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Cover letter

CME as requested for October has been submitted per your request.

LB

37-year-old man referred for assistance with his persistent asthma, atopic dermatitis and chronic conjunctivitis

Clinical vignette

37-year-old man is referred to the allergy service for assistance with his persistent asthma, atopic dermatitis and chronic conjunctivitis.

His asthma has been well controlled along with allergic rhinitis with an inhaled corticosteroid/long acting beta agonist therapy as well as intranasal steroids since childhood. He has had multiple courses of oral steroids, but was never admitted the hospital. While living in Italy, his atopic dermatitis and asthma had been controlled with seasonal exacerbations of chronic red eyes, tearing, droopy upper eyelids, at times with a glassy appearance, as well as nasal congestion and runny nose that never completely resolve. His symptoms became worse during college. His visual acuity decreased after graduating and presently works in an accounting department with over 8 hours a day of computer work. He chronically used antihistamines to control his sneezing with increasing ocular discomfort. He has started to constantly “squint” with mild blurring of vision, increasing sensitivity to light without pain. His ophthalmologist noted increased curvature of the cornea (OS) with mild keratitis. He had been treating him for the past 12 years as he has had increasing involvement around both eyes with scaling that has led to crusting on the eyelids and involving the eyelashes. He recently started using over the counter ocular lubricants on a regular basis as his eyes have started to feel gritty. He states that “the itch” is extremely bothersome, and he chronically rubs his eyes. He also notes that his eyes are constantly “gritty” and is constantly blinking.

This has progressed to a stringy mucus discharge treated with multiple courses of topical steroids. Baseline intraocular pressure was 16 mm and 22 mm and some lens opacifications posterior pole (OD) after topical treatment with limited injection. His atopic dermatitis has required ongoing oral steroid treatment. He developed a progressive ropey discharge of his eyes in the morning. With increasing complaints of his atopic dermatitis and his asthma starting to require increasing doses of inhaled bronchodilators.

Family history: He was born in Italy and moved at 8 years of age to the United States. His father has asthma; brother and sister have atopic dermatitis; parents and several siblings have allergic rhinoconjunctivitis; mother and maternal grandfather have glaucoma; cataracts in both sets of grandparents.

Physical examination: The head was atraumatic and normocephalic. There is increased redness and swelling around both eyes and cheeks, with increased creases below his eyes, and a peculiar absence of the lateral eyebrows with eyelids being slightly asymmetrical. There is thickening of both lids with redness, fissuring and swelling. The conjunctiva has diffuse fine areas of pinhead shaped and sized lesions of the upper and lower tarsal conjunctiva, diffuse multiple blood vessels and increased thickness of the clear portions of the conjunctiva and a white stringy semisolid thread of white mucus in the inferior fornix. The upper right eyelid was touching the iris with the left upper eyelid touching the pupil. (The ophthalmologist’s records note small areas of loss of epithelium from the cornea with the application of fluorescein.) There were white lines running across the inside

portions of the lower palpebral portion of the conjunctiva. There is noted thinning of the eyelashes with some that appear to be turning inwards and irritating the ocular surface. Nasal mucosa is pale and boggy with a stringy nasal opaque to yellow mucus covering the posterior oropharynx. The ears demonstrate cerumen partially occluding left tympanic membrane. There is no pretragal or submental nodes. The lung exam is significant for mild bilateral end expiratory wheezes with a prolonged expiratory phase of respiration; no nasal flaring or accessory muscle use is appreciated. Skin examination is significant for thickened, pigmented skin in the antecubital fossa. The rest of the physical examination is normal.

Testing: A white blood cell count of 7800 cells/mm³ with 1260 eosinophils/mm³ compared to 10,100 cells/mm³ with 220 eosinophils/mm³ – 6 weeks ago on 40 mg of prednisone. Total serum IgE was 836 IU/ml. Eosinophils in giemsa stained stringy exudate. Spirometry demonstrated an FEV1 of 74% (83% post bronchodilator). Delayed skin tests to candida and tuberculin did not reveal reactivity at 24, 48 and 72 hours. Skin-prick testing revealed normal, immediate responses to histamine and saline with minimal reaction to grass and weed pollen with moderate reactions to oak, maple and birch. There was strong reactivity to dust mite.

Background

The patient clearly has a spectrum of atopic disease affecting the classic target organs of the skin, nose and lungs as well as the eyes. The most immediate problem has been involving the ocular surface with a recent acute process. All of the other features suggest an ongoing active atopic disease state that includes asthma, allergic rhinitis, atopic dermatitis that is associated with a form of chronic conjunctivitis, atopic keratoconjunctivitis (AKC) versus vernal that is seen more commonly in children (Table 1).

