Topics in OCULAR ANTIINFLAMMATORIES

A CONTINUING MEDICAL EDUCATION PUBLICATION

ISSUE 4

# Serious Allergic Conditions of the Ocular Surface

**JODI I. LUCHS, MD**

**Patients with atopic or vernal keratoconjunctivitis are at risk for vision loss from the effects of continuous ocular surface inflammation. Prompt diagnosis, adequate antiinflammatory treatment, including the use of cell-active agents, and careful monitoring are mainstays of effective management.**

Within ophthalmology, the past decade has been marked by an increasing awareness of the importance of the ocular surface and the potentially disastrous consequences of chronic, severe inflammation. Of the allergy-related inflammatory states that affect the eye, vernal keratoconjunctivitis (VKC) and atopic keratoconjunctivitis (AKC) are the most serious and pose the greatest overall threat to corneal health and vision.

In hot, dry climates—including parts of the Mediterranean region, Africa, and the Middle East—these aggressive, chronic ocular surface inflammatory diseases are relatively common and contribute significantly to ocular morbidity and corneal blindness. Fortunately, both conditions are comparatively rare in the US, although their apparent prevalence may be increasing due to better access to healthcare and the migration of susceptible populations to the US.[1,2]

Treatment of VKC and AKC patients requires a high level of vigilance for several reasons: 1) compared to milder ocular allergic conditions, such as seasonal or perennial allergic conjunctivitis (SAC and PAC), in VKC and AKC the underlying immune defect is more severe and the clinical manifestation more aggressive; 2) while there is some variability in disease severity over time (due to seasonal exposures and other factors), inflammation in VKC and AKC tends to be unrelenting and chronic; and 3) the risk of disease-related and treatment-related complications is far greater in VKC and AKC.

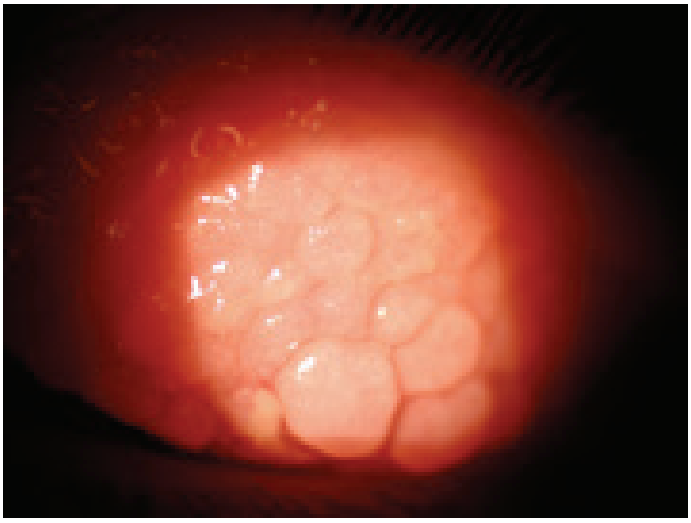

**FIGURE 1** Giant papillae on upper tarsal surface in a VKC patient. *(Image courtesy of the author.)*

## ASSOCIATIONS

As with many allergic conditions, patients with serious ocular allergic conditions commonly have overlapping immune-related disorders. Patients with VKC and AKC are

**See INSIDE for:**
**Issues in Long-term Antiinflammatory Therapy**
*by Michael B. Raizman, MD*

**TARGET AUDIENCE** This educational activity is intended for ophthalmologists and ophthalmologists in residency or fellowship training.

**LEARNING OBJECTIVES** Upon completion of this activity, participants will be able to:

1. Adopt strategies for effective treatment of serious ocular allergy that minimize risk of medication side effects .
2. Employ strategies for minimizing corticosteroid side effects in patients who require chronic management of severe ocular inflammation.

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*Topics in Ocular Antiinflammatories* is jointly sponsored by Candeo Clinical/Science Communications, LLC, and the University of Florida College of Medicine. This publication is administered by an independent editorial board and supported by an unrestricted educational grant from Bausch + Lomb, Inc.



