

Ocular allergy

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Purpose of review

Ocular allergy is often encountered by allergists, ophthalmologists, pediatricians, and primary care physicians. An understanding of the immunologic mechanisms, the differential diagnosis, the clinical features, and the treatment of ocular allergy will be useful to all physicians who encounter these patients.

Recent findings

Basic and clinical research has provided a better understanding of the cells, mediators, and immunologic events which occur in ocular allergy. New pharmacological agents, including more potent mast cell stabilizers, and low-dose corticosteroids, have improved the efficacy and safety of ocular allergy treatment.

Summary

Physicians who currently treat ocular allergy have a greater familiarity with the signs and symptoms of allergic disease, a better understanding of the mechanisms and clinical features of allergic conjunctivitis, and improved therapeutic tools to deliver satisfactory outcomes in the management of ocular allergy.

Keywords

allergic conjunctivitis, atopic keratoconjunctivitis, ocular allergy, vernal keratoconjunctivitis

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Introduction

Ocular allergy is often encountered by allergists, ophthalmologists, pediatricians, and primary care physicians. An understanding of the immunologic mechanisms, the differential diagnosis, the clinical features, and the treatment of ocular allergy will be useful to all physicians who encounter these patients. Basic and clinical research has provided a better understanding of the cells, mediators, and immunologic events which occur in ocular allergy. New pharmacological agents, including more potent mast cell stabilizers, and low-dose corticosteroids, have improved the efficacy and safety of ocular allergy treatment. Physicians who currently treat ocular allergy have a greater familiarity with the signs and symptoms of allergic disease, a better understanding of the mechanisms and clinical features of allergic conjunctivitis, and improved therapeutic tools to deliver satisfactory outcomes in the management of ocular allergy.

The eye, like the respiratory tract, can be a target of acute allergic reactions. The most common ocular allergic condition is seasonal allergic conjunctivitis (SAC), and most SAC occurs in the spring, summer, and fall. Perennial allergens, such as animal dander, dust, and molds, can also affect the eye. The target tissue of the eye is the conjunctiva, the mucous membrane which covers most of the eye, and also lines the inside of the

upper and lower eyelids. The anatomy and physiology of the conjunctiva are similar to the nasal mucosa, and allergic reactions in the two locations are similar.

Differential diagnosis

The triad of conjunctival redness, itching and swelling is an accurate description of allergic conjunctivitis [1] (Table 1). Redness (injection) tends to be mild, and swelling (chemosis) is often prominent. The combination of mild redness and prominent swelling gives the conjunctiva a pinkish or milky appearance. Most ocular allergies are associated with itching. Whereas the symptom of itching is most closely associated with ocular allergy, some patients with blepharitis, dry eye, and irritative, nonallergic conjunctivitis also complain of itching. Typical features of ocular allergy are

- (1) conjunctival injection (mild to severe),
- (2) conjunctival edema (chemosis) (mild to severe),
- (3) itching,
- (4) discharge (mild),
- (5) trantas dots (vernal or atopic),
- (6) corneal plaques (vernal or atopic), and
- (7) cataracts (atopic).

Some useful questions will help distinguish ocular allergy from other types of ocular inflammation, and support the diagnosis of this condition.

Table 1 Types of ocular allergy and key immunologic mechanism

Types of ocular allergy	Key immunologic mechanism
Seasonal allergic conjunctivitis	IgE
Perennial allergic conjunctivitis	IgE
Vernal keratoconjunctivitis	IgE
Atopic keratoconjunctivitis	IgE and cell-mediated immunity
Contact allergy	Cell-mediated immunity
Giant papillary conjunctivitis	Irritative, not a true allergy

‘What is the location of the itching?’ If the itching is localized to the conjunctiva, then itching is consistent with a diagnosis of allergic conjunctivitis. If itching is localized to the eyelids, or the periorbital skin, the patient may have blepharitis, contact dermatitis, atopic eczema, or psoriasis. Sometimes, it is difficult for patients to determine the location of itching, and the physician must rely on the examination to determine whether the focus of inflammation is the conjunctiva or the skin.