Chronic conjunctivitis is considered for any conditions lasting more 3 weeks as that is the upper limit for cases of viral infections and most bacterial infections to resolve without treatment. The patient has a form of chronic conjunctivitis with acute infectious episode.

AKC has been thought to be relatively uncommon is a rare disorder, but may be more apparent in clinical practice as approximately 5% of atopic dermatitis patients have some ocular involvement¹. In its most severe form, AKC can be a life-long, sight-threatening condition that predominantly affects mainly adults, but occasionally children, who have systemic atopic disease – particularly atopic dermatitis². AKC is a highly symptomatic disorder with severe itching, watering, stickiness, and redness of the eyelids and eye, and sometimes causes ocular pain. The symptoms of redness and itching that overlap with dry eye disease syndromes can be objectively measured with the ocular surface disease index validated instrument (OSDI) that can be clinically used in the office setting³. However, if pain is noted that an immediate consultation with an ophthalmologist is warranted. There is usually facial eczema involving the eyelids and the lid margins show blepharitis (chronic inflammation of the lash follicles and meibomian glands) spilling over and causing additional inflammation of conjunctival surface. (Table 2) The lid margins are thickened and hyperemic,

posteriorly rounded, sometimes keratinized, and the lid anatomy may be distorted with what is seen as a droopy eyelid.

The disease of the ocular surfaces involves changes in the tear biofilm as clearly demonstrated with increases IgE antibody, histamine, bradykinin, tryptase, interferon-gamma, IL-6 and IL-10 occurring over a 24 hour period with typical early and late phase reaction mediator release⁴. The combined effects of these mediators yield the various signs and symptoms of allergic conjunctivitis including redness, itching, and tearing overlaps early and late phase allergic reactions thus requiring the combinations of various chronic ocular allergy treatments to maximize therapeutic effects⁵⁻⁷. However, there also appears to be a barrier defect on the AKC ocular surface similar to atopic dermatitis as looser cell noted tight junctions between epithelial cells have been noted that may facilitate allergen penetration⁸.

Different configurations exist - outward (ectropion); inward (entropion) and as this patient has inturning of (trichiasis) and loss of some of the eyelashes (madarosis) that may lead to notching. The conjunctival surface having a grade 1-2 being most intense on the inferior palpebral conjunctiva with limited involvement of the superior tarsal conjunctiva. Peripheral vascularization of the cornea may be commonly seen. Examination with a biomicroscope commonly reveals inferior punctate epithelial erosions with persistent epithelial defects in the more chronic conditions. The detection of increased intraocular pressure may not be associated with any clinical signs or symptoms. When the cornea is involved, blepharospasm due to photophobia along with blurring of vision and causes the patient to require time in the morning to get acclimated. Pain is not a feature of the acute forms of ocular allergy, but can be involved in the more chronic forms when they involve the cornea (mimicking a corneal abrasion). This should generate an immediate referral to an eye care specialist (e.g. ophthalmologist) to assist in the care of the corneal surface. There is no preauricular lymphadenopathy as that is more commonly seen in viral conjunctivitis. The description of a "glassy appearance" suggests the presence of conjunctival edema with hyperemia since the swelling of the bulbar surface causes it to be more diffusely pink than red.

Designed to protect, moisten, and cleanse the ocular surface, the eyelids are the first line of defense for the eye. The palpebral skin is extremely thin compared to the dermal thickness elsewhere on the human body (0.55 mm compared to the thickness of the 2 mm integument of the face), which explains the common extensive involvement of the eyelid in minor inflammatory insults.

The whole conjunctiva is affected and shows intense infiltration, papillae that may be giant, linear and stellate scars, and often shrinkage with remodeling of the surface noted in this patient with white linear lines on the inferior eyelid. Marked limbal inflammation (limbitis) may develop. The cornea is subject to epithelial defects and progressive scarring, and neovascularization, thinning and secondary corneal infections (herpetic, bacterial, and fungal) may occur. Involvement of the cornea is what commonly causes the "pain" similar to a corneal abrasion. Alterations in the volume or quality of the tear film may cause severe dry eye. Corneal plaque similar to that of vernal disease is sometimes seen. Associations between AKC and eye rubbing, keratoconus, atopic cataract, and retinal detachment are recognized. Keratoconus that this patient demonstrates is an excessive curvature to the cornea that interferes with the

proper focus of light and thus leads to visual impairment that requires corneal transplant. The skin of the eyelids may demonstrate induration, scaling and lichenification. Dennie – Morgan’s lines in the infraorbital region is a fold or line in the skin below the lower eyelid caused by edema in atopic dermatitis and is used as a diagnostic marker for allergy.