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more likely than unaffected peers to have comorbid atopic conditions, including asthma, eczema, and rhinitis. Approximately 55% to 60% of VKC and AKC patients are skin test-positive for allergens, indicating the presence of circulating allergen-specific IgE.

A family history of atopy is also common in VKC and AKC patients.[1,3] Studies in Europe have found increased rates of autoimmune conditions, such as psoriasis and thyroiditis, in family members of VKC patients.[4,5]

## PATHOPHYSIOLOGY

VKC and AKC are managed differently from milder forms of ocular allergy. The main objective in treating SAC and PAC is to alleviate patients' ocular itching, typically by prescribing a mast cell stabilizer/antihistamine combination agent. If the itch is severe or there are additional signs or symptoms, a pulse of low-dose corticosteroid (eg, loteprednol etabonate 0.2%) can be helpful. Identifying and avoiding allergen triggers can also be a viable strategy in SAC and PAC.

By contrast, while treating symptoms and avoiding triggers are important, the goal of treatment in VKC and AKC is to suppress or rebalance overactive immune mechanisms on a long-term basis while monitoring closely for complications.

These vital clinical distinctions stem from key differences in pathophysiology.[1] SAC and PAC-related symptoms are thought to result mainly from IgE-related mast cell degranulation. While genetic-based immune dysregulation may be present in individuals with SAC, SAC is primarily an allergen-driven condition. In contrast, VKC and AKC are complex, immune-driven diseases.

Research points to the importance of T helper (Th) lymphocytes and eosinophils (as well as other cell types including mast cells) in the pathophysiology of VKC and AKC.[6] Exposure to outside antigens may exacerbate the process; however, it is an underlying defect (or defects) in regulation of the inflammatory cascade that drives the pathology in VKC and AKC.

The immunopathology of VKC and

## TOPICS IN OCULAR ANTIINFLAMMATORIES, ISSUE 4

**STATEMENT OF NEED**

The indications for topical ophthalmic antiinflammatory drugs (both steroidal and nonsteroidal) are evolving rapidly, as new agents and new applications emerge. Many of these are novel—eg, the perioperative use of nonsteroidal antiinflammatory drugs (NSAIDs) to prevent cystoid macular edema—and/or fly in the face of older thinking—eg, the use of steroids to calm inflammation and reduce the risk of melting or scarring from infection. Neither of these important applications is on-label.

In addition, new steroidal and nonsteroidal agents continue to come to market, expanding the utility of both classes. Antiinflammatory drugs are now used for: the treatment of ocular surface disease and allergic conjunctivitis; prevention of perioperative pain and inflammation in ocular surgery; infection management; cystoid macular edema prophylaxis following cataract surgery; haze prevention in PRK; and much more.

What has regrettably not followed this expansion of indications, formulations, and new molecular entities are protocols for drug selection and use.[1] These are vital because significant differences in safety, tolerability, and efficacy exist between and within both antiinflammatory drug classes. C-20 ester steroids, for example, have a demonstrated lower risk of intraocular pressure (IOP) elevation than ketone steroids.[2,3] Since a range of steroid formulations and concentrations is available, clinicians need up-to-date information about the indications and optimum uses for each.[3]

Although topical NSAID formulations have been associated with significant adverse events (keratopathy ranging from superficial punctate keratitis to corneal melt), recent work shows these to be uncommon and less severe with newer formulations.[4] Indeed, novel NSAIDs make use of lower concentrations and less frequent dosing, potentially impacting safety profiles and reducing risk from long-term use.[5]

Although both are "antiinflammatory," steroids and NSAIDs act at different points in the inflammatory cascade, and thus offer opportunities for physicians to fine-tune their drug selection. And although they are frequently used together, whether or not the two drug classes can act synergistically is controversial. In the context of recent clinical data, a clear mechanistic understanding of each drug class generally—and of newer formulations specifically—will equip clinicians to make effective, evidence-based prescribing decisions across the many situations that call for ocular inflammation control.

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**DATE OF ORIGINAL RELEASE** November 2013. Approved for a period of 12 months.