‘Is there a history of allergy?’ Most people with allergy have had previous allergic episodes, often during the allergy season. If one is to make an initial diagnosis of ocular allergy in a patient who has never had allergy, it is important to inquire about previous hay fever, asthma, and eczema. A family history of allergy will also help support a new diagnosis of allergy. An initial diagnosis of allergy in an adult, especially an older adult, is uncommon. There are two exceptions. During a particularly severe allergy season, individuals with low-grade allergies sometimes develop symptoms which warrant a doctor’s visit. When an individual moves to a new location, they may have allergic symptoms for the very first time. For example, if a ragweed-sensitive individual moves from California, where ragweed is not a prominent allergen, to the midwest, where ragweed is abundant, they may experience their first onset of allergic symptoms.

‘Are we in the allergy season?’ Most allergy occurs during the pollen season, usually occurring during the spring, summer, and fall months. It is less common to encounter allergic conjunctivitis patients during the winter months, when pollen counts are low. Accordingly, it is rare to make an initial diagnosis of allergic conjunctivitis during the winter months. An exception would be the patient who is allergic to perennial allergens, such as animal dander, dust mites, or fungi.

‘Is there exposure to perennial allergens?’ It is useful to ask about pets and other animal exposure. Cat allergy is particularly common. Guinea pig and rabbit allergy are common among laboratory workers. Some people are exposed to perennial allergens at work, particularly those working in dusty environments. It is helpful to ask these people if symptoms improve when they are away

from work, or while on vacation. Patients often ask if they could be allergic to fumes, perfumes, sprays and cosmetics. In my experience, these substances may cause irritative conjunctivitis, but rarely allergic conjunctivitis.

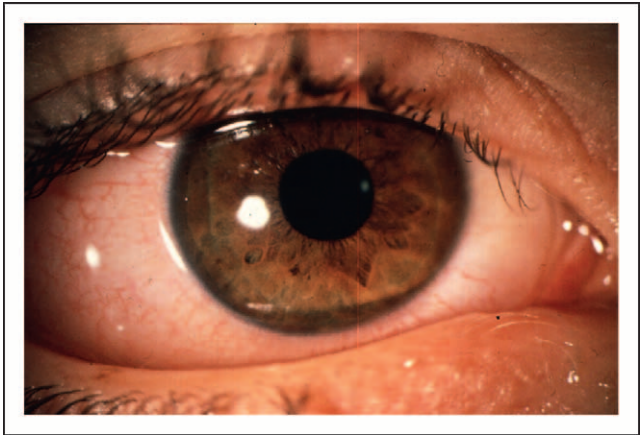
Types of ocular allergy

There are numerous classifications of ocular allergy, and it seems prudent to select one which takes into consideration our current understanding of immunologic mechanisms and their relationship to systemic disease. The simple classification below distinguishes between IgE-mediated and cell-mediated conditions. It also includes one disease, giant papillary conjunctivitis, which has certain signs suggestive of allergy, but is probably a strictly irritative phenomenon.

Seasonal and perennial allergic conjunctivitis

Seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC) are the most common forms of ocular allergy (Fig. 1). Estimates vary, but these types of allergy are said to affect at least 15–20% of the population [2]. Signs and symptoms of these two conditions are the same. The difference is the specific allergens to which the patient is allergic. SAC is usually caused by airborne pollens. Signs and symptoms usually occur in the spring and summer, and generally abate during the winter months. PAC can occur throughout the year with exposure to perennial allergens. Diagnostic features of SAC and PAC consist of itching, redness, and swelling of the conjunctiva. Redness, or conjunctival injection, tends to be mild to moderate. Conjunctival swelling, or chemosis, tends to be moderate, and somewhat more prominent than one would expect for a mild amount of redness. Itching is a fairly consistent symptom of SAC and PAC. It is sometimes said that ‘if it itches,

Figure 1 Mild conjunctival redness (injection) and moderate swelling (chemosis) typical of acute seasonal and perennial allergic conjunctivitis



it must be allergy, and if does not itch, it cannot be allergy'. This is probably an overstatement. Itching may, in fact, be associated with blepharitis, dry eye, and infection. Still, patients who complain of itching should be considered likely candidates for ocular allergy.