Exudates can take different forms with watery exudates seen in viral conjunctivitis. The most common type of exudate as manifested in this patient's most recent form of conjunctivitis, mucopurulent (or catarrhal) representing a mixture of mucous and pus clearly suggesting a bacterial infection. In some of the chronic forms of allergic conjunctivitis such as vernal keratoconjunctivitis, a thick, tenacious “*mucoïd exudate*” that can be peeled off as a string from the conjunctival surface and this commonly has eosinophils in them when stained with giemsa.

An important component of the eye examination is the presence of ptosis as it notes the position of the eyelid in respect to the pupil. The normal eye has the lid just touching the iris, but not the pupil while the exophthalmic eye has the eyelid not touching the iris at all, displaying the white of the sclera between the eyelid and the iris. In ptosis, the eyelid covers most of the upper iris and may cover some of the pupil. This suggests additional pathology to be sought either in the eyelid or orbit with either the formation of papillae on the upper eyelid, oculomotor nerve palsy or aging.

The past history of severe ocular involvement with a droopy eyelid/ptosis when living in Italy suggests the possibility of vernal conjunctivitis or an early form of atopic conjunctivitis. (Table1) The involvement of the cornea in AKC is more commonly reported in older patients. The absence of contact lens use, or a foreign body also makes the diagnosis of giant papillary conjunctivitis unlikely. Giant papillary conjunctivitis is more commonly associated with a milder form of ocular pruritus than VKC. In VKC enlarged papillae up to 7-8mm in diameter may form on the tarsal conjunctivae, is a classic hallmark of this disease, and forms a “cobblestone appearance”. VKC is commonly a disorder of children or young adults which this patient may have had as a child as it appears to occur more frequently in warm/tropical climates.

As with atopic dermatitis, there is tendency for increased colonization with cutaneous staphylococcus on the skin as well as on around the eyes and eyelids. The development of staphylococcal blepharitis involves soft scales around lash roots that eventually leads to madarosis and trichiasis. In more extensive disease, the anterior lid margin may have ulcerations, notching and microabscesses that eventually evolve to become cystic lesions (hordeolums, styes). Patients often complain of dry eye symptoms as the tear biofilm is altered which adds to the altered tear film in patients with underlying AKC. The conjunctiva commonly involves papillae and phlyctens (pinkish yellow nodule in corneal or conjunctiva that usually develops into ulcer). Fluorescein examination of the corneal surface demonstrates punctate erosions along with marginal infiltrates. It is commonly associated with atopic dermatitis of the eyelids

The management of AKC is difficult and patients cannot be cured. Allergic conjunctivitis especially chronic forms are associated with dry eye syndromes⁹⁻¹¹

("hyperosmolarity" in the tear film) whereas seasonal allergic inflammation does not appear to be associated with permanent tear film instability¹². Ophthalmic preservatives may aggravate ocular allergies with the possibility of developing an allergic response¹³, but may also cause cytotoxicity of conjunctival epithelium¹⁴. As antihistamines also demonstrate anticholinergic activity especially the older forms, these will actually worsen symptoms of dry eyes while improving the nasal symptoms of allergic rhinoconjunctivitis. It is crucial to control the facial eczema and lid margin inflammation as much as possible. Topical mast cell inhibitors are used chronically. A "burst" of topical steroids for 3-7 days e.g. loteprednol approved for treatment of allergic conjunctivitis, but the more potent steroids should be reserved for the more severe cases in consultation with an ophthalmology.

Atopic dermatitis alone is a risk factor for subcapsular cataract formation while anterior are more specific, posterior cataracts are increased from the use of steroids¹⁵. Steroids are associated with ocular adverse effects (intraocular pressure, cataracts) depending on duration, dose and route being the primary factors (oral > ophthalmic > dermatological > Inhaled corticosteroid > Intranasal steroids)¹⁶.

Allergen immunotherapy is beneficial at decreasing future allergic symptoms by increasing the threshold to the allergens associated with the ocular as well as nasal signs and symptoms. Immunomodulation for inflammation related to dry eye disease and AKC includes topical cyclosporine, and potentially omalizumab and other immunophilins that have been used in the treatment in as well as selective glucocorticoid receptor antagonists and nanoparticles¹⁷.

