mast cell stabilizers in the past which seem to keep his ocular problems in remission. On this occasion, nothing seems to help his itchy eyes.
8. **At this point, what is the best course of action for this patient?**
   A. Initiate topical steroids
   B. Refer the patient to an ophthalmologist
   C. Refer the patient to an allergist
   D. Prescribe a systemic antihistamine
   E. Prescribe systemic steroids

The patient is started on topical prednisolone acetate QID by an ophthalmologist and develops significant relief. He is seen in follow-up one week later and both eyes appear white and quiet. The topical steroid is tapered down and kept at a low baseline dosage of once daily. The patient is followed every 3-4 months to make sure he does not develop cataracts or glaucoma.

9. **This patient has a propensity to have an ocular infection caused by which of the following organisms?**
   A. Adenovirus
   B. Herpes simplex virus
   C. HIV
   D. Cytomegalovirus
   E. Staphylococcal aureus

**Discussion: Atopic Conjunctivitis (AC)**

Similar to vernal conjunctivitis, atopic conjunctivitis (AC) is a chronic allergy-related eye condition that requires monitoring by an ophthalmologist and/or dermatologist. Unlike patients with vernal conjunctivitis, patients with AC often have concomitant atopic disease such as eczema, dermatitis, and/or asthma. There is a strong association of AC and a family history of atopic disease. Patients with AC have episodes of intense ocular itching and redness year round with no seasonal variation and no climate predilection. The pathophysiology of AC is also complex like VC and involves IgE-mediated hypersensitivity and reduced T-cell related immune function. This reduced immune function most likely predisposes patients with AC to viral infections involving the eye such as herpes simplex virus.[19,20,21]

The ocular findings in AC are more extensive and potentially damaging than VC. The inflammation associated with AC can involve virtually every structure of the eye and cause potential blindness. The eyelids of patients with AC can reveal blepharitis and signs of over-colonization by staphylococcal bacteria. Within the conjunctiva, large papillae and conjunctival scarring (symblepharon) can be found due to chronic inflammation. When the cornea is involved, the condition is termed atopic keratoconjunctivitis (AKC). In AKC, the cornea can develop dry eye syndrome damage (punctate keratitis), extensive vascular scarring, and shield ulcers. Patients with AKC also have a higher risk of developing keratoconus, a progressive disorder that results in corneal thinning and vision loss. Patients with AKC and severe keratoconus may not have useful vision with spectacles unless they wear contact lenses. The presence of ocular inflammation on the conjunctiva and cornea, however, can make it difficult for AKC patients to safely wear contact lens in order to see. A cornea transplant in an AKC-keratoconus patient can also be problematic because of a higher risk of rejection due to the underlying disease. Patients with AC or AKC can also develop vision-threatening cataracts at an earlier age. AC is a severe inflammatory eye condition that causes potential blindness.
These patients must be identified by primary care clinicians and promptly referred to ophthalmologists.

Because AC is a chronic condition, the goal of treatment is to reduce the duration of symptomatic exacerbations and to prevent future flare-ups. Topical/oral antihistamines and steroids can help reduce ocular symptoms of itching and discomfort. Topical mast cell stabilizers may help prevent flare-ups in some patients but most will require the long-term use of stronger immunosuppressive agents. Low-dose topical steroids used routinely can prevent flare-ups but require monitoring by an ophthalmologist for cataract and glaucoma side effects. The chronic use of topical steroids however can increase the risk of developing microbial infections in the eye.[22] This can be problematic in AC patients as they have a higher risk of developing herpes simplex eye infections because of altered cellular immunity.[19,20,21] Systemic cyclosporine is used to keep patients with AC in remission but requires intensive monitoring because of hypertension and renal damage risks.[23] Alternatively, topical cyclosporine has been used for AC prophylaxis (FDA off-label use) in order to avoid steroid-related complications and the problems associated with systemic cyclosporine.[24,25] Systemic and topical tacrolimus, a T-cell immunomodulator, have also been used for treating atopic dermatitis and AC (FDA off-label use).[26,27]

Case Study 6
A 24-year-old female presents to your office for 3 weeks of intense ocular itching and discharge in both eyes. She denies any history of atopic disease or previous eye problems. She is myopic and wears soft contact lenses. She admits to occasionally sleeping in them and cleans them sporadically. She does not remember the name of her cleaning solution. She forgot to wear them today and is wearing her backup pair of glasses. Her vision is 20/25 in the right eye and 20/30 in the left eye aided by her glasses in each eye. You stain the corneas of both eyes and they appear normal.