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AKC involves degranulation of conjunctival mast cells and eosinophils on a regular basis; this results in an ongoing release of large quantities of chemokines, cytokines, lytic proteins, and growth factors that cause ongoing inflammation, cellular damage and tissue remodeling on conjunctival and corneal surfaces.[6-8]

Although commonly discussed side by side, VKC and AKC are distinct diseases with different types of underlying immune dysfunction.[7] VKC has been associated with a paucity of Th1 cells, increased numbers of Th2 cells, and excess eosinophilic production of IL-3, IL-5, and IL-6.[1,6,7] AKC is associated with overstimulation of Th1 cells and excess eosinophilic production of IL-4 and IL-8.[6-8]

## CLINICAL CHARACTERISTICS OF VKC

Consistent with their immunohistopathology, VKC and AKC share some clinical manifestations. VKC, named for its springtime ("vernal") onset in the first few years of the disease, commonly affects children in the first two decades of life, with boys more often affected than girls. Children tend to "outgrow" the disease by the end of puberty, but remain at risk for the development of AKC later in life.[1]

VKC can be quite dramatic in its presentation, which may be characterized by severe bilateral ocular itch, red conjunctivae, swelling, tearing, photophobia, foreign body sensation, and the presence of a thick ropey discharge. Lids are typically spared.[1] Patients will often be referred from a pediatrician after failing to improve following one or more rounds of topical antibiotic for suspected bacterial conjunctivitis.

VKC may be predominantly tarsal, limbal, or mixed in presentation. The hallmark characteristic of the tarsal type is giant cobblestone papillae on the upper tarsal conjunctiva (Figure 1). In the limbal type, small white dots (Trantas dots) on the limbus represent collections of eosinophils.[2] Corneal involvement, more common when there is tarsal involvement, may include superficial punctate keratitis, small epithelial defects, or larger oval-shaped defects (shield ulcers) (Figure 2). Centrally located shield ulcers can scar and cause vision loss; they are typically sterile but can become infected.[9] Corneal involvement can also lead to keratoconus and keratoglobus; permanent visual acuity reduction occurs in about 6% of VKC patients.[1,2,10]

## PRESENTATION: AKC

AKC is the ocular manifestation of a system-wide immune dysregulation that also affects the skin (atopic dermatitis or eczema), nose (allergic rhinitis), and bronchioles (asthma). It typically presents in patients in their 20s through 40s and who have a history of atopic disease, and it may occur among patients formerly affected by VKC.

Compared with VKC, the presentation in AKC is subtle, most notably including bilateral itch (generally worse than the itch associated with SAC or PAC) and diffuse fine papillae on the upper and lower tarsal conjunctivae. This fine papillary reaction remains present even when symptoms are well controlled, a finding that distinguishes AKC from allergic conjunctivitis. AKC patients also complain of burning, tearing, foreign body sensation, and photophobia. The eyes may appear inflamed, red, and show a mucous discharge. Eczema on the eyelids or elsewhere is helpful in making the diagnosis but is not always present.

Long-term inflammation can affect the lids, conjunctiva, and cornea, leading to corneal thinning and scarring, symblepharon, severe keratoconus, and potentially to corneal blindness.[10,11]

## CORE CONCEPTS

- AKC and VKC are uncommon but serious inflammatory disorders of the ocular surface with potentially sight-threatening consequences.
- VKC is characterized by a severe presentation, typically in the first or second decade of life: giant papillae on the upper tarsal plate, thick ropey discharge, and Trantas dots. Corneal shield ulcers can compromise vision.
- A majority of patients with AKC have comorbid non-ocular manifestations of atopy.
- AKC can lead to debilitating conjunctival and corneal cicatrization and symblepharon development; careful monitoring of the ocular surface is required.
- Patients with AKC or VKC may have allergen-specific environmental triggers; however an underlying immune system abnormality, likely T-cell-related, is the basis of the disease.
- Baseline management consists of topical antihistamine/mast cell stabilizers and systemic antihistamine; some patients require chronic or intermittent topical corticosteroids.
- Calcineurin inhibitors may be used for long-term maintenance of immune control on the ocular surface.
- Strategic use of corticosteroids to manage inflammation can help prevent bad outcomes.