Lasik surgery has been noted to have increased complication in patients with ocular allergies and especially in AKC¹⁸. However, a number of these patients require corneal surgery, which, in the presence of AKC, is a high-risk procedure.

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Table 1. **Atopic versus Vernal Conjunctivitis**

	Vernal	Atopic
Age	Younger	Older
Gender predilection	Males	Nil
Duration of disease	Self-limiting	Chronic
Time of year	Spring	Perennial
Conjunctival involvement	Superior tarsus	Inferior tarsus
Cicatrization	Absent	Common
Cornea	Shield ulcer	Persistent epithelial defect
Corneal scarring	Mild	Severe
Corneal vascularization	Rare	Common

When the chronic conjunctivitis concomitantly involves the cornea, they are termed *keratoconjunctivitis*.

Vernal conjunctivitis and superior limbic keratoconjunctivitis primarily involve the upper palpebral eyelid while toxic conjunctivitis from topical medications involves the lower eyelid. They commonly have papilla involving the upper tarsus causing it to causes it to droop (ptosis) associated with a mucoid discharge. The cornea can become severely involved with the development of a corneal ulcer, superior corneal punctate epithelial erosions, epithelial macroerosions, shield ulcers and plaques, pseudogerontoxon and peripheral vascularization.

Table 2. **Characteristics of chronic blepharitis**

		Anterior blepharitis		
	Sign	Staphylococcal	Seborrheic	Posterior blepharitis
Lashes	Deposit	Hard	Soft	
	Loss	++	+	
	Distorted or trichiasis	++	+	
Lid margin	Ulceration	+		
	Notching	+		++
Cyst	Acute hordeolum	++		
	Meibomian			++
Conjunctiva	Phlycten	+		
Tear film	Foaming			++
	Dry eye	+	+	++
Cornea	Punctate erosions	+	+	++
	Vascularization	+	+	++
	Infiltrates	+	+	++
Associated dermatitis		Atopic	Seborrheic	Acne rosacea

The involvement of the periocular tissue can take up several forms with significant involvement of the eyelids as noted in chronic blepharitis, molluscum contagiosum and atopic keratoconjunctivitis that also extensively involve the conjunctival surface. Blepharitis (inflammation of the eyelid) may involve crusting, redness and swelling of the anterior lid margin. Examination of the posterior lid margin reveals either a squared (normal) or rounded margin (indicating chronic disease) in ocular allergic disorders. In chronic lid margin disorders, the meibomian gland orifices are unevenly dilated and their secretion is yellow and semi-solid (may even form a solid wax) in contrast to the normal clear fluid that is produced.

Figure 1. A stepwise approach to the treatment of AKC until adequate control of the condition is achieved is presented. A stepwise approach reflected the intensity of cellular involvement and the mediators that are in the tear biofilm from the allergic inflammation. Topical therapeutics represent the mainstay of treatment. Consideration of discontinuation \ of oral antihistamine due to their potential anticholinergic effect that increases the drying of the surface that already has a tear film stability. Topical agenst including multiple action agents, steroids and/or immunophilins are use in stages and in combination. Surgery would be required for those developing severe keratoconus with corneal transplants. Lasik surgery is not recommended in these patients. (modified from Heustein S, Bielory L. – reference 1)



Figure

Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Quiescent	Mild Intermittent	Moderate Persistent	Severe	Very Severe	Remodeling (scarring)
No Treatment	<hr/> Oral Steroids <hr/> Short bursts of Topical Steroids <hr/> Topical cyclosporine or tacrolimus <hr/> Topical Vasoconstrictors / lubricants / Cool compresses <hr/> Disposable contact lenses Daily administration of topical ophthalmic multiple action antihistamine / mast cell stabilizing agents NSAIDS				
	Corneal Transplant (Surgery for Keratoconus)				
	Oral antihistamines Avoidance Treatment of comorbidities (e.g. atopic dermatitis, asthma, allergic rhinitis, dry eye syndrome) that includes immunotherapy, inhalational and intranasal steroids, omalizumab, immunophilins (pimerolimus, tacrolimus), ophthalmic cyclosporine				

Questions

1. Which formulation of daily steroid use is associated with the highest frequency of cataract development?

- a. Oral prednisone
- b. Topical ophthalmic steroids
- c. Inhaled corticosteroids
- d. Intranasal steroids
- e. Topical dermatological steroids

Answer: oral

Steroids are associated with ocular adverse effects, but to different degrees. Long-term oral and ophthalmic steroids have the highest likelihood to generate intraocular adverse effects such as significant increase in intraocular pressure and cataracts. However, he has been treated with intermittent courses limited to 2 weeks duration of topical ophthalmic steroids, but the patient has required extensive courses of oral steroids for control of his atopic dermatitis asthma. The concomitant use of long term inhaled corticosteroids (more than a year) for asthma may also increase the steroid impact as it has also been associated an increased potential for growth effects in children and intraocular effects in adults. Intranasal steroids may also add to the cumulative burden of steroid use. Independently oral > ophthalmic> dermatological> inhaled corticosteroid>Intranasal steroids. Short course treatment with modified topical steroids approved for allergic conjunctivitis is appropriate in many patients.