Vernal keratoconjunctivitis

Vernal keratoconjunctivitis (VKC) is a disease of warm climates and warm weather months [3,4]. It is more common in the tropics than in northern climes. However, it is not unusual to see occasional vernal conjunctivitis patients throughout the United States and Canada. Young people are typically affected. VKC may begin before puberty, and it usually resolves by age 20 years [5]. Patients often have a strong history of allergy to pollens, or other types of allergic conditions, such as atopic dermatitis, allergic rhinitis, or asthma. Symptoms include ocular itching, redness, swelling and discharge. Itching may be quite severe, and even incapacitating. Patients are often photophobic, sometimes intensely so. The most characteristic sign is giant papillae on the upper tarsal conjunctiva (Fig. 2). These 'cobblestone-like' swellings may be several millimeters in diameter. Usually, 10–20 are found on the tarsal conjunctiva, and they can be seen easily by 'flipping' the upper eyelid. There may be a tenacious mucous discharge between the giant papillae. As one might expect, the giant papillae are filled with inflammatory cells and edema. Neutrophils, plasma cells, mononuclear cells, and eosinophils are found in abundance. There is also a great deal of mast cell activity within the giant papillae. Mast cells can be seen in various stages of degranulation throughout the conjunctival stroma. Mast cells may also be found in the conjunctival epithelium, a location in which they are not normally present. The tears of VKC patients contain high levels of IgE and mast cell mediators

Figure 2 Giant papillae of the upper tarsal conjunctiva in vernal keratoconjunctivitis

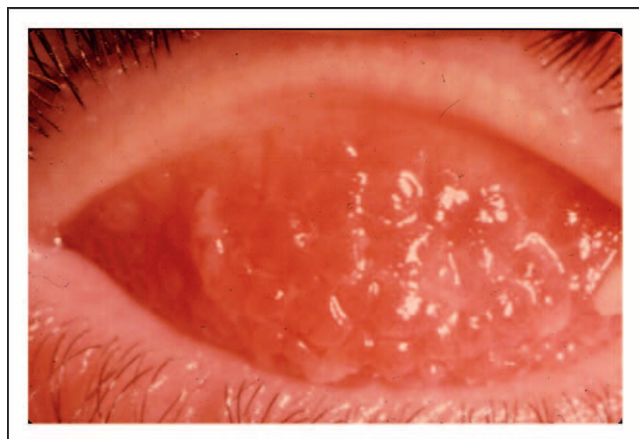
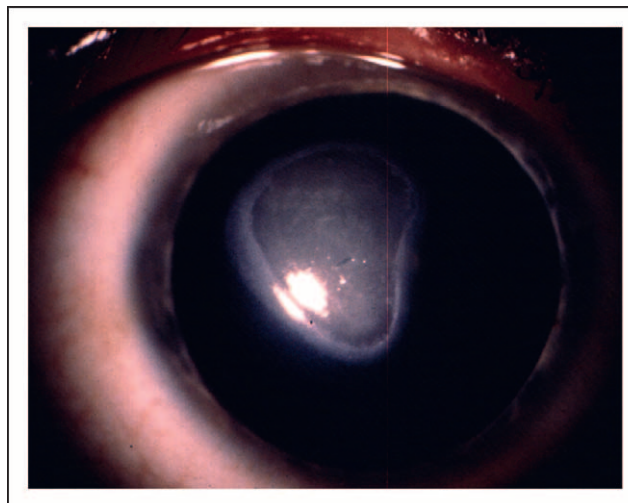


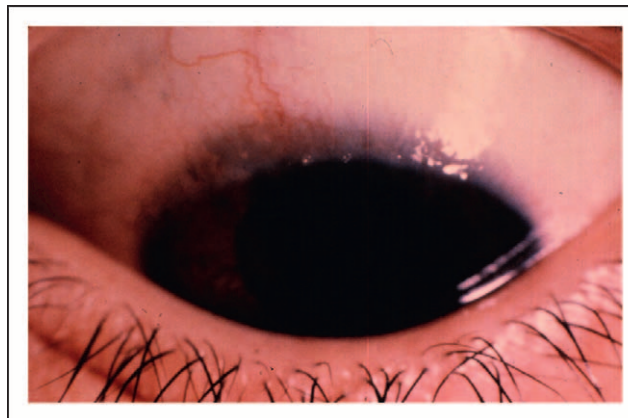
Figure 3 Corneal plaque in vernal conjunctivitis



[6,7]. Histamine, leukotrienes, prostaglandins, and kinase may be found in the tears of VKC patients.