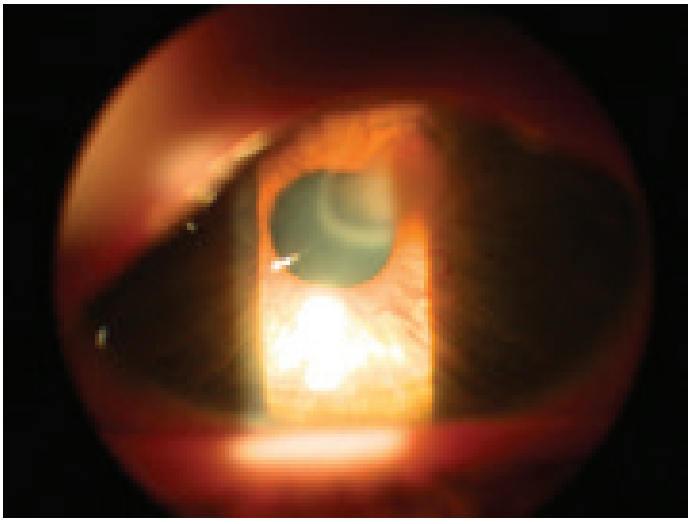

**FIGURE 2** Shield ulcer associated with VKC. *(Image courtesy of the author.)*

## MANAGEMENT: VKC

Antiinflammatory treatment helps prevent the development of shield ulcers in patients with VKC. Topical dual-acting antihistamine/mast cell stabilizing agents and oral antihistamines form the foundation of treatment. Immune modulators that target T cells, such as cyclosporine or tacrolimus, may be used for long term adjunctive management.[7,12]

Short courses of topical ocular corticosteroids are intermittently necessary for flares of inflammation associated with the presence of very large papillae, which signal an increased risk for shield ulcers. Corticosteroids are also needed in the treatment of shield ulcers, which are usually sterile. (An antibiotic may be used adjunctively to cover for infection.) The challenge for clinicians is to achieve adequate inflammatory control with the least cumulative corticosteroid exposure.

To reduce corticosteroid exposure, it may be useful to gain the upper hand quickly with high potency corticosteroids and minimize risk for rebound inflammation via a carefully monitored taper. For the treatment of giant papillae, my practice is to start with an agent such as topical ocular prednisolone acetate or difluprednate, tapering the dose once the papillae respond. I may introduce an adjunctive agent such as cyclosporine during the corticosteroid taper. Careful patient monitoring helps prevent rebound inflammation.

Some patients may require continual low-dose corticosteroids, for example, a drop every other day to maintain control of inflammation. One must rely on clinical judgment and make every effort to use agents with the best safety profiles at the lowest effective doses.

## MANAGEMENT: AKC

A similar management strategy applies to the treatment of AKC. Patients are generally maintained on topical antihistamine/mast cell stabilizing agents, systemic antihistamines, topical cyclosporine, with corticosteroids added for flare-ups. Some patients require chronic corticosteroids. The main management difference between AKC and VKC is the need for more frequent monitoring of the ocular surface in AKC. Patients with signs of disease progression—including shortening of the fornix, progressive conjunctival scarring, corneal keratinization or neovascularization, or limbal stem cell deficiency—require more aggressive management in the form of systemic immunosuppression.

Used adjunctively, immunotherapy may be beneficial to the subset of patients who are skin-test-positive for specific allergens.

## THERAPEUTIC ADVANCES

The development of topical antihistamine/mast cell stabilizing agents has enabled significant improvement in the ability to control inflammation associated with AKC and VKC. The calcineurin inhibiting agent cyclosporine is available in topical ophthalmic formulation and is commonly used off-label for the treatment of serious ocular allergic conditions; higher concentrations of cyclosporine can be pharmacy-compounded. Tacrolimus is another calcineurin inhibiting immunosuppressant under investigation for topical ophthalmic use and is showing promise.[7,12]

The introduction of topical ophthalmic loteprednol has broadened topical corticosteroid options. Its ester-based chemical structure allows for rapid deactivation on the ocular surface which reduces overall patient exposure and risk for side effects.[13] Its high therapeutic index makes it a strong choice for patients with repeated needs for corticosteroids over the long term.