2. In patient with atopic keratoconjunctivitis who complains of increasing tearing, redness, itching and with scaling along the upper and portions of lower eyelashes with an increasing ropey discharge that requires constant “drawing out” (pulling off the eye surface) through the day after patient’s known pollen season. On closer examination the scaling appear to clinging to the bases of the eyelashes. The recommended initial treatment is:

- a. Topical antibiotic (e.g. moxifloxacin)
- b. Dual Action Agents/Antihistamine (e.g. Alcaftadine, Bepotastine, Olopatadine)
- c. Topical steroid (e.g. loteprednol)
- d. Tobradex (tobramycin/dexamethasone)
- e. Improved lid hygiene (e.g. lid scubbing)

Answer: E. Patients with any of the forms of allergic conjunctivitis may develop a bacterial conjunctivitis that is associated with a glue eye especially upon awakening and commonly starts unilaterally before involvement of both eyes, and requiring the use of topical antibiotic. Patients with chronic forms commonly become colonized with staphylococcal species when they develop blepharoconjunctivitis and will have staphylococcal collarettes attached to the

bases of the eyelashes. This not an infection, but a colonization that is associated with perpetually generating a stimulus to the ocular stimulus with symptoms tearing, redness, and itching that mimics and compound the underlying allergic inflammatory process. One of the key features is the collarettes around the eyelashes. The primary treatment is focused on lid hygiene such as scrubbing the eyelids with nontearing solutions e.g. several of the baby shampoos with a cotton swab or warm disposable towelletes. The scrubbing should be performed with a single stroke to the medial canthus, disposing the cotton swab or towellete and repeating this procedure several times. The use of dual action agents may be considered and commonly are required as adjunctive therapy in these patients, but are limited in their effect when the patient has a clear form of staphylococcal blepharoconjunctivitis. Although topical steroids become an option in the treatment of allergic conjunctivitis for severe acute forms and in the exacerbations of the more chronic forms, the FDA steroid approved for allergic conjunctivitis is loteprednol. Combination antibiotic and steroids are limited to more severe forms and patient should be more thoroughly examined for potential viral infection and intraocular pressure as dexamethasone is a potent topical steroid that can easily increase intraocular pressure within days and may cause proliferation of a viral conjunctivitis due to suppression of local immune defense.

3. Which of the following statements about intraocular pressure is true
- Inhaled corticosteroids for asthma has not been reported to be associated with increased intraocular in patients who had taken oral steroids in the past
 - Increased intraocular pressure (>22 mm) is associated with the development of ocular injection
 - A family history of glaucoma increases the chance of developing glaucoma on steroids
 - increased intraocular pressure has been reported with high concentrations of benzalkonium chloride (BKC) in topical solutions
 - increased ocular pressure is commonly seen in patients on beta-blockers

Answer: C

Increased ocular pressure may not be associated with any clinical signs or symptoms. The concept of ophthalmic preservatives impact on the ocular surface has always been a slight quandary since when used normal conjunctival tissue it serves its function with limited adverse effects. However, when applied to inflamed conjunctival surfaces (as seen in various forms of conjunctivitis) their chronic use leads to exacerbations of the underlying inflammatory process including our patients that suffer from allergic conjunctivitis. It has not been associated with increased intraocular pressure. A family history is very important historical point associated with the development of glaucoma. Increased intraocular pressure does not commit the patient to the development of glaucoma that is commonly seen with values over the 30 mm and is then commonly associated with the development of redness , but increases the likelihood and

thus is commonly treated to maintain values below 22mm. Beta blockers are associated with lowering systemic blood pressure and intraocular rpressure.

4. Improvement of the ocular symptoms of AKC involves all of the following except

- a. Intermittent use of topical ophthalmic steroids
- b. Treatment of staphylococcal blepharoconjunctivitis
- c. Discontinuation of oral antihistamines
- d. Use of Lasik surgery to correct his vision
- e. Surgery for keratoconus
- f. Use of topical cyclosporine

Answer: D

The treatment of AKC involves a variety of medical and even surgical interventions such as corneal transplants for severe keratoconus that interferes with vision. Oral Antihistamines increase the tear osmolarity by its drying effects and can increase subjective symptoms rather relieve them and it is recommended to avoid these agents if possible. Lasik surgery has a higher complication rate in patients with chronic allergic inflammation.

