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Ocular Allergic Disease

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Ocular allergic disease is a common and potentially serious problem for the comprehensive ophthalmologist. The spectrum of disease ranges from minor ocular allergy to severe and chronic sight-threatening conditions that have a major impact on quality of life. Ocular allergic disease affects approximately 20% of the population. In Canada, approximately 6 million people suffer with this disorder, with Ontario accounting for 55% of these individuals. From a financial perspective, it is estimated that, in North America, ocular allergy costs an estimated $250 million per annum due to lost workplace productivity. Therefore, it is important for the ophthalmologist to be familiar with ocular allergic disease. This issue of *Ophthalmology Rounds* focuses on the diagnosis and management of this prevalent condition.

Four essential factors must be considered in the work-up of patients with presumed ocular allergy:

- Environmental factors (eg, pollens) that may cause acute seasonal allergic conjunctivitis, and climatic conditions, which play an important role in vernal keratoconjunctivitis.
- Genetic factors; there is a 4-fold increase in a child's chance of developing ocular allergy if one parent is atopic. If both are affected, the chances increase 10-fold.
- Medications may act as allergens or as immune modulators. For example, some drugs (eg, oral antihistamines) can dry ocular mucous membranes, aggravating the effects of external allergens on the eye. Other drugs (eg, topical mast cell stabilizers) at greater concentrations stimulate mast cells, exacerbating the effects of ocular allergy.
- Mechanical factors, like eye rubbing and contact lens (CL) wear, can also exacerbate allergy symptoms. CLs are implicated in causing one type of ocular allergy: giant papillary conjunctivitis.

Diagnosis and diff e rential diagnosis

The conjunctiva is frequently inv o lved in allergic reactions because this mucous membrane is directly exposed to environmental allergens. Since the majority of ocular allergic conditions affect the conjunctiva, it has become common practice to group all ocular allergic diseases under the common heading, "allergic conjunctivitis." However, according to our current understanding of the pathophysiology and clinical course of this disease, a more precise classification has been proposed in which 4 distinct subtypes of ocular allergy are classified. The spectrum of severity ranges from uncomfortable and irritative, but not sight-threatening diseases (eg, seasonal allergic conjunctivitis and giant papillary conjunctivitis), to conditions that can cause corneal ulceration with scarring and are potentially blinding (such as vernal and atopic keratoconjunctivitis).

Itching is the most common symptom in patients presenting with allergic conjunctivitis. Chemosis and conjunctival injection are frequently associated signs although, in most cases, they are subtle. An exception may occur in acute allergic reactions, especially when associated with vigorous eye-rubbing, where chemosis can be severe. Lid edema is another sign of allergic eye disease. The differential diagnosis of ocular allergy includes other ocular surface disorders (eg, keratitis sicca and blepharitis).

4 distinct subtypes of ocular allergy

Allergic conjunctivitis

Seasonal allergic conjunctivitis (SAC) is the most prevalent form of ocular allergic disease, affecting 5% to 22% of the population. It is closely associated to the cycles of airborne plant-related allergens. Fortunately, it is a self-limiting condition due to type I hypersensitivity. It is often referred to as "acute allergic conjunctivitis" and accounts for approximately 50% of all ocular allergies. It is typically accompanied by seasonal allergic rhinitis. It is the ocular

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form of hay fever and is often the predominant presentation in hay fever sufferers. As the name implies, its occurrence is seasonal, due to exposure to grass, tree pollen, or ragweed. In Ontario, the causative factors are tree and flower pollen in early spring, grass pollen in the late spring and early summer, and ragweed in late summer and early fall. During July and August, the presence of grass and ragweed overlap and this is the worst period for affected patients.

The predominant symptom of SAC is a bilateral low-grade ocular and periocular itching, but other symptoms (eg, redness, burning, excessive tearing, and the presence of a stringy white mucous discharge) may be present. Symptoms are bilateral, although they may be asymmetric. Occasionally, patients may complain of photophobia and many have a history of other allergic disorders, food allergies, or sensitivity to pets. On ocular examination, signs may be absent or consist of mild injection. There may be a mild papillary reaction involving the tarsal conjunctivae. Mild chemosis may be present in the bulbar conjunctiva.