10. **What is the next step in the management of this patient?**
   A. Evert the upper eyelids
   B. Palpate the preauricular lymph nodes
   C. Contact the patient’s optometrist who prescribed her contact lenses
   D. Inspect the patient’s contact lenses, cleaning solution, and storage case
   E. Prescribe a topical antihistamine-mast cell stabilizer
Figure 9 – Right upper eyelid everted

The patient’s upper eyelids are everted and the following lesions are seen on upper tarsal conjunctival in both eyes.

11. **What is the patient's diagnosis?**
   A. Seasonal allergic conjunctivitis
   B. Perennial allergic conjunctivitis
   C. Atopic conjunctivitis
   D. Giant papillary conjunctivitis (GPC)
   E. Conjunctival papilloma

12. **What should you do for the patient?**
   A. Have the patient stop the contact lenses immediately and use her glasses for an extended period
   B. Prescribe a topical antihistamine-mast cell stabilizer
   C. Contact the patient’s ophthalmologist and arrange for an appointment or referral
   D. All of the above
   E. None of the above

**Discussion – Giant Papillary Conjunctivitis**

Giant papillary conjunctivitis (GPC) is the result of a complex allergic inflammation cascade that often occurs from poor contact lens hygiene, exposed sutures from eye surgery procedures, ocular prosthesis use (prosthetic eye), and foreign bodies. Exposure to external entities causes ocular irritation, redness, and itching that eventually results in the formation of large giant papillae on the surface of the upper tarsal conjunctiva (Figure 9). Soft contact lenses tend to become coated with protein deposits that build from the lids and conjunctiva. These deposits then behave like a sponge and soak up any environmental allergens that can cause ocular allergy eye symptoms. GPC has been reported to occur with virtually any type of contact lens, including soft, hard, and even newer generation silicone hydrogel lenses.[28]
Currently, there is lack of clinical data and standardized guidelines for proper contact lens hygiene.[29] In our fast-moving society, many contact lens companies offer convenience in cleaning lenses with several “no-rub” cleaning solution products. Further contributing to the problem, there are even soft contact lenses available that are FDA approved for overnight or extended duration use without the need to be removed for cleaning.[30] As a result these products, both patients and eye care providers have become careless in enforcing proper contact lens hygiene. Clinical studies have shown that these “no-rub” cleaning solutions are not effective in removing protein deposits from soft contact lenses.[31] There was also a recent recall of many cleaning solutions because of an outbreak of fungal keratitis.[32,33] There is also increasing evidence that even these new silicone-hydrogel contact lenses, when used for overnight or for extended periods without proper hygiene, are just as dangerous in causing vision-threatening bacterial keratitis (corneal ulcers) as previous generations of lenses.[34,35]

Checklist questions that should be asked of all ocular allergy patients are the use of soft contact lenses and their contact lens cleaning practices. With any history of contact lens use, there are two very important things that the primary care clinician must do when examining the eye. The first task is to evert the upper eyelid inspecting for giant papillae on the upper tarsal conjunctival surface that is found in GPC. The second and most important task is to stain the cornea with fluorescein to rule out abrasions or ulcerations (see Part 1 – Infectious Conjunctivitis). Once the diagnosis established, the most important thing is to discontinue and throw away any contact lenses. This patient should be started with a topical antihistamine – meso stabilizer and refer to an ophthalmologist as they will most likely need a stronger agent such as a topical steroid. Again, primary care clinicians should not dispense topical steroids, as they do not have the capability to monitor for steroid side effects such as cataracts and glaucoma. The structural changes in GPC can take weeks or months to resolve, but symptomatic relief can occur immediately with discontinuation of all contact lenses and the use of topical antihistamine-mast cell stabilizers.

**Case Study 7:**

A 50-year-old male presents with 3-week history of an itchy, red right eye. ([Figure 10](#)) He is being treated for glaucoma by his ophthalmologist. Recently, he was started on a new glaucoma medication to control his eye pressure. This medication was used only on his right eye as a trial to see if the eye pressure would be lower relative to the left eye. The patient is convinced that this new medication is the cause of his itchy, red right eye. The patient does not use any contact lenses and does not have any history of seasonal allergies. His left eye is completely normal. His vision is 20/20 in each eye while wearing his spectacles.
13. Which of the following medications is most likely the cause of the patient’s itching symptoms?