Bepharoconjunctivitis aggravates the ocular surfaces in patients already having an allergic inflammatory response of the mucosal surface and requires concomitant treatment to maximize the clinical outcome. Ophthalmic steroids are often required to be part of the treatment regimen for patients with AKC with loteprednol being the only one FDA approved for allergic conjunctivitis. The use of topical cyclosporine may also be required to control the cell mediated inflammation in addition to potentially treating the concomitant dry eye condition of the allergic inflammatory surface of the eye.

5. The tear film covering the eye after an allergic response contains of the following except

- a. IgE
- b. IgA
- c. Low osmolarity (low sodium content)
- d. Tryptase
- e. Bradykinin

Answer C:

Tear film analysis in allergic patients reveals the presence of IgE antibody, histamine, and tryptase. Preformed mediators (histamine, tryptase, bradykinin) of inflammation are released immediately on allergen exposure, and the newly formed "de novo" mediators (leukotrienes, prostaglandins) are released within hours peaking in 8-24 hours. The combined effects of these mediators yield the various signs and symptoms of allergic conjunctivitis including redness, itching, and watery discharge that combines early phase reactions with late phase and thus many patients with chronic ocular allergy disorders do benefit from the use

of topical steroids. The various mediators in the tear film and the potential cellular infiltration into the conjunctival surface provides the basis of treatment of patients with atopic keratoconjunctivitis. The increase in salt content is associated with increasing osmolarity and provides a similar biofilm to patients with dry eye syndromes. The conjunctival surface is bathed in a thin layer of tear film that appears at approximately 2 to 4 weeks after birth. Traditionally the tear film has been described as simply containing an outer lipid layer, a middle aqueous layer, and an inner mucoprotein layer. A more recent model of tear film structure describes an aqueous layer with a gradient of mucin that decreases from the ocular surface to the overlying lipid layer. Goblet cells distributed along the conjunctival surface produce this mucin, which decreases the surface tension of the tear film, thus maintaining a moist hydrophobic corneal surface. The outermost lipid component of the tear film decreases the evaporation rate of the aqueous tears. The aqueous portion of the tear film contains a variety of solutes, including electrolytes, carbohydrates, ureas, amino acids, lipids, enzymes, tear-specific prealbumin, and immunologically active proteins, including immunoglobulin A (IgA), IgG, IgM, IgE, trypsin, histamine, lysozyme, lactoferrin, ceruloplasmin, vitronectin, and cytokines.

6. What signs of atopic keratoconjunctivitis are not found in the figure?



- a. madarosis
- b. DeHorteghe's sign
- c. Horner's Trantas dots
- d. Periocular edema
- e. Blepharoconjunctivitis

Answer: C. The figure demonstrates the loss eyelashes (madarosis) with swelling around the eyelid commonly seen in examinations with blepharoconjunctivitis associated with atopic keratoconjunctivitis. There is also thinning and loss of the lateral third of his eyebrow (DeHortelhe's sign) due to excessive rubbing of the eyes.

Ocular Surface Disease Index[®] (OSDI[®])²

Ask your patients the following 12 questions, and circle the number in the box that best represents each answer. Then, fill in boxes A, B, C, D, and E according to the instructions beside each.

Have you experienced any of the following during the last week?	All of the time	Most of the time	Half of the time	Some of the time	None of the time
1. Eyes that are sensitive to light? . . .	4	3	2	1	0
2. Eyes that feel gritty?	4	3	2	1	0
3. Painful or sore eyes?	4	3	2	1	0
4. Blurred vision?	4	3	2	1	0
5. Poor vision?	4	3	2	1	0

Subtotal score for answers 1 to 5

Have problems with your eyes limited you in performing any of the following during the last week?	All of the time	Most of the time	Half of the time	Some of the time	None of the time	N/A
6. Reading?	4	3	2	1	0	N/A
7. Driving at night?	4	3	2	1	0	N/A
8. Working with a computer or bank machine (ATM)?	4	3	2	1	0	N/A
9. Watching TV?	4	3	2	1	0	N/A

Subtotal score for answers 6 to 9

Have your eyes felt uncomfortable in any of the following situations during the last week?	All of the time	Most of the time	Half of the time	Some of the time	None of the time	N/A
10. Windy conditions?	4	3	2	1	0	N/A
11. Places or areas with low humidity (very dry)?	4	3	2	1	0	N/A
12. Areas that are air conditioned? . . .	4	3	2	1	0	N/A