Perennial allergic conjunctivitis (PAC) is also referred to as chronic allergic conjunctivitis because it persists throughout the year. Like the acute form, this is a type I hypersensitivity response that involves both an early and late phase hypersensitivity reaction. It has a documented prevalence of 0.03%, and 87% of patients experience seasonal exacerbations. It most often results from exposure to constantly present household allergens (eg, animal dander, dust mite feces, moulds, and pollen). Exacerbations may occur in the spring or fall due to increased exposure to dust mites and fungal allergens at this time.

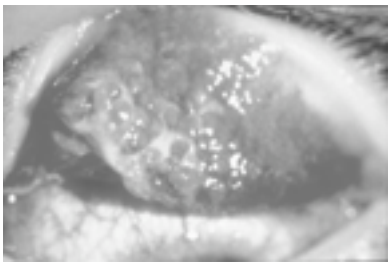
The clinical signs and symptoms associated with PAC are similar to those of SAC, although they tend to be milder and more persistent. Most cases are bilateral, but a unilateral presentation can occur if an antigen, such as animal dander, reaches one eye by hand contact.

Vernal keratoconjunctivitis (VKC)

VKC is a recurrent, bilateral, and usually self-limiting ocular inflammatory disease. It is a potentially sight-threatening condition, occurs most frequently between the ages of 3 and 20 years, and is more prevalent in male children. Seasonal exacerbations are characteristic, hence the term "vernal" (spring). Invariably, these children have a family history of hay fever, allergy, atopy, or asthma. VKC tends to resolve after puberty. It is particularly common in hot dry climates (around the Mediterranean, West Africa, Pakistan and India).

Symptoms include intense itching, photophobia, and blurred vision. Patients tend to rub their eyes a lot and suffer from a stringy or ropey discharge. Pseudoptosis may be present and, on everting the eyelid, there is the classic cobblestone appearance of the upper tarsal conjunctiva and copious stringy discharge (Figure 1). Horner-Trantas dots are collections of degenerated epithelial cells and eosinophils that may be found around the limbus. The inflamed tarsal conjunctiva can cause a superficial punctuate keratitis. The coalescence of these defects may result in a shield ulcer (Figure 2), which is usually oval and shield-shaped, on the upper one-third of the cornea underneath the upper eyelid. The shield ulcer is in direct contact with the cobblestone papillae. The base of the ulcer contains a plaque of fibrin, mucus, and debris from eosinophil granules that act as toxins and inhibit the closure of the epithelial defect. Healing is promoted by removal of the plaque. The concurrent inflammation also attracts neovascularization from the limbus. When these lesions heal, a subepithelial ringlike scar may remain in the damaged area. The combination of punctate epithelial keratitis and increased mucous discharge may result in a filamentary keratitis. The skin of the lids and the lid margin are relatively uninvolved compared to atopic conjunctivitis. Eye-rubbing is a significant problem and may account for an increased incidence of keratoconus in these patients.

Figure 1: Cobblestone appearance of upper tarsal conjunctiva in VKC. Note the copious discharge in-between the cobblestones



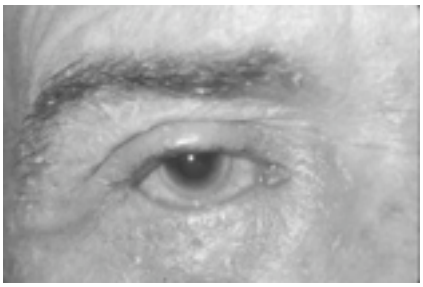
Atopic keratoconjunctivitis (AKC)

AKC is a chronic condition that affects about 3% of the population. Both type I and type IV hypersensitivity mechanisms are thought to be involved. This potentially severe, sight-threatening disease can present at any age, but is most common in patients in their late teens or early 20s who have a family history of hay fever, allergy, atopy, or asthma. No racial or geographic predilection has been reported. The condition does not exhibit the seasonal variability that is common with other allergic disorders. Nonetheless, exacerbations have been noted in the winter, possibly the result of dryness associated with home heating. Concomitant skin manifestations are typical; patients often report a history of eczema. Dermatitis is usually evident in the periocular region (Figure 3). The eyes are affected in approximately 25%-50% of patients with atopic dermatitis.