The cornea may be affected in VKC. A punctate keratitis, known as keratitis epithelialis vernalis of El Tobgy, may begin in the central cornea. The dots may coalesce to form a syncytial opacity. This often leads to a whitish or grayish plaque beneath the epithelium (Fig. 3). These vernal plaques may interfere with vision and lead to central scarring of the cornea. This is one of the few instances in which ocular allergy can be associated with visual morbidity. Plaques can be removed by superficial keratectomy, but they rarely resolve without surgical intervention. Histologically, plaques consist of mucin and epithelial cells which are literally ground into the central cornea. VKC patients may also demonstrate Trantas dots (Fig. 4), small white dots usually at the

Figure 4 Trantas dots in vernal conjunctivitis



superior limbus. The dots represent almost pure collections of eosinophils [5]. These cells collect in crypts which are formed by invaginations at the junction of the cornea and conjunctiva. Trantas dots tend to appear when VKC is active, and disappear when symptoms abate.

Atopic keratoconjunctivitis

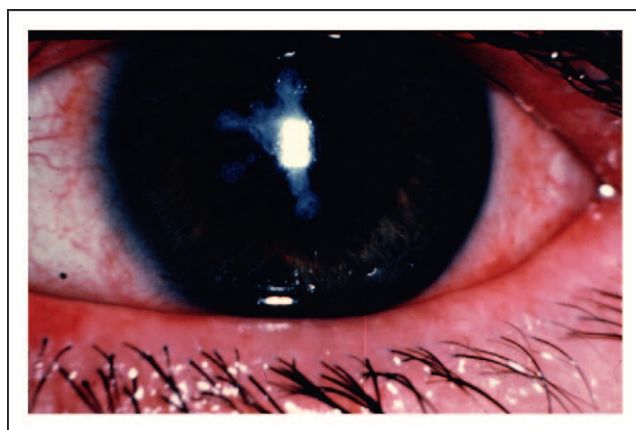
Atopic keratoconjunctivitis (AKC) is the ocular counterpart of atopic dermatitis, or atopic eczema [8[•]]. Eczematous lesions may be found on the eyelids (Fig. 5), or any place on the body. Skin lesions are red and elevated. They often occur in the antecubital or popliteal regions. Typically, eczematous lesions are itchy, and scratching them makes them more itchy. Ocular findings vary. The eyelid skin may have a fine sandpaper-like texture. There may be mild, or severe, conjunctival injection and chemosis [9]. Giant papillae may, or may not, be present. Conjunctival scarring is common. Trantas dots may also be present. AKC is said to be associated with keratoconus. If this association exists, it is relatively uncommon. Most atopic patients do not have keratoconus, and most keratoconus patients do not have AKC. It has been suggested that eye rubbing, precipitated by ocular itching, may lead to keratoconus. Whereas this may be an interesting theory, there does not seem to be much evidence that rubbing the eye could create an ectatic corneal condition like keratoconus. AKC patients may also develop atopic cataracts (Fig. 6). Typically, these are anterior, shield-like cataracts, but nuclear, cortical and even posterior subcapsular cataracts may develop. Corticosteroid therapy of AKC may contribute to cataract development [10]. However, atopic cataracts were documented long before corticosteroids were available for medical use. It is not unusual for AKC patients to have cataract surgery at a young age.