A. Topical beta-blocker
B. Topical carbonic anhydrase inhibitor
C. Topical alpha-adrenergic receptor agonist
D. Topical prostaglandin analogue
E. None of these

Discussion - Medication-Induced Allergic Conjunctivitis

Most cases of allergy-related eye disease result in bilateral involvement because of the systemic wide exposure to environmental allergens. Unilateral involvement usually implies iatrogenic or self-inflicted causes. Thus, an important checklist question for primary care clinicians is to inquire about the use of any medications used in the eye. Topical eye pressure lowering eye drops for glaucoma, in particular, are well known among ophthalmologists for causing allergy-related eye symptoms.[36] Of all the glaucoma agents available, topical alpha-adrenergic agonists are most likely to cause ocular itching and redness.[37] If a patient has this problem, contact the patient’s ophthalmologist before discontinuing glaucoma eye medication, as the eye pressure may become elevated upon discontinuation.

Case Study 8

A 64-year-old male corporate executive has decided to retire early from his profession. He has chronic bilateral “red eyes” for decades and is simply tired of co-workers commenting about his eyes. He disdains public appearances and often wears sunglasses indoors to conceal the appearance of his eyes. Both of his eyes itch and he has tried various topical antihistamines and topical steroids off and on over the years with variable results. He admits to frequently using over-the-counter topical vasoconstrictors to keep his eyes white. The patient has seen several doctors over the years including allergists, primary care specialists, and ophthalmologists - all of whom he states have failed to take care of his eyes. The patient denies contact lens use and any history of atopic disease. He has a dog and cat that he is quite fond of and they have slept in his bed each night for the past 12 years. The patient states that when he takes a vacation away from his home in Georgia, his eyes do not trouble him at all. On examination, his vision is 20/20 in each eye with his current spectacles. Inspection of both eyes reveal large papillae throughout his upper and lower conjunctival surface (Figure 11-13). There are no defects noted on the corneas by fluorescein staining.
Figure 11. Right upper eyelid everted

Figure 12. Periocular skin appearance

Figure 13. Right lower conjunctival fornix
14. Which of the following are appropriate in the management of this patient?
   A. Recommend that the dog and cat never enter his bedroom
   B. Replace the pillows and mattress and put plastic covers over the new ones
   C. Recommend HEPA certified air filter in the house and bedroom
   D. Refer the patient to an allergist
   E. Suggest to the patient that he retire to another part of the country where there are fewer environmental irritants
   F. Refer the patient to an ophthalmologist so he can receive long-term suppression with topical antihistamine/mast cell stabilizers and topical steroids
   G. Use topical vasoconstrictors to remove ocular redness sparingly (i.e. emergency social events such wedding anniversaries, birthdays, job interviews, etc)
   H. A, B, and C
   I. D, E, F, and G
   J. All of the above

Discussion - Putting It All Together And Future Therapies
This clinical case highlights several of the important principles highlighted in previous cases:

- Always evert the upper eyelids and stain the corneas with fluorescein
- Provide immediate relief of ocular symptoms
- Discuss strategies for improving the cosmetic appearance of the eyes
- Referral to an allergist to identify the offending allergens and for consideration of immunotherapy
- Minimize current and future allergen exposure through home hygiene and non-pharmacological interventions
- Minimize future flare-ups with appropriate pharmacotherapy
- Referral to an ophthalmologist for monitoring and prevention of therapy-related side effects

When ocular allergy-related conditions affect the patient’s personal life (i.e., career or family), it is important to consult an allergist to help identify potential exacerbating allergens. This will help the patient make educated decisions on how to alter their lifestyle in an effort to minimize allergen exposure. When ocular allergy symptoms cannot be controlled with conventional therapy (i.e., topical antihistamines, mast cell stabilizers), patients should be referred to ophthalmologists for more intensive pharmacotherapy. The current armamentarium for the treatment and prevent of allergic conjunctivitis is limited to antihistamines, mast cell stabilizers, NSAIDs, and steroids. However, the future is bright for patients as there are currently several FDA clinical trials being conducted for allergic conjunctivitis. Off-label use of topical cyclosporine has also been used successfully to treat chronic allergic eye conditions.\[38,39\] Newer class agents directed at specific molecular and chemical targets within the allergic inflammatory cascade, if effective, would undoubtedly reduce the societal burden of allergic conjunctivitis. The primary care clinician will continue to be the instrumental gatekeeper in helping all patients with allergy-related eye disease.
References