In the pipeline is a new class of agents known as selective glucocorticoid receptor agonists (SEGRAs), designed to be a safer version of corticosteroids. SEGRAs are structurally similar to steroids and bind the same glucocorticoid receptor ubiquitous in cells; however, SEGRAs elicit only some of corticosteroids' downstream actions. SEGRAs maintain the transrepressive actions of steroids, which underlie their anti-inflammatory efficacy, but are "dissociated" from transactivation, which is thought to underlie side effects such as increased intraocular pressure and cataract formation.[14] Should they arrive on the market, SEGRAs could have a substantial impact on the treatment of chronic ocular inflammation.

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# Issues in Long-term Antiinflammatory Therapy

**MICHAEL B. RAIZMAN, MD**

**Corticosteroids are highly effective antiinflammatory agents that enable clinicians to treat ocular inflammation aggressively. However, the potency of corticosteroid agents must be balanced against their potential to cause vision-threatening side effects, especially in prolonged antiinflammatory treatment. Appropriate corticosteroid use involves more than just minimizing side effects; rather corticosteroid treatment should aim to preserve vision by controlling both inflammation and complications.**

## CORE CONCEPTS

- Despite the potential for serious ocular and systemic side effects, corticosteroids remain the first line therapy in patients with severe chronic ocular inflammatory disease.
- Elevated IOP and cataract formation are two major ocular side effects of long-term corticosteroid use. They can usually be managed by standard means.
- Corticosteroids induce the same ocular side effects, irrespective of the route of administration.
- The risk of IOP elevation and cataract is roughly proportional to an agent's antiinflammatory potency, the dosage, duration of treatment, and for topical agents, ocular penetration.
- Predisposing risk factors for corticosteroid-induced hypertension and glaucoma include POAG, family history of POAG, diabetes, high myopia, connective tissue disease, and young age.
- Immunosuppressive therapy, including use of novel biologic agents, offers an alternative treatment option for patients with severe chronic intraocular inflammation or patients resistant to or intolerant of corticosteroids.

Corticosteroids were introduced to ophthalmology more than 50 years ago, and because they are our most potent antiinflammatory agents they have been a mainstay in the treatment of inflammatory eye disease ever since.[1] Corticosteroid efficacy, however, comes at a price: their broad spectrum of action can give rise to serious adverse side effects, including glaucoma and posterior subcapsular cataract. The dangers increase with prolonged use.

Despite these risks, long-term corticosteroid use (ie, use for more than 3 months) continues to be an essential aspect of managing a number of serious ocular conditions, including post-graft corneas to prevent rejection, noninfectious uveitis, postoperative inflammation, and retinal conditions that require chronic inflammatory control. To effectively preserve vision and reduce ocular morbidity in these situations, the clinician must have strategies for minimizing risk and be prepared to deal with complications, should they occur.

### ADVERSE EFFECTS

Chronic corticosteroid therapy, local or systemic, can generate a variety of ocular side effects. Among these, elevated intraocular pressure (IOP) and cataract formation are most common. Other ocular side effects of corticosteroids include delayed epithelial and stromal healing, exacerbation of microbial infection, and potentiation of herpes simplex viral infections.[2]

Corticosteroids differ in their propensity to induce complications, and the risk of adverse effects typically parallels the agent's antiinflammatory potency.[2] Stronger corticosteroids, such as prednisolone, dexamethasone, and difluprednate, are more likely to cause serious side effects and are less safe for chronic antiinflammatory therapy. They are usually indicated for acute and severe inflammation. Other corticosteroids, such as loteprednol etabonate and fluorometholone, are less potent but more suitable for maintenance treatment because of their lower propensity to cause elevated pressure and cataract formation.[3-5] In addition to the corticosteroid's strength, the risk of side effects is also related to the dosage, duration of treatment, and in the case of topical treatment, ocular penetration.[2,6] Loteprednol is particularly safe, as it is converted to an inactive metabolite in the anterior chamber.