The major ocular symptoms are itching, burning, and photophobia. Eczematous lid involvement with scaling and redness can be a differentiating sign. Other findings include punctuate epithelial keratitis, persistent epithelial defects, scarring of the cornea, and neovascularization. These patients are prone to develop other ocular conditions such as keratoconus, anterior or posterior subcapsular cataract, secondary glaucoma, bacterial or herpetic superinfections, retinal detachment

Figure 2: Shield ulcer in a patient with VKC.

Figure 3: Eczematoid blepharitis in a patient with AKC.



and, very rarely, crystalline lens dislocation secondary to eye-rubbing.

Giant papillary conjunctivitis (GPC)

GPC is a reversible condition, most commonly associated with CL wear, exposed sutures, a scleral buckle, or a prosthesis. It appears to be a response to mechanical trauma and not due strictly to allergic mechanisms. However, it is still included as one of the forms of ocular allergy. The pathophysiology here is both a type I and type IV hypersensitivity reaction. It is estimated that about 20 million people use CLs. GPC occurs in 10%-15% of soft CL wearers and in 1%-5% of hard CL wearers. With soft contact lens wear, GPC usually develops within months while, with hard contact lenses, GPC development can occur after a few years. The clinical diagnosis is made on the basis of a history of CL wear with an increasing intolerance to the lenses. There is typically also a history of itching (more when the lenses are removed), blurring of vision, mucous discharge with adherence of the eyelids at night. The diagnostic sign is the presence of giant papillae (ie, >0.3 mm in diameter) involving the upper tarsal plate.

Pathophysiology of ocular allergic disease

The allergic response is typically elicited by ocular exposure to an allergen that causes cross-linkage of membrane-bound IgE, which triggers mast cell degranulation. This results in the release of a cascade of allergic and inflammatory mediators, including histamine, and the synthesis of arachidonic acid resulting in the production of prostaglandin and leukotrienes that are associated with increased mucous secretion and cellular infiltration.

Mast cells are normally found in the vascular stroma (substantia propria) of the conjunctiva. There are approximately 50 million mast cells in the human conjunctiva, but they are identifiable in the epithelium only in pathologic situations. In all forms of allergic eye disease, a large number of mast cells can be identified in the conjunctiva. In AKC, VKC, and GPC, there is also an increase in the number of conjunctival T cells, particularly CD4-memory cells, resulting in an increase in the CD4/CD8 ratio. Histamine is stored in granules in the mast cells and is readily released. There are approximately 5 to 10 picograms of histamine per individual mast cell. There are 2 histamine receptor subtypes in the eye (H-1 and H-2). Histamine binding of these receptors produces the itching sensation resulting from the activation of the H1 receptor and vasodilatation from the H2 receptor.

The early phase of the allergic reaction continues for approximately 20 minutes after allergen activation. The mast cells are responsible for this phase. When activated, they release histamine and other proinflammatory mediators (eg, prostaglandin D2, leukotriene C4, platelet activating factor, and tryptase). Histamine, protease tryptase, leukotrienes, and eosonophils can be detected in the tears. The late phase, when basophils are involved, occurs 2-9 hours after activation and histamine, but not tryptase or eosinophils, is detected in the tears.[1] Clinical signs indicate that the allergic response lasts for a longer period due to an influx and infiltration of the conjunctiva with inflammatory cells, such as eosinophils, neutrophils, and Th2 cells. Eosinophil major basic protein has been shown to be cytotoxic to corneal epithelium and is involved in the more severe and chronic forms of allergic ocular disease (eg, VKC and AKC).