Subtotal score for answers 10 to 12

Add subtotals A, B, and C to obtain D
(D = sum of scores for all questions answered)

Total number of questions answered
(do not include questions answered N/A)

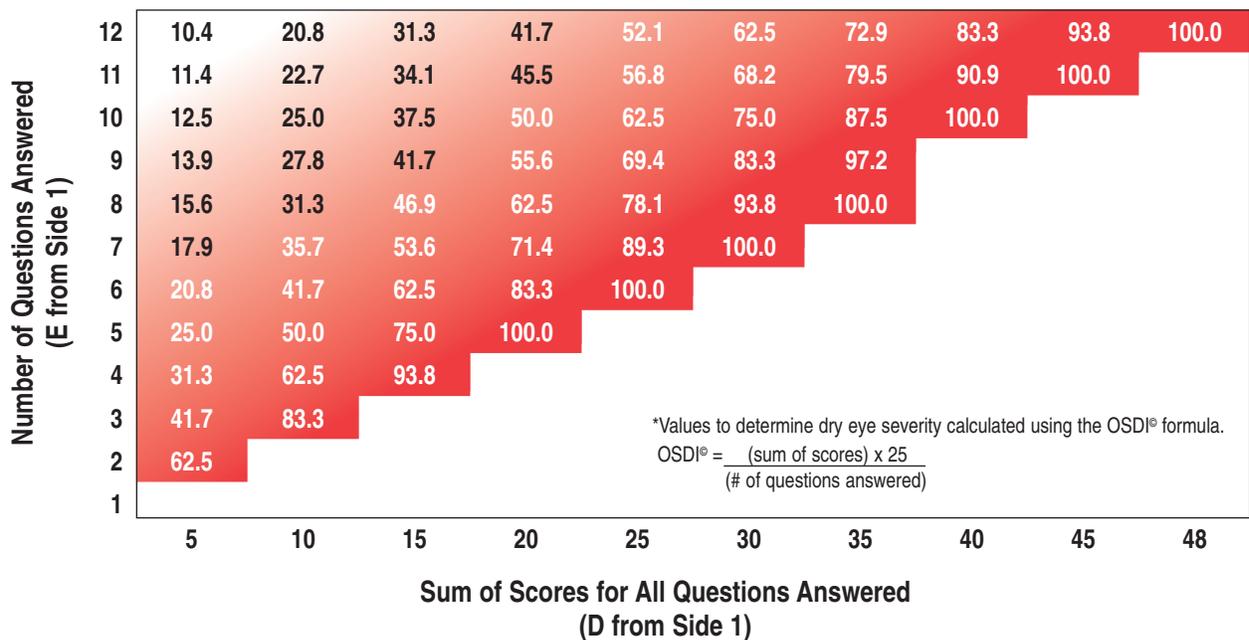
Please turn over the questionnaire to calculate the patient's final OSDI[®] score.

Evaluating the OSDI® Score¹

The OSDI® is assessed on a scale of 0 to 100, with higher scores representing greater disability. The index demonstrates sensitivity and specificity in distinguishing between normal subjects and patients with dry eye disease. The OSDI® is a valid and reliable instrument for measuring dry eye disease (normal, mild to moderate, and severe) and effect on vision-related function.

Assessing Your Patient's Dry Eye Disease^{1, 2}

Use your answers D and E from side 1 to compare the sum of scores for all questions answered (D) and the number of questions answered (E) with the chart below.* Find where your patient's score would fall. Match the corresponding shade of red to the key below to determine whether your patient's score indicates normal, mild, moderate, or severe dry eye disease.



Normal Mild Moderate Severe

.....
 Patient's Name: _____ Date: _____

How long has the patient experienced dry eye disease? _____

Eye Care Professional's Comments: _____

1. Data on file, Allergan, Inc.
 2. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. *Arch Ophthalmol.* 2000;118:615-621

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I certify that the statements I have made above are true, complete, and correct to the best of my knowledge and belief.

Signature: _____ Date: _____

Request for Taxpayer Identification Number and Certification

Give Form to the
requester. Do not
send to the IRS.

Print or type
See Specific Instructions on page 2.