### ROUTE OF ADMINISTRATION

Ophthalmic corticosteroids can be given topically, intravitreally, by subconjunctival or periocular injection, or systemically. Topical drops are the most commonly used corticosteroid therapy, but drug administered this way does not penetrate in adequate concentration beyond the crystalline lens. Treatment of profound inflammation in the posterior segment typically requires use of intraocular, periocular, or oral corticosteroids.[6]

Locally administered corticosteroids are generally not associated with systemic side effects. There is, however, a potential risk for systemic absorption and adrenal suppression.[2] No matter the route of administration, including systemic, all corticosteroid therapies cause the same adverse effects in the eye, primarily IOP elevation and cataract formation.

### INTRAOCULAR HYPERTENSION

Corticosteroids affect the trabecular meshwork and elevate the IOP by increasing aqueous humor outflow resistance.[7,8] While potent corticosteroids may elevate IOP within a few

weeks, weaker steroids typically require a longer treatment period to do so.[9]

Corticosteroid responsiveness varies widely among individuals in the normal population. When treated with topical corticosteroids for 4 to 6 weeks, about 4 to 6% of the population will develop a significant IOP rise (greater than 15 mmHg) and are considered "high responders."[10,11] One-third of the population will have a moderate pressure elevation (6 to 15 mmHg). The rest of the population are "nonreponders," with an IOP rise less than 6 mmHg.

Certain risk factors predispose a patient to corticosteroid-induced hypertension. These include primary open angle glaucoma (POAG) or a family history of POAG, diabetes, high myopia, and connective tissue disease.[12-17] Young children are more likely to be responders than adults.[7] Corticosteroid should be used with caution (if at all) in at-risk patients, and careful monitoring of IOP is necessary.

Corticosteroid-induced IOP elevations generally return to baseline upon withdrawal of the treatment, but in some cases the ocular hypertension may persist and result in glaucomatous optic nerve damage and visual field loss. The reversibility of corticosteroid-induced hypertension may be associated with duration of the corticosteroid treatment.[18] Similar to POAG, corticosteroid-induced glaucoma is managed with glaucoma medications and laser or surgical intervention.

## CATARACT FORMATION

The association between corticosteroid therapy and posterior subcapsular cataract is well established.[19] Corticosteroids are thought to cause cataract by binding to lens proteins with subsequent oxidation.[2] The relative risk of corticosteroid agents is not fully understood but is thought to depend on length of administration and the agent's antiinflammatory potency.[2] But even weaker corticosteroids such as fluorometholone have been reported to cause cataract after 4 months of topical treatment.[20]

## ORAL CORTICOSTEROIDS

Oral corticosteroids can raise the IOP and cause cataract; and they also have many systemic side effects: gastric ulcers, weight gain, psychological disturbances, osteoporosis, diabetes, hypertension, and growth suppression in children, among others.[21]

Because oral therapy is associated with significant systemic side effects, clinicians have become increasingly interested in the local delivery of corticosteroids to the eye. But oral corticosteroids continue to play an important role in the management of severe chronic inflammation, particularly when the patient has an underlying systemic disease or when the ocular disease is bilateral. One advantage of oral therapy is that it can be easily discontinued, whereas intraocular or periocular corticosteroids can be difficult to remove if problems arise.

Long-term use of moderate- and high-dose systemic corticosteroids has become much less common due to the risk of side effects and the availability of steroid sparing alternatives. When using systemic corticosteroid, maintaining the patient on the lowest possible dose that controls the inflammation can minimize adverse effects. Patients on long-term corticosteroid therapy, particularly elderly patients, should receive calcium and vitamin D to prevent osteoporosis.