Management

The management of ocular allergy can be somewhat confusing because many different modalities of treatment are available. Bielory's review of ocular allergy management lists 28 different treatment options.[2] As a general principal, treatment is based on severity of symptoms and how much they interfere with the individual's quality of life. A reasonable approach to management is a stepped-care approach, with environmental modulation and avoidance of known or suspected allergens as the first step, progressing to pharmacotherapy in a graded manner. For mild symptoms, artificial tears may be all that is required and this comprises the first tier of management. The majority of patients can be managed with one of the newer antihistamine/mast cell stabilizer/anti-inflammatory drops, which form the second tier. Steroids, either topical or systemic, and other immunomodulatory medications comprise the third tier.

General supportive measures

Avoidance of inciting allergens is advised by staying indoors during high pollen counts, keeping windows closed when possible, washing the hair and clothes after being outdoors, and avoiding soaps, cosmetics, and detergents. Other helpful maneuvers include the use of air conditioners and electronic filters, plastic bedcovers, removing carpets, and avoiding pets. Eye rubbing should be avoided because the mechanical irritation causes the release of inflammatory mediators, which perpetuates the itch-rub-itch-cycle. Artificial tears, used 4-8 times a day, improve the barrier function of the tear film, dilutes allergens and mediators, and helps to flush them out of the eye. They also mitigate against the drying effect of systemic antihistamines. Nonpreserved tear substitutes are recommended and refrigeration increases their comfort. Cold compresses or ice packs several times a day can provide considerable relief, especially from itching.

Medical care

Topical vasoconstrictors

Topical vasoconstrictors, including tetrahydrozoline, phenylephrine, and other vasoconstrictors, are sympathomimetic agents that decrease vascular congestion by alpha-adrenoreceptor stimulation. These drugs have no effect on the allergic reaction itself and they do not alleviate the major complaint of itching. Adverse side-effects include pupil dilation, even at low concentrations, that could trigger an attack of acute angle-closure glaucoma in prone individuals. These preparations may themselves cause burning and itching. Prolonged use of vasoconstrictors can lead to tachyphylaxis, causing the

patient to use the drops more frequently. Discontinuation may cause rebound hyperemia.[2] As a general class of anti-allergy medicines, their usefulness is limited, and their potential to cause problems often outweighs their potential benefits.

Antihistamines

Antihistamines are more effective for the treatment of ocular allergy when administered topically compared to systemically. Topical administration delivers a high concentration of drug directly to the target site and, consequently, the onset of action is faster (within minutes). Also, drug interactions and unwanted side-effects occasionally seen with oral antihistamines are avoided. Side effects such as sedation, dizziness, tinnitus, nervousness, and insomnia are less common with the newer generation systemic antihistamines. Although 3rd generation systemic antihistamines are not sedating, they can cause drying of the ocular surface, thereby exacerbating the symptoms of patients suffering with ocular allergy.[3] Table 1 presents an overview of commercially available topical anti-allergy ocular medications, their mechanisms of action, and potential side-effects. Below is an overview of the common anti-allergy drops.