It may seem that the appearance of VKC and AKC is similar. Both may be associated with giant papillae and

Figure 5 Atopic keratoconjunctivitis with eczematous skin lesions of the eyelids



Figure 6 Anterior shield-like cataract associated with atopic keratoconjunctivitis

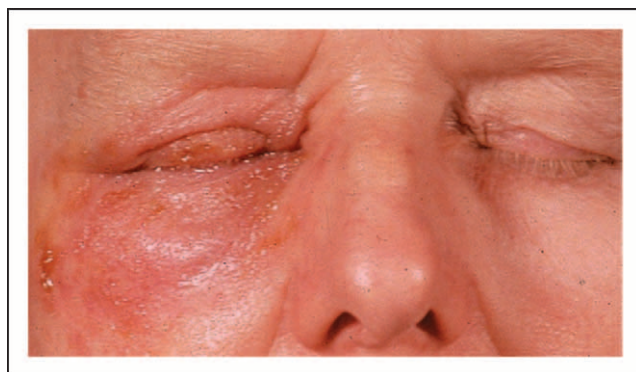


Trantas dots. In fact, there probably is some overlap between these two conditions. VKC, however, resolves by age 20 years, whereas AKC can persist throughout life.

Contact allergy

Contact allergy, or contact dermatitis, is not an IgE-mediated allergy, and can be considered in a different category than the aforementioned allergic conditions [11]. Contact allergy is mediated by lymphocytes, rather than antibody. Allergens are generally simple chemicals, low molecular weight substances that combine with skin protein to form complete allergens. Examples include poison ivy, poison oak, neomycin, nickel, latex, atropine and its derivatives. Although contact allergic reactions usually occur on the skin, including the skin of the eyelids (Fig. 7), the conjunctiva may also support contact allergic reactions. Initial sensitization with a contact allergen may take several days. Upon re-exposure to the allergen,

Figure 7 Contact allergy to neomycin eyedrops



an indurated, erythematous reaction slowly develops. The reaction may peak 2–5 days after re-exposure. The delay in development of the reaction is due to the slow migration of lymphocytes to the antigen depot. The term ‘delayed hypersensitivity’ is sometimes given to these reactions, in contrast to ‘immediate hypersensitivity’, a term which emphasizes the rapid development of IgE antibody-mediated reactions. Contact allergic reactions are generally associated with itching. Treatment consists of withdrawing, and avoiding future contacts with the allergen. Patch testing is sometimes used to identify unknown allergens. Severe reactions can be treated with topical or systemic corticosteroids.

Giant papillary conjunctivitis

Giant papillary conjunctivitis (GPC) is not a true ocular allergy, but rather an irritant phenomenon (Fig. 8), which induces giant, medium, or small papillae in the superior palpebral conjunctiva. GPC used to be classified as an allergic phenomenon because of conjunctival changes similar in appearance to vernal conjunctivitis [12]. However, the incidence of systemic allergy in GPC patients is similar to that of the general population, and the stimuli for the papillary conjunctival changes are inert substances rather than allergens. For example, GPC may be caused by limbal sutures, contact lenses [13], ocular prostheses, and limbal dermoids. When these irritative stimuli are removed, the conjunctival papillary changes resolve. The conjunctival tissues may contain mast cells, basophils, or eosinophils, but not to the extent of an allergic reaction. There is no increase in IgE or histamine in the tears of GPC patients. Since the advent of disposable contact lenses, the frequency of GPC is low. It appears that protein build-up on the

surface of contact lenses, and irregular edges were the main reason for the close association between contact lenses and GPC.

Diagnostic tests

The diagnosis of ocular allergy is primarily clinical, but there are laboratory tests that can be useful in supporting the diagnosis [14^{••}]. Allergists can perform skin testing for specific allergens by scratch tests or intradermal injections of allergen. In-vitro tests for IgE antibodies to specific allergens also exist. There are also commercial tests for total IgE levels in tears. Conjunctival smears can provide supportive evidence of ocular allergy. Conjunctival scrapings can be stained with a variety of stains and viewed under light microscopy. Presence of eosinophils, mast cells, or basophils, would support the diagnosis of ocular allergy.