## INTRAVITREAL TREATMENT

Intravitreal corticosteroids are highly effective and now often used in the treatment of chronic non-infectious uveitis and macular edema due to retinal vein occlusion and after cataract surgery. They can be delivered by injection (eg, triamcinolone) or implantation of a sustained-release device (fluocinolone or dexamethasone) into the vitreous.

Use of intravitreal corticosteroids, however, is associated with significantly higher risk of IOP elevation and cataract formation. Cataract formation is common with single injections of triamcinolone, and the risk increases with multiple injections. Almost all eyes with the long-acting fluocinolone acetonide implant develop marked cataract within 3 years, and up to 40% may require trabeculectomy.[22]

Adverse effects of intravitreal therapy can also arise from the injection or implantation procedure. These side effects, including endophthalmitis, bulbar perforation, choroidal injection, intravitreal hemorrhage, and retinal detachment, can occur following any intraocular injection but fortunately are very rare.[6]

Periocular injection of corticosteroids also carries inherent risks such as ptosis, bulbar perforation, choroidal injection, and hemorrhage. Though less potent than intravitreal injections, the risk of cataract and elevated intraocular pressure is much lower, making periocular injections useful alternatives in many situations.

## FACTORING IN THE RISK

Corticosteroid-induced glaucoma and cataract are sight-threatening complications, but so is severe ocular inflammation. In many cases, the severity of the ocular inflammation leaves the clinician with little or no alternative to corticosteroid use. The clinician must evaluate each patient individually and weigh the clinical benefits of the antiinflammatory therapy against the known risks.

If controlling a patient's serious chronic inflammation requires aggressive corticosteroid treatment, clinicians should initiate treatment and manage the side effects, should they occur, as needed with standard means. Of course, there are some situations in which the risk of glaucoma or cataract makes sustained corticosteroid therapy unacceptable. In children, for example, it is best to avoid cataract or glaucoma surgery. If ocular inflammation is threatening the young patient's vision, and the risk of elevated IOP or cataract is high, it may be the wiser course to consider an alternative, non-corticosteroid treatment such as systemic immunosuppressive therapy.

## IMMUNOSUPPRESSIVE THERAPY

Immunosuppressive therapy can benefit patients by better controlling ocular inflammation and/or reducing the risk

of corticosteroid side effects. Immunosuppressives play an important role in the treatment of severe chronic intraocular inflammatory disease, particularly in patients with poor response to corticosteroid treatment or at risk of serious corticosteroid side effects.[23] Certain conditions such as Behçet's disease require early use of immunosuppressive medications. Immunosuppressive agents are recommended for patients who require chronic oral corticosteroid therapy (more than 3 months) at doses greater than 5 to 10 mg per day.[23]

More clinicians are now becoming familiar with systemic immunosuppressive medications and there is a trend to use these agents more frequently, both as primary therapy and as secondary corticosteroid-sparing agents. Conventional immunosuppressive agents, including antimetabolites, alkylating agents, and T-cell inhibitors, can have serious side effects and the patients should be closely monitored in follow-up care.

Newer biologic agents such as tumor necrosis factor (TNF)-α inhibitors further expand the treatment options for sight-threatening ocular inflammation. Biologic therapy offers more specific suppression of damaging immune responses by targeting particular cytokines, chemokines, and cellular receptors and may be associated with fewer side effects.

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## EXAMINATION QUESTIONS TOPICS IN OCULAR ANTIINFLAMMATORIES | ISSUE 4

This CME program is sponsored by the University of Florida College of Medicine and supported by an unrestricted educational grant from Bausch + Lomb, Inc. **Directions:** Select the one best answer to each question in the exam (Questions 1–10) and in the evaluation (Questions 11–16) below by circling one letter for each answer. Participants must score at least 80% on the questions and complete the entire Evaluation section on the form below. The University of Florida College of Medicine designates this enduring material for a maximum of 1.0 *AMA PRA Category 1 Credit™*. There is no fee to participate in this activity. You can take the test online at **http://cme.ufl.edu/toai**.