- Azelastine hydrochloride 0.5%, is a derivative of phtalazinon that is metabolized to the active metabolite desmethylazelastine. It has multiple actions: it is an anti-histamine, anti-leukotriene, and a serotonin-blocker, and it also has mast cell stabilizing action. Indications are seasonal and perennial allergic conjunctivitis and ocular allergy syndromes. Contraindications include sensitivity to benzalkonium chloride (BAK). Side effects are stinging in the eye upon instillation and a bitter taste that can be reduced with punctual occlusion. Azelastine is very effective in reducing itch within minutes and has a long-lasting effect. Dosing is usually 2 times a day, but may be increased to 4 times a day.
- Emedastine 0.01% is a H1 selective antagonist, with dose-dependent inhibition of histamine-induced conjunctival permeability. It has no effect on cholinergic, dopaminergic, or adrenergic receptors. The indication for its use is SAC or acute allergy. Contraindication is sensitivity to BAK. In Europe, a preservative-free Minim preparation is available. It is not safe during pregnancy (animal studies) and since renal and hepatic excretion have not been studied, it should be avoided in the elderly and in patients with renal and hepatic insufficiency. It is a very effective medication to counter itch and acute allergy. Its prolonged use has not been studied. Dosage is twice a day.
- Levocabastine 0.05% is a carbenoid derivative with anti-histaminic action. It is actually the "gold-standard" for laboratory studies in histamine inhibition. Indications are SAC and VKC. It is very effective in acutely relieving itch, but has no role in prolonged treatment of allergy. Contraindication is an allergy to BAK. It has been shown to be teratogenic and is contraindicated during pregnancy. Dosage is usually twice a day, but may be increased to 3 or 4 times a day for acute and severe episodes.
- Ketotifen-fumarate 0.025% is a antihistamine with a weak anti-cholinergic action. It is mast-cell stabilizing in vitro. Indications are SAC and acute allergy. Side effects can be local irritation and allergic reaction, punctuate keratopathy, headache, drowsiness, dry eyes, and dry mouth.
- Second-generation anti-allergy eye drops contain a combination of antihistamines and vasoconstrictors and tend to be more effective than either agent alone. They can usually be purchased over the counter (OTC). Again, the benefits of topical vasoconstrictors must be weighed against their potential side effects.

Table 1: An overview of topical anti-allergic preparations, their mechanisms of action, and potential side-effects

Preparation	Mechanism	Side effects
Azelastine 0.05%	MCI, anti-H1, anti-LT,anti-5OH	Bitter, stings
Cromoglycate 2%	Anti-H1, MCI Prophylaxis	Contact dermatitis Stings
Emedastine 0.05%	Anti-H1 also acute Relief of itch	Burns Dyspnea
Ketotifen 0.025%	Anti-H1, MCI	Itch, contact allergy, urticaria
Levocabastine 0.05%	Anti-H1 acute relief of itch	Irritation
Nedocromyl 2%	MCI, prophylaxis	Contact dermatitis Burns
Opalatadine 0.1%	Anti-H1, MCI	Itch, burns, edema

Anti-H1 = H1-blocking agent, MCI = mast cell inhibitor, Anti-LT = anti-leukotrienes, Anti-5OH (5-hydroxypropafenone) = antiserotoninergic

Mast cell stabilizers

Mast cell subtypes vary in different tissues and in different species in such parameters as neutral protease content and responsiveness to therapeutic agents. Therefore, mast cell stabilizers that were not developed for ocular use may not be effective in the eye. The exact mechanism for their action is not fully understood. What is known, however, is that, when used prophylactically, they are very effective in preventing mast cell degranulation, thus preventing histamine release and the cascade of reactions resulting in ocular allergy symptoms. However, they do not block histamine receptors or prevent the production of newly formed mediators and, therefore, do not relieve existing symptoms. Their effect on stabilization of mast-cells is biphasic, meaning that, at low concentrations, there is stabilization, while at higher concentrations, degranulation of histamine is actually stimulated. The only exception to this biphasic mechanism is olopatadine, which has a dose-dependent stabilizing effect only. In order to be effective, treatment must commence 2-3 weeks before the allergy season. A meta-analysis perfomed by Owen et al[5] found that patients using mast cell stabilizers were 4.9 times (95% CI, 2.5-9.6) more likely to perceive benefit than those receiving a placebo.

Mast cell stabilizers include chromolin sodium, and nedocromyl. Ketotifen is a multiple action drug with mast cell inhibiting properties, as are opalatadine and azelastine.