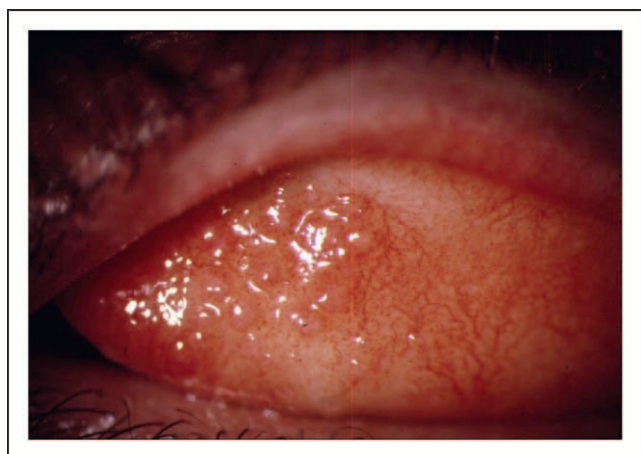
Treatment

Treatment of ocular allergy is usually tailored to fit the severity of signs and symptoms (see below). Treatment options for ocular allergy includes

- (1) avoidance of allergen,
- (2) cold compresses,
- (3) oral antiallergics,
- (4) vasoconstrictor/antihistamine eye drops,
- (5) mast cell stabilizers eye drops, and
- (6) corticosteroid eye drops.

If symptoms are mild, no treatment is necessary. Many patients tolerate mild itching and redness of the eyes during the allergy season without resorting to medication. If the allergen can be identified, and avoided, allergic symptoms may be mild, or nonexistent. Many patients with ocular allergy use oral antiallergics on a regular basis. The effect of these oral medications may be sufficient to control ocular symptoms. Antiallergic eyedrops may be useful. Over-the-counter preparations containing a vasoconstrictor, usually naphazoline hydrochloride, and an H₁ antihistamine, usually antazoline, or pheniramine, are readily available. They are especially useful for reducing conjunctival injection. Adverse reactions are extremely rare with these combination drugs. Concern has sometimes been expressed about a ‘rebound’ vasoconstriction with these drugs. If rebound vasodilatation does occur, it is mild, and harmless. Several mast cell stabilizers are available [15,16], both over the counter, and by prescription. They are effective for treating the signs and symptoms of mild to moderate allergic conjunctivitis. They also have a high safety profile. These drugs inhibit the release of mast cell mediators. Some have been shown to have antihistaminic properties, and some have antichemotactic effects.

Figure 8 Giant papillary conjunctivitis caused by contact lens wear



Mast cell stabilizers are used once or twice a day. They can be used throughout the allergy season without concern for adverse reactions. For severe allergic conjunctivitis, corticosteroid eye drops are an order of magnitude more potent than mast cell stabilizers [17,18]. Low-dose corticosteroids, particularly those which have little glaucomagenic potential, are preferred. Fluorometholone and loteprednol etabonate are among the preferred corticosteroid eye drops for ocular allergy. Patients receiving corticosteroid eye drops should be monitored for glaucoma and cataracts every 4 months. One should keep in mind that intranasal corticosteroid sprays have been associated with elevated intraocular pressures, and glaucoma damage [19]. There may be some benefit from the use of topical cyclosporine eye drops in the treatment of ocular allergy [20]; however, oral cyclosporine and other antimetabolites have no role in the treatment of ocular allergy.

Conclusion

Ocular allergy is common, but fortunately, most cases are mild, and associated with airborne pollens, and seasonal allergic rhinitis. Occasionally, severe ocular allergy in the form of VKC, or AKC, is encountered. It is usually possible to distinguish ocular allergy from other types of ocular inflammation by considering history, seasonality, and symptomatology. The triad of redness, swelling and itching is a useful, and fairly reliable, description of allergic conjunctivitis. Treatment should be tailored to address the severity of the signs and symptoms. Avoidance, cold compresses, and oral antihistamines are effective for mild allergic conjunctivitis. Vasoconstrictor/antihistamine eye drops and mast cell stabilizers are useful for mild to moderate ocular symptoms. Corticosteroid eye drops may be needed for severe allergic signs and symptoms. Careful attention should be paid to potential corticosteroid-related side effects. Frequent eye exams, with monitoring of intraocular pressure and cataract formation, are necessary precautions when topical, nasal, or oral corticosteroids are used.

Acknowledgement

Conflicts of interest

None declared.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
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Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

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