1. Which of the following characteristics differentiate(s) VKC and AKC from allergic conjunctivitis?
   A. Mast cell involvement
   B. Severity of symptoms
   C. Danger of treatment-related complications
   D. B and C

2. Giant papillae on the upper tarsal conjunctiva is a distinguishing feature of:
   A. Seasonal allergic conjunctivitis
   B. VKC
   C. Symblepharon
   D. All of the above

3. What percentage of the population will have significant IOP increases after a month on steroid drops?
   A. Less than 1%
   B. 4% to 6%
   C. 15% to 30%
   D. Over 30%

4. A corticosteroid's ability to cause serious side effects is related to its:
   A. Antiinflammatory potency
   B. Dosage
   C. Length of administration
   D. All of the above

5. Which dietary supplements are recommended for patients on long-term systemic corticosteroid therapy?
   A. Calcium and vitamin D
   B. Vitamins A and E
   C. Omega-3 fatty acids
   D. None of the above is correct

6. Which of the following is NOT true of shield ulcers?
   A. Etiology is always infectious
   B. More common in tarsal VKC than limbal VKC
   C. Can lead to permanent visual loss
   D. Respond to treatment with topical corticosteroids

7. Which of the following best describes the pathophysiologic basis for VKC and AKC?
   A. Allergen-driven seasonal event
   B. Immune-driven; exacerbations may be allergen-related
   C. Medicamentosa: allergic reaction to topical medication
   D. None of the above

8. Which of the following conditions is NOT known to predispose a patient to corticosteroid-induced ocular hypertension?
   A. POAG
   B. High blood pressure
   C. High myopia
   D. Diabetes

9. Which of the following statements is NOT correct?
   A. Systemic corticosteroids can elevate IOP and cause cataract
   B. Stronger corticosteroids are generally more likely to cause side effects
   C. There is zero risk of systemic side effects from topical corticosteroids
   D. Intravitreal therapy has significantly higher rates of ocular hypertension and cataract

10. Which of the following is NOT a component of AKC management at present?
    A. Systemic antihistamines
    B. Selective glucocorticoid receptor agonists (SEGRAs)
    C. Topical dual acting antihistamine/mast cell stabilizers
    D. Calcineurin inhibitors

## EXAMINATION ANSWER SHEET TOPICS IN OCULAR ANTIINFLAMMATORIES | ISSUE 4

This CME activity is jointly sponsored by the University of Florida and Candeo Clinical/Science Communications, LLC, and supported by an unrestricted educational grant from Bausch + Lomb, Inc. Mail to: University of Florida CME Office, PO Box 100233, Gainesville, FL 32610-0233. DIRECTIONS: Select the one best answer for each question in the exam above (Questions 1–10). Participants must score at least 80% on the questions and complete the entire Evaluation (Questions 11–16) to receive CME credit. CME exam expires October 31, 2014.

**ANSWERS:**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **1.** | A | B | C | D | **6.** | A | B | C | D |
| **2.** | A | B | C | D | **7.** | A | B | C | D |
| **3.** | A | B | C | D | **8.** | A | B | C | D |
| **4.** | A | B | C | D | **9.** | A | B | C | D |
| **5.** | A | B | C | D | **10.** | A | B | C | D |

**EVALUATION:**

1=Poor 2=Fair 3=Satisfactory 4=Good 5=Outstanding

11. Extent to which the activity met the identified
    Objective 1: 1 2 3 4 5
    Objective 2: 1 2 3 4 5
12. Rate the overall effectiveness of how the activity:
    Related to my practice: 1 2 3 4 5
    Will influence how I practice: 1 2 3 4 5
    Will help me improve patient care: 1 2 3 4 5
    Stimulated my intellectual curiosity: 1 2 3 4 5
    Overall quality of material: 1 2 3 4 5
    Overall met my expectations: 1 2 3 4 5
    Avoided commercial bias/influence: 1 2 3 4 5
13. Will the information presented cause you to make any changes in your practice? Yes No
14. If yes, please describe: _____
15. How committed are you to making these changes? 1 2 3 4 5
16. Are future activities on this topic important to you? Yes No

If you wish to receive credit for this activity, please fill in the following information. Retain a copy for your records.

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