Drugs with >1 mechanism of action

This is the newest generation of ocular allergy medications. Their advantage is the rapid sympto-

matic relief produced by immediate histamine receptor antagonists, coupled with the long-term disease-modifying benefit of mast cell stabilizers. Olopatadine (Patanol) acts as a mast cell stabilizer, H1 receptor antagonist and inhibits cytokine secretion. Azelastine (Optivar) and Nedocromil (Alocril) have some inhibitory effect on inflammatory cells. Ketotifen (Zaditor) is a drug that acts as a histamine receptor antagonist and mast cell stabilizer. Ketotifen is a relatively selective, noncompetitive antagonist of histamine H1 receptors and a mast cell stabilizer, inhibiting the release of inflammatory mediators from mast cells. In addition, it has been shown to modulate the actions of eosinophils via several distinct mechanisms other than mast cell stabilization, including a direct effect on the endothelium, inhibiting the synthesis and expression of cellular adhesion molecules that play a key role in the recruitment of eosinophils; antagonism of the activity of platelet activating factor, thereby inhibiting the recruitment and activation of eosinophils; inhibition of eosinophil chemotaxis and activation induced by eotaxin and IL-5; and a direct stabilizing effect on eosinophils, thus preventing degranulation.[6]

In antigen challenge tests, both olopatadine and ketotifen were found to be very efficient in rapidly reducing signs and symptoms of seasonal allergic conjunctivitis within minutes, including redness, itching, tearing, chemosis, eye lid swelling and mucous discharge.[7]

Nonsteroidal anti-inflammatory drugs (NSAIDs)

This class of drugs functions by inhibiting prostaglandin (PG) production. PGE_2 and PGI_2 are extremely pruritogenic to the conjunctival mucosa. NSAIDs diminish ocular itching and hyperemia by inhibiting these factors. It may take 2 weeks of topical use to have an effect.

Topical corticosteroids

Corticosteroids reduce the transcription of proinflammatory genes (eg, the gene for phospholipase A2) and thus reduce the amount of PGs produced. However, corticosteroids also promote the release of phospholipase A2 inhibitor (Lipocortin) from leukocytes.

There is no clear understanding of the mechanism at the cellular and plasma levels.[8] Glucocorticoids inhibit the production of interleukins (ILs), among them IL-4 and IL-5 that are the primary ILs produced by ocular surface mast cells. Steroids also reduce transcription of eotaxin and may induce apoptosis of eosinophils and T-cells.[9] Topical steroids do not have an immediate effect on ocular itching caused by allergies. Their effect is based on attenuating the late phase response.

In view of their potential side effects, including cataracts, increased intraocular pressure, and corneal melts, corticosteroids are typically reserved for patients not responsive to other therapy or for use in the severe forms of allergy, such as AKC or VKC, and acute exacerbations of VKC. The regimen is a high dose of dexamethasone or prednisolone 8 times daily for 1 week and then rapid tapering. Topical mast cell stabilizers or a combined medication should be started concurrently.

The use of supratarsal injections of steroids in severe VKC has been described. Holsclaw et al[11] found that patients injected supratarsaly with dexamethasone sodium or triamcinolone experienced relief in signs and symptoms within 1 to 5 days and could subsequently be maintained on conventional therapeutic regimens. One patient injected with triamcinolone had a rise in intraocular pressure. The frequent administration of topical steroids can achieve the same effect, while avoiding some of the potential complications of a supratarsal injection. Beside the well-known complications of secondary cataract and glaucoma, one should consider the potential for causing skin problems like necrosis, depigmentation, and subcutaneous atrophy. Supratarsal injection is not our preferred method of therapy.

Cyclosporine A (CsA)

Cyclosporine A is an immunomodulator and inhibits CD4+ T lymphocyte proliferation via calcium-dependent, specific, reversible inhibition of transcription of IL-2. This reduces the production of a range of cytokines, inhibiting the activation and/or maturation of various cell types, including those involved in atopy. The drug has direct inhibitory effects on eosinophil and mast cell activation and release of mediators, which is important in the treatment of allergic inflammation.