Name (as shown on your income tax return)
STARx Technical Corporation

Business name/disregarded entity name, if different from above

Check appropriate box for federal tax classification:
 Individual/sole proprietor C Corporation S Corporation Partnership Trust/estate
 Limited liability company. Enter the tax classification (C=C corporation, S=S corporation, P=partnership) ▶
 Other (see instructions) ▶

Exempt payee

Address (number, street, and apt. or suite no.)
400 Mountain Avenue

City, state, and ZIP code
Springfield, NJ 07081

List account number(s) here (optional)

Requester's name and address (optional)
Totality Consultant

Part I Taxpayer Identification Number (TIN)

Enter your TIN in the appropriate box. The TIN provided must match the name given on the "Name" line to avoid backup withholding. For individuals, this is your social security number (SSN). However, for a resident alien, sole proprietor, or disregarded entity, see the Part I instructions on page 3. For other entities, it is your employer identification number (EIN). If you do not have a number, see *How to get a TIN* on page 3.

Social security number								
			-			-		

Note. If the account is in more than one name, see the chart on page 4 for guidelines on whose number to enter.

Employer identification number									
2	2	-	3	5	6	4	2	4	9

Part II Certification

Under penalties of perjury, I certify that:

- The number shown on this form is my correct taxpayer identification number (or I am waiting for a number to be issued to me), and
- I am not subject to backup withholding because: (a) I am exempt from backup withholding, or (b) I have not been notified by the Internal Revenue Service (IRS) that I am subject to backup withholding as a result of a failure to report all interest or dividends, or (c) the IRS has notified me that I am no longer subject to backup withholding, and
- I am a U.S. citizen or other U.S. person (defined below).

Certification instructions. You must cross out item 2 above if you have been notified by the IRS that you are currently subject to backup withholding because you have failed to report all interest and dividends on your tax return. For real estate transactions, item 2 does not apply. For mortgage interest paid, acquisition or abandonment of secured property, cancellation of debt, contributions to an individual retirement arrangement (IRA), and generally, payments other than interest and dividends, you are not required to sign the certification, but you must provide your correct TIN. See the instructions on page 4.

Leonard Bielory, M.D.

Sign Here Signature of U.S. person ▶ Date ▶

General Instructions

Section references are to the Internal Revenue Code unless otherwise noted.

Purpose of Form

A person who is required to file an information return with the IRS must obtain your correct taxpayer identification number (TIN) to report, for example, income paid to you, real estate transactions, mortgage interest you paid, acquisition or abandonment of secured property, cancellation of debt, or contributions you made to an IRA.

Use Form W-9 only if you are a U.S. person (including a resident alien), to provide your correct TIN to the person requesting it (the requester) and, when applicable, to:

- Certify that the TIN you are giving is correct (or you are waiting for a number to be issued),
- Certify that you are not subject to backup withholding, or
- Claim exemption from backup withholding if you are a U.S. exempt payee. If applicable, you are also certifying that as a U.S. person, your allocable share of any partnership income from a U.S. trade or business is not subject to the withholding tax on foreign partners' share of effectively connected income.

Note. If a requester gives you a form other than Form W-9 to request your TIN, you must use the requester's form if it is substantially similar to this Form W-9.

Definition of a U.S. person. For federal tax purposes, you are considered a U.S. person if you are:

- An individual who is a U.S. citizen or U.S. resident alien,
- A partnership, corporation, company, or association created or organized in the United States or under the laws of the United States,
- An estate (other than a foreign estate), or
- A domestic trust (as defined in Regulations section 301.7701-7).

Special rules for partnerships. Partnerships that conduct a trade or business in the United States are generally required to pay a withholding tax on any foreign partners' share of income from such business. Further, in certain cases where a Form W-9 has not been received, a partnership is required to presume that a partner is a foreign person, and pay the withholding tax. Therefore, if you are a U.S. person that is a partner in a partnership conducting a trade or business in the United States, provide Form W-9 to the partnership to establish your U.S. status and avoid withholding on your share of partnership income.

The health care provider will successfully complete review of the clinical case of chronic allergic conjunctivitis in an atopic patient.

Learning points

- Atopic keratoconjunctivitis (AKC) is a chronic allergic inflammatory disease that is at the severe end of a spectrum of allergic conjunctival diseases.
- AKC can involve the cornea and conjunctiva bilaterally, and at times can lead to visual loss from corneal complications.
- Chronic involvement of the eyelids (blepharitis) is common and is an important component of the treatment intervention.
- Tear film abnormalities with “hyperosmolarity” are noted in chronic allergy consistent dry eye syndromes.
- Current treatment options includes a stepwise, multidisciplinary approach that involving medical interventions of topical and systemic immunomodulating agents, as well as surgery (corneal transplantation) for keratoconus