Both topical and oral cyclosporine A have been shown to be effective in managing the symptoms and reducing the amount of topical steroid use in AKC.[10] A commercially available 0.05% emulsion of cyclosporine A (Restasis®) improved signs and symptoms in patients with steroid-resistant AKC.[11] In Canada, Restasis is not readily available and can only be obtained from The Emergency Drug Release Program in Ottawa.

Mitomycin-C

Mitomycin-C (MMC), like the other alkylating agents, acts in a manner similar to radiation. It selectively inhibits DNA synthesis and is non-cell-cycle specific. At high concentrations, cellular RNA and protein synthesis are also suppressed. Without correctly configured new DNA and RNA molecules, cell migration and mitosis are inhibited, resulting in a decreased rate of cell proliferation. Rapidly dividing cells are most sensitive and it has a non-specific inhibitory effect on the proliferation of both inflammatory cells and fibroblasts, which are responsible for the symptoms and signs associated with allergic conjunctivitis. Topical MMC was found to be safe at low doses and the application of 0.01% MMC drops for 2 weeks led to a significant decrease in mucous discharge, conjunctival hyperemia, and limbal edema in patients with VKC.[13] However, the risk-benefit ratio should be very carefully considered before prescribing a drug with the toxic potential of MMC.

FK506 (tacrolimus hydrate)

Tacrolimus is a macrolide immunosuppressant and is used for immunomodulation after organ transplantation. FK506 ointment is currently available for treatment of atopic dermatitis. It strongly

inhibits cytokine production by T cells in vitro and suppresses delayed-type cutaneous responses in mice by inhibiting the activation of sensitized Th1 cells already accumulated in the dermis. Although FK506 inhibits histamine release and cytokine production by mast cells and basophils in vitro, the ointment does not suppress the immediate-type response in rats. In a study on an animal model, Sengoku et al[14] examined the effect of FK506 eye drops on ocular allergy and demonstrated that the drops inhibited late and delayed type response and were equivalent in their effectiveness to steroids. Vichyanond et al[16] reported a very favourable effect with 0.1% FK506 eye ointment in the treatment of 10 patients with VKC. An ophthalmic preparation of topical tacrolimus is not currently available in Canada

Conclusion

Ocular allergy is one of the most common external disease problems facing the comprehensive ophthalmologist. This issue has reviewed the diagnosis of ocular allergy, discussed the 4 distinct subtypes of allergic ocular disorders, and reviewed the pathophysiology of this disease to help in the management of these patients. As a general principal, management is based on the severity of symptoms and how much they interfere with an individual's quality of life. The general supportive measures and specific pharmaco-therapies presented in this article will help the comprehensive ophthalmologist in dealing with patients presenting with ocular allergy of varying severity.

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June 3, 2005 47th Departmental Research Day
Clement McCulloch Lecturer – Dr. Mark Tso
John Hopkins University, Baltimore, MD
U of T – JJR MacLeod Auditorium
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Stella.pang@sickkids.ca

June 22-25, 2005 Canadian Ophthalmological Society (COS)
Shaw Conference Centre, Edmonton, AB
Contact: Kimberley Ross at 1-800 267-5763
Email: kross@eyesite.ca

July 6-9, 2005 Ophthalmological Society of the West Indies (OSWI) Freeport, Bahamas
Contact: OSWI10@hotmail.com

September 29, 2005 VPP – Dr. Brian Leonard, Ottawa, Ontario
"International Ophthalmology"

October 13, 2005 World Sight Day

October 15-18, 2005 American Academy

December 2-3, 2005 Walter Wright Day
The Old Mill, Toronto, Ontario
"Eye Care: What Works? What Doesn't?"

Note: This year's VPP Rounds will be held at St. Michael's Hospital, 30 Bond Street, Toronto – Paul Marshall Lecture Theatre, B1- Queen, Queen Street entrance (near Second Cup). Next year's (September 2005 – May 2006) VPP rounds will be held at the Hospital for Sick Children, 555 University Avenue, Toronto – Main Lecture Theatre